

BUKTI KORESPONDENSI
Jurnal Internasional Bereputasi
Sebagai Syarat Khusus

Judul Artikel : Evaluation of pulpal anesthesia and injection pain using IANB with preheated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis—a randomized clinical study.

Penulis : Namita Gandhi, Nimisha Shah, **Dian Agustin Wahjuningrum**, Sweetly, Purnomo, Riana Nooshian, Suraj Arora and Ajinkya M. Pawar

Jurnal : PeerJ Vol. 10:e14187; ISSN = 2167-8359

Penerbit : PeerJ

1	Manuscript was submitted to Journal “PeerJ”	Received: 16 Mei 2022
	Thank you for submitting your article for review - Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis- A Randomized Clinical Study	
2.	Decision: Accepted for Publication	14 September 2022
3.	Proof Check	10 Oktober 2022
4.	Published online	19 Oktober 2022
5.	Published on PeerJ Vol. 10:e14187	19 Oktober 2022

PeerJ

Dan Agustin Wahjuningrum

New submission

Submissions

Reviewing

JOURNALS PUBLISH COMMUNITIES

COVID-19 notice: PeerJ aims to continue publishing your research during this pandemic. We ask for your patience if you experience any delays as a result of the challenges that the world is now facing.

My submissions

MY ARTICLES

- My submissions**
- Impact factor
- Create submission

MANUSCRIPTS

- Reviewing

PROFILE

- View profile
- Edit profile
- ORCID Connect

SETTINGS

- Email and profile link
- Password

NOTIFICATIONS

- Content alerts
- Metrics, offers, and activity
- Push notifications

PAYMENTS AND PLANS

- Payments and receipts
- Individual plan
- Group plan

PeerJ	Awaiting Decision	2022-04-24 04:02:11 (NEW)	Computed tomography-based assessment of alveolar bone and soft tissue pneumatization...	Admin Agustin M Pawan - Created 14 Sept	Review PDF
PeerJ	Reviewed	2022-04-24 04:02:11 (NEW)	"Pro Enkephalins: Build Up" an important aspect of endolekith treatment: Competitive and...	Admin Agustin M Pawan - Created 5 April	Review PDF
PeerJ	Published	2022-05-17 16:11:11 (PUBLISHED)	Location angle of second molar-social canal in mandibular molars of an Indian population...	Admin Agustin M Pawan - Created 12 Nov 2021 - Published 19 October 2022	
PeerJ	Published	2022-05-17 16:11:11 (PUBLISHED)	Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered...	Admin Agustin M Pawan - Created 12 Nov 2021 - Published 19 October 2022	
PeerJ	Reviewed	2021-11-07 16:00:21 (PUBLISHED)	Comparative evaluation of the effects of two pulpal medications on pain and bleeding...	Admin Agustin M Pawan - Created 7 November 2021 - Published 11 May 2022	

PeerJ

Dan Agustin Wahjuningrum

New submission

Submissions

Reviewing

JOURNALS PUBLISH COMMUNITIES

COVID-19 notice: PeerJ aims to continue publishing your research during this pandemic. We ask for your patience if you experience any delays as a result of the challenges that the world is now facing.

Article status: **Published** Type: **Research Article** Journal: **PeerJ**

Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis- A Randomized Clinical Study

Overview Payment: 0 authors

This manuscript was published on October 19, 2022.

Your peer-review comments:

Editor's Decision **ACCEPT**

Thank you for submitting this manuscript. I look forward to seeing it published soon.

Comments from the reviewers

Reviewer 2
Basic reporting
no comment

Article fees paid

- Optional graphical abstracts and CC BY/NC

Remaining available

Home

Dian Agustini Waljuningrum

New submission

Submissions

Reviewing

JOURNALS PUBLISH COMMUNITIES

Experimental design
no comment

Variety of the findings
no comment

Additional comments
no comment

Reviewer 1

Basic reporting
The introduction and basic reporting are excellent, the article does not need changes in this section.

Experimental design
The materials and methods are well described, the methodology is of a high level. I believe the article is valid for how the study was developed.

Variety of the findings
The results are well described in clear and easily readable tables. The results are interesting, linked to the research methodology, and represent an excellent result.

Additional comments

SECTION

SUBJECTS

Anesthetics and Pain Management Clinical Trials Dentistry Oral and Maxillofacial Surgery

KEYWORDS

Buffered Local anesthesia Pain scale Irreversible pulpitis Endodontics

ABSTRACT

Background. Efficacy of 2% Lidocaine is reduced in a hot tooth. Local anesthetic agents can

Home

Dian Agustini Waljuningrum

New submission

Submissions

Reviewing

JOURNALS PUBLISH COMMUNITIES

be preheated and buffered to increase their effectiveness. The present investigation was carried out due to a limited information concerning adult patients with symptomatic irreversible pulpitis in mandibular teeth. **Methods.** A total of 252 individuals were included in the clinical trial in accordance with the selection criteria only after clinical study was registered with the Clinical Trial Registry of India (CTRI/2020/09/027796). Scores on the VAS and EPT on a 1–10 scale were recorded prior to the commencement of therapy. In this double-blinded study, patients were randomly divided by a Co-investigator using computer randomisation (www.randomizer.org) into three groups, Group A: IANB with 2% lignocaine preheated at 42°C (injected at 37 °C) (N=84), group B: IANB of 2 % lignocaine buffered with 0.18ml of 8.4% sodium bicarbonate (N=80) and group C: 2 % lignocaine (N=88). Excluding the dropouts of individuals (n=11), where in the anaesthesia failed, a total of 241 people were finally assessed 15 minutes after profound anaesthesia, endodontic access, and intraoperative pain were quantified using VAS. Pain on injection for all three groups was recorded immediately after IANB with VAS. The analysis was performed using One Way ANOVA with Tukey's Post Hoc Test and Paired T-Test using SPSS version 21. **Results.** Preheated, Buffered, and conventional 2% lignocaine showed statistically significant reduction in intraoperative pain (P <0.001) compared to pre-operative but on inter-group comparison preheated and buffered showed highly significant pain reduction compared with conventional 2% lignocaine (P <0.001). **Conclusions.** Warm and buffered LA were effective in reducing intraoperative discomfort than conventional LA. Preheated local anesthetics caused the least pain, followed by buffered local anesthetics, while conventional local anesthetics caused the most pain (Sumandeep Vidyapeeth Institutional Ethics Committee) SVI/EC/ON/Dent/BNFC/18/D19047, date of approval 22/11/2019 and the clinical trial registry of india no. CTRI/2020/09/027796).

AUTHORS

Narita Gandhi
Department of Conservative Dentistry and Endodontics, K M Shah Dental College and Hospital, Sumandeep Vidyapeeth, Vadodra, Gujarat, India

Naraina Shah
Department of Conservative Dentistry and Endodontics, K M Shah Dental College and Hospital, Sumandeep Vidyapeeth, Vadodra, Gujarat, India

PeerJ

Dian Agusti Wahjuningrum

New submission

Submissions

Reviewing

Submissions

Reviewing

Reviewing

- Dian Agusti Wahjuningrum**
Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga, Surabaya City, East Java, Indonesia
- Sweety Permana**
Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga, Surabaya City, East Java, Indonesia
- Riana Nurdiana**
Conservative Dentistry and Endodontics, Nair Hospital Dental College, Mumbai, Maharashtra, India
- Baqi Anwar**
Department of Restorative Dental Sciences, College of Dentistry, King Khalid University, Abha, Saudi Arabia
- Ajwaja M Pawar**
Conservative Dentistry and Endodontics, Nair Hospital Dental College, Mumbai, Maharashtra, India

FILES

Response Files Download all files

Comments_3-round_NS_PeerJ.docx REBUTTAL (15KB)

Final_NS_English_and_References.docx TRACKEDCHANGES (5KB)

Primary Files

Final_NS_English_and_References_CLEAN.docx MANUSCRIPT (4KB)

Table_1_Corrected.docx TABLE (15KB)
Comparison of visual analog scale (vas) pre and post with paired t-test for groups.

Table_2.docx TABLE (14KB)
Comparison between the groups for vas score (pre-intra) by tukey's post hoc test. The values marked with (*) and **) exhibited significant difference.

Table_3.docx TABLE (14KB)
Comparison between the groups for pain on injection (VAS SCORE).

Fig_1_73435_1T_xxxff.pdf FIGURE (21KB)
CONSORT 2010 flow diagram.

Supplemental Files

MASTERCHART.xlsx SUPPORTING TABLE (2KB)
Master-chart raw data

NOT FOR PUBLICATION

Dr_Namita_Dandhi.pdf SUPPORTING HUMAN STUDIES-APPROVAL (5KB)
Institutional Ethics committee clearance

NOT FOR PUBLICATION

ctri_registration.pdf SUPPORTING CLINICAL TRIAL-APPROVAL (1KB)
Registration with the Clinical Trial Registry of India

NOT FOR PUBLICATION

consent_form.pdf SUPPORTING CLINICAL TRIAL-CONSENT (11KB)
Clinical trial/tissue consent form

Fwd: [PeerJ] We've received your submission: " Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis- A Randomized Clinical Study" (#2022:16:67550:0:0:CHECK)
1 pesan

From: PeerJ <info@peerj.com>
Date: 16 Mei 2022 at 12:45:07 PM IST
To: Dian Agustin <dian-agustin-w@fkg.unair.ac.id>
Subject: [PeerJ] We've received your submission: " Evaluation of pulpal anesthesia..."
(#2022:11:67550:0:0:CHECK)
Reply-To: PeerJ <info@peerj.com>

PeerJ

Dear Dian Agustin,

Thank you for submitting your article for review - Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis- A Randomized Clinical Study.

It will now be checked by PeerJ staff, who will email you if any changes are required. Many of our staff are on lockdown in response to COVID-19, therefore there may be a delay in processing your revision submission. We thank you for your patience in this difficult time.

Please note that it is currently the weekend in the US where our staff are based, so please expect a slight delay.

After passing checks, it will be assigned to an Academic Editor, who will invite reviewers to carry out peer-review.

If you have a reviewer discount or similar, please enter your code now.

You will receive an email update at each stage, and you can check the status of your article at any time.

[View your Submission](#)

This is a great time to complete your PeerJ profile. Even the basics of a profile photo and institutional info will leave readers with a richer understanding of you and your work.

[Complete your Profile](#)

In under 3 minutes

With kind regards,
The PeerJ Team

ID-73630 / PeerJ

Need help? Just reply to this email.

Publisher of: *PeerJ— Life & Environment, PeerJ Computer Science, PeerJ Physical Chemistry, PeerJ Organic Chemistry, PeerJ Inorganic Chemistry, PeerJ Analytical Chemistry and PeerJ Materials Science*

Follow us on [Twitter](#), [Facebook](#), [Instagram](#) and our [Blog](#)

2021, PeerJ, Inc. PO Box 910224 San Diego, CA 92191, USA

Fwd: Your accepted PeerJ submission: "Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis- A Randomized Clinical Study"
(2022:05:73630:2:0:ACCEPTED)

1 pesan

From: Jacqueline Thai <jackiethai@peerj.com> Date: 14 September 2022 at 4:38:04 AM IST

To: Dian Agustin Wahjuningrum <dian-agustin-w@fkg.unair.ac.id>

Subject: Your accepted PeerJ **submission**: "Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth **with** symptomatic **irreversible** pulpitis- A Randomized Clinical Study" (2022:05:73630:2:0:ACCEPTED)

Reply-To: production@peerj.com

PeerJ

Dear Dian Agustin,

Congratulations again on the acceptance of your article - Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% **lignocaine in teeth with symptomatic irreversible pulpitis- A Randomized Clinical Study**.

Please complete the tasks below. Reply directly to this email.

After you complete these tasks we will begin producing your final PDF.

Production tasks

Please complete all required queries to proceed with publication. Please reply directly to this email for ALL queries.

1: [REQUIRED] Now that the article has been accepted, you should pay the one-off Article Processing Charge through the payment grid <https://peerj.com/manuscripts/73630/payments/>.

Alternatively, you could pay for individual Memberships for each co-author in which case each of the following author(s) need to upgrade their plans: Namita Gandhi, Dr Nimisha Shah, Dian Agustin Wahjuningrum, Sweetly Purnomo, Riana Nooshian, Suraj Arora

All authors have access to the payment link and any author can pay for any other author if they choose. We accept: major credit cards (Visa, American Express, MasterCard, Discover, JCB, Diners Club), ACH payments from US bank accounts, or Alipay (China-based payers).

2: [REQUIRED] Can you please confirm whether you and your co-authors are happy for us to publish the peer review history alongside the manuscript at this time? There is no extra charge for this service and no further work is required from you to include it.

The peer review history consists of all the reviewers' comments from each iteration, including the reviewers' names where they have agreed to reveal their names; all previous versions of the manuscripts; all the responses to reviewers. Including the peer review history increases engagement and views, and has been cited as a helpful learning tool regardless of how the process went. It's also been well received as a demonstration that your article went through a rigorous peer review process.

3: [REQUIRED] Figure 1: Please remove the top and bottom borders of the figure that include "Materials and Methods" and "28". This text and those borders should not be included in the figure.

By reply email, please provide complete replacement figures measuring a minimum of 900 pixels and a maximum of 3000 pixels on all sides, saved as PNG or vector PDF format without excess white space around the images. Do

not supply figures in Word processing files. Do not change any other contents of the figures.

4: [NO ACTION NEEDED] Funding is not permitted in the Acknowledgements. Funding is required to appear in the Funding Statement which is published with the article. This text has been removed from the Acknowledgements: The authors extend their appreciation to the Deanship of Scientific research at King Khalid University, Abha, Saudi Arabia for their support through the Short Research Project under grant number (RGP-1/347/43).

It has been moved to the Funding Statement where it is required to appear, edited to comply with our policy, and replaces the previous statement "The authors did not receive any funding.":

The authors received support from the Deanship of Scientific research at King Khalid University, Abha, Saudi Arabia through the Short Research Project under grant number (RGP-1/347/43).

5: We are able to arrange for the creation of a graphical abstract or a video abstract (a 3-4 minute interview with a video journalist) for your article. If you commissioned either option, they would be linked to from your published article and may help to improve the reach and understanding of your research.

An example graphical abstract is at <https://peerj.com/articles/11466/> and the artist would work directly with you to come up with the final image. An example video abstract is at <https://www.youtube.com/watch?v=IsnoFVQe0Ik> and in this case the journalist would interview you over Skype for -30 minutes before creating a 3-4 minute video from that material.

This is an optional commissioned service in addition to your publication fee but we have tried to make these additional fees as low as possible. For example, you could pay for your article fee via our APC payment, and commission both a graphical abstract and a video abstract all for less than the cost of article publication at most other Open Access publishers.

- Cost for a graphical abstract: \$299
- Cost for a video abstract: \$550
- Scheduling: we aim to complete and publish the material alongside your published article (though that is not essential of course and we can work with you on the publication date)
- License: Materials are created under the Open Access CC BY license.

If you are interested in either option, please select the desired item from this page and complete payment: <https://peerj.com/manuscripts/73630/payments/>.

Complete production tasks

With kind regards,

Jackie Thai

Head of Publishing Operations, PeerJ

ID-73630 / PeerJ

Need help? Email support@peerj.com

Publisher of: *PeerJ — Life & Environment, PeerJ Computer Science, PeerJ Physical Chemistry, PeerJ Organic Chemistry, PeerJ Inorganic Chemistry, PeerJ Analytical Chemistry and PeerJ Materials Science*

Follow us on [Twitter](#), [Facebook](#), [Instagram](#) and our [Blog](#)

2022, PeerJ, Inc. PO Box 910224 San Diego, CA 92191, USA

[peerj] Proof ready for checking (PEERJ_73630)

1 pesan

PeerJ Staff <production@peerj.com>

10 October 2022 pukul 23.56

Balas Ke: PeerJ Staff <production@peerj.com>

Kepada: Ajinkya Pawar <ajinkya@drpawars.com>, Dian Agustin Wahjuningrum <dian-agustin-w@fkg.unair.ac.id>

PeerJ

Dear Dian Agustin,

Please download and check your proofing PDF. Then upload it with your changes.

Note: You only have one round of checks, so please collect feedback from all necessary co-authors before returning it.

[Download Proofing PDF](#)

Next steps

- Mark up the Proofing PDF with your requested changes. Please do not implement the changes, just mark them up.
- Or, supply a list of corrections in a text file.
- Only review the Proofing PDF that you download from this email.
- You may need to upload multiple files e.g. your Proofing PDF + replacement figures. Add all files to a single zip file before uploading.

When ready, upload your changes:

Upload Changes

Yours,

Jacqueline Thai

Head of Publishing Operations, PeerJ

Need help? Email support@peerj.com

Publisher of: *PeerJ — Life & Environment, PeerJ Computer Science, PeerJ Physical Chemistry, PeerJ Organic Chemistry, PeerJ Inorganic Chemistry, PeerJ Analytical Chemistry and PeerJ Materials Science*

Follow us on [Twitter](#), [Facebook](#), [Instagram](#) and our [Blog](#)

© 2022, PeerJ, Inc. PO Box 910224 San Diego, CA 92191, USA

Your article is published

1 pesan

PeerJ <info@peerj.com>

Balas Ke: PeerJ <info@peerj.com>

Kepada: Dian Agustin Wahjuningrum <dian-agustin-w@fkg.unair.ac.id>

19 October 2022 pukul 05.19

PeerJ

Dear Dian Agustin,

Congratulations, your article - Evaluation of pulpal anesthesia and injection pain using IANB with pre heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis—a randomized clinical study - is now published!

This is great news, why not share it:

My article has been published today in @PeerJLife
<https://peerj.com/articles/73630> #
AnesthesiologyandPainManagement #ClinicalTrials
#Dentistry #DrugsandDevices

Send Tweet

(you can edit before sending)

So, what now?

To put it simply - this is just the beginning! Authors who actively share their article in

the first year **receive more views, feedback and citations.**

You and your co-authors invested huge amounts of time and effort to create this article. If you believe it will benefit your academic community (or a wider readership), now is the time to get it out there!

First - keep track of your article's usage

As an author you have access to exclusive PeerJ analytics tools. Now that you are published, you'll get a rich data set of daily usage across all of your publications at PeerJ. Also discover how download and citation rates of published articles are affected by a manuscript's title length, choice of open or hidden review history, and more.

[Analytics Dashboard](#)

Next - start sharing

Your **Impact Toolkit** is a great place to begin sharing and see how it affects usage with the analytics tools above. Choose from a range of sharing tasks, from tweeting to wikipedia edits:

[Impact Toolkit](#)

On behalf of the PeerJ team, congratulations again for successfully publishing your article and contributing to the scientific record.

We are proud to have helped you get there.

With kind regards,

The PeerJ Team

Spread The Word about PeerJ

Help us make fair and fast Open Access publishing the norm.

Enable your advocate dropdown for quick sharing tasks, and visit our Spread The Word pages for more ideas.

Spread The Word

ID-67550 / PeerJ

Need help? Email support@peerj.com

Publisher of: *PeerJ — Life & Environment, PeerJ Computer Science, PeerJ Physical Chemistry, PeerJ Organic Chemistry, PeerJ Inorganic Chemistry, PeerJ Analytical Chemistry and PeerJ Materials Science*

Follow us on [Twitter](#), [Facebook](#), [Instagram](#) and our [Blog](#)

2022, PeerJ, Inc. PO Box 910224 San Diego, CA 92191, USA

**To
The Academic Editor,
PeerJ**

Subject: Submission of Revision.

Dear Academic Editor and Respected Reviewers,
Thank you very much for reviewing our article and providing us with encouragement and guidance. This would undoubtedly enhance our paper's credibility and substantiation.

We hereby present a revised version of our manuscript that addresses all of the comments made by the distinguished reviewers.

Please find the responses to the comments raised by each reviewer below.

Best regards

Dian Agustin Wahjuningrum
Submitting Author

Reviewer 1

Basic reporting

I think this section is now complete.

Our Response: We'd like to thank the highly rated critic for his kind compliments.

Experimental design

Materials and Methods all well written.

Our Response: We'd like to thank the highly rated critic for his kind compliments.

Validity of the findings

Results are important and linked to the thesis.

Our Response: We'd like to thank the highly rated critic for his kind compliments.

Additional comments

I think the article is now suitable for publication.

Our Response: We'd like to thank the highly rated critic for his kind compliments.

Reviewer 2

Basic reporting

Please have the manuscript edited by professional English editing service.

Our Response: We acknowledge the respected evaluator's remarks. We've finalised the manuscript to be more sound. Hopefully, this is now suitable.

Experimental design

The number of patients in each group in Abstract, Materials and Methods, Results, and flow diagram do not match.

Please correct every part of the manuscript.

Our Response: We appreciate the respected evaluator's views. In this regard, we made the modifications indicated throughout the manuscript. Hopefully, this is now acceptable.

Additional comments

For more detail, please see the PDF file and word file with track changes.

Our Response: We'd like to thank the distinguished assessor for his complimentary remarks. With this amended paper submission, we have made all of the modifications advised by the reviewer in the annotated PDF.

1 **Evaluation of pulpal anesthesia and injection pain**
2 **using IANB with pre-heated, buffered and**
3 **conventional 2% lignocaine in teeth with**
4 **symptomatic irreversible pulpitis- A Randomized**
5 **Clinical Study.**

6
7 Namita Gandhi¹, Nimisha Shah¹, Dian Agustin Wahjuningrum^{2,*}, Sweetly Purnomo², Riana
8 S. Nooshian⁴, Suraj Arora³, Ajinkya M. Pawar^{4,*}

9
10 ¹Department of Conservative Dentistry and Endodontics, K M Shah Dental College and
11 Hospital, Sumandeep Vidyapeeth, Vadodara, Gujarat, India.

12 ²Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga,
13 Surabaya City, East Java 60132, Indonesia.

14 ³Department of Restorative Dental Sciences, College of Dentistry, King Khalid University,
15 Abha, P.O. Box 960, Postal Code: 61421, Saudi Arabia.

16 ⁴Department of Conservative Dentistry and Endodontics, Nair Hospital Dental College,
17 Mumbai 400008, Maharashtra, India.

18
19 ***Corresponding Authors**

20 **Ajinkya M. Pawar**

21 Department of Conservative Dentistry and Endodontics, Nair Hospital Dental College,
22 Mumbai, Maharashtra, India

23 Email address: ajinkya@drpawars.com

24
25 **Dian Agustin Wahjuningrum**

26 Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga,
27 Surabaya City, East Java, Indonesia

28 Email address: dian-agustin-w@fkg.unair.ac.id

31 Abstract

32

33 **Background.** Efficacy of 2% Lignocaine is reduced in a hot tooth. Local aesthetic agents can
34 be preheated and buffered to increase their effectiveness. The present investigation was
35 carried out due to a limited information concerning adult patients with symptomatic
36 irreversible pulpitis in mandibular teeth. Efficacy can be improved by preheating and
37 buffering LA. Due to limited information in adult patients with symptomatic irreversible
38 pulpitis in mandibular molars the present study was conducted.

39 **Methods.** A total of 252 individuals were included in the clinical trial in accordance with the
40 selection criteria only after clinical study was registered with the Clinical Trial Registry of
41 India (CTRI/2020/09/027796). After registration of the clinical study to the Clinical Trial
42 Registry of India (CTRI/2020/09/027796) and informed consent, 252 patients were enrolled
43 as per selection criteria. Scores on the VAS and EPT on a 1–10 scale were recorded prior to
44 the commencement of therapy. Before starting the treatment a 1–10-point scale VAS and EPT
45 scores were noted. In this double-blinded study, patients were randomly divided by a Co-
46 investigator using computer randomisation (www.randomizer.org) into three groups, Group
47 A: IANB with 2% lignocaine preheated at ~~42°~~ 42° c (injected at 37 °c) (N=84), group B:
48 IANB of 2 % lignocaine buffered with 0.18ml of 8.4% sodium bicarbonate (N=80) and group
49 C: 2 % lignocaine (N=88). Excluding the dropouts of individuals (n=11), where in the
50 anaesthesia failed, a total of 241 people were finally assessed 15 minutes after profound
51 anaesthesia, endodontic access, and intraoperative pain were quantified using VAS. 15-
52 minutes after profound anaesthesia, endodontic access, and intraoperative pain were recorded
53 using VAS. Pain on injection for all three groups was recorded immediately after IANB with
54 VAS. The analysis was performed using One Way ANOVA with Tukey's Post Hoc Test and
55 Paired T-Test using SPSS version 21.

56 **Results.** Preheated, Buffered, and conventional 2% lignocaine showed statistically significant
57 reduction in intraoperative pain ($P < 0.001$) compared to pre-operative but on inter-group
58 comparison preheated and buffered showed highly significant pain reduction compared with
59 conventional 2% lignocaine ($P < 0.001$).

60 **Conclusions.** Warm and buffered LA were effective in reducing intraoperative discomfort
61 than conventional LA. When compared to conventional LA, warmed and buffered LA were
62 more successful in reducing intra-operative pain. Preheated local anesthetics caused the least
63 pain, followed by buffered local anesthetics, while conventional local anesthetics caused the
64 most pain. (Sumandeep Vidyapeeth Institutional Ethics Committee)

65 SVIEC/ON/DentBNPG18/D19047; date of approval 22/11/2019 and the clinical trial registry
66 of India no.: CTRI/2020/09/027796).

67

68 **Keywords.** Buffered; Endodontics; Irreversible Pulpitis; local anesthesia; pre-warm-

69 Irreversible Pulpitis; Endodontics

70 Introduction

71 In order to minimise discomfort during different dental, endodontic, and minor
72 surgical treatments, local anaesthetic (LA) is necessary (Queiroz et al., 2015). In the majority
73 of patients, it is challenging to achieve enough anaesthetic success for a "hot" tooth. Local
74 anaesthesia (LA) is a requirement for reducing pain during various dental, endodontic, and
75 minor surgical procedures (Queiroz et al., 2015). In most of the patients, it is difficult to
76 achieve adequate anesthesia in patients with "hot" tooth. According to the literature, inferior
77 alveolar nerve blocks (IANB) using lignocaine in mandibular posterior teeth had a failure rate
78 of 44%–81% (Claffey et al., 2004; Potoenik et al., 2000). There are a number of causes,
79 including local tissue acidosis brought on by the production of lactic acid and its by-products,
80 hyperalgesia offered on by inflamed pulp, and a lower resting membrane potential, but the
81 most widely accepted theory is that tetrodotoxin-resistant sodium channels are to penalise
82 (TTXr). Lignocaine makes it four times harder for these channels to close, and inflammation
83 doubles the production of these molecules (Wells et al., 2007; Badrian et al., 2016). The
84 literature estimates a 44%–81% failure rate for inferior alveolar nerve blocks (IANB) with
85 lignocaine in mandibular posterior teeth (Claffey et al., 2004; Potoenik et al., 2000). Various
86 reasons like local tissue acidosis due to the formation of lactic acid and by products,
87 hyperalgesia due to inflamed pulp, and lower resting membrane potential, but most accepted
88 theory is tetrodotoxin-resistant sodium channels (TTXr). These channels are four times more
89 difficult to get closed up by lignocaine, and inflammation doubles the expression of these
90 molecules (Wells et al., 2007; Modaresi et al., 2016).

91 Various techniques used to boost the success rate of IANB in hot tooth are, change in
92 injection technique (Meechan, 1999), supplementary anesthesia technique (Yadav, 2005;
93 Bhalla et al., 2021), change in anesthetic liquid, etc. (Nagendrababu et al., 2020) Changes in
94 injection method (Meechan, 1999), supplemental anaesthesia techniques (Yadav, 2005;
95 Bhalla et al., 2021), changes in anaesthetic liquid, etc. (Nagendrababu et al., 2020) are a few
96 of the approaches utilised to increase the success rate of IANB in hot teeth. Lignocaine
97 containing adrenaline usually have a pH range between 2.9 - 4.4 (Malamed et al., 2013).
98 This pH is recommended to prolong the shelf life and to prevent oxidation of LA, but at the
99 same time it shows reduction in its efficacy, burning sensation, slow anesthesia onset.

100 When used for mandibular or maxillary anaesthesia, elevating the pH of lignocaine by
101 neutralising it with 8.4% sodium bicarbonate accelerates the dissociation rate and increases
102 the concentration of uncharged base ions crossing the nerve membrane. Elevating the pH of

103 Lignocaine by neutralizing it with 8.4% sodium bicarbonate increases the dissociation rate
104 and increases the concentration of uncharged base ions crossing the nerve membrane, hence
105 more effective when used for mandibular or maxillary anesthesia. (Kattan et al., 2019).

106 Warming LA to 42°C is another effective way to boost its effectiveness (Aravena et
107 al., 2018; Tirupathi & Rajasekhar, 2020; Hogan et al. 2011). The LA molecule may infiltrate
108 the nociceptor, causing sodium channels to block more promptly. This could be the result of
109 local anaesthetics' temperature-dependent, decreasing pKa (dissociation constant) value
110 (Allen et al., 2008). According to Powell (1987), lignocaine has a pKa of 7.57 at 40°C and
111 7.92 at 25°C. As a result, warming lignocaine may expedite the initiation of local anaesthetic
112 and enhance its effectiveness. Another proven method to increase the efficacy of LA is
113 warming it to 42°C (Aravena et al., 2018; Tirupathi & Rajasekhar, 2020; Hogan et al. 2011).
114 The LA molecule may penetrate the nociceptor, resulting in faster blocking of sodium
115 channels. This may occur due to the pKa (dissociation constant) value of local anaesthetics
116 being temperature-dependent and decreasing when warmed (Allen et al., 2008). Powell
117 (1987) states that the pKa of lignocaine is 7.57 at 40°C and 7.92 at 25°C. Hence, warming
118 lignocaine may speed the onset of local anesthesia and improve its quality.

119
120 The speed, location, and pH of the anaesthetic solution are only a few of the many
121 aspects of local anaesthesia delivery that might induce pain. As a result, patients get anxious
122 and postpone away necessary surgeries. A research by Gümüş & Aydinbelge (2020)
123 demonstrated that pre-warming LA decreases injection discomfort. In a similar context,
124 Palanivel et al., (2020) revealed that buffered LA caused the least discomfort during
125 administration. Many factors cause pain during local anesthesia administration, including the
126 speed of injection, the site of injection, and the pH of the anesthetic solution. This results in
127 patient anxiety and the deferment of needed procedures. A study by Gümüş and Aydinbelge
128 (2020) proved that injection pain is reduced by pre-warming LA. Similarly, a study by
129 Palanivel et al., (2020) showed that buffered LA had the least pain on administration.

130
131 Since there is sporadic literature comparing the efficacy of preheated, buffered, and
132 conventional LA on adult population, the present double-blinded randomized clinical study
133 was designed aiming to evaluate the pulpal anesthesia and injection pain using IANB with
134 pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible
135 pulpitis. The null hypothesis was that there is no difference in efficacy of pulpal anesthesia

136 and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in
137 teeth with symptomatic irreversible pulpitis

138

139 **Materials and Method**

140 **Study design, Ethical Approval, and Clinical Trial Registry.**

141 This double-blind randomized clinical study was approved by the Sumandeep Vidyapeeth
142 Institutional Ethics Committee (SVIEC/ON/DentBNPG18/D19047; date of approval
143 22/11/2019), India. The protocol was developed and registered at the clinical trial registry of
144 India (CTRI/2020/09/027796). The current superiority trial was reported according to
145 Consolidated Standards of Reporting Trials (CONSORT) guidelines (*Schulz et al., 2010*).
146 Written informed consent was obtained from all participants in this study.

147

148 **Sample size.**

149

150 —In a one-way ANOVA study, sample sizes of minimum 60, 60 and 60 were
151 obtained from the 3 groups whose means were compared. The total sample of 180 subjects
152 achieves 80% power to detect differences among the means versus the alternative of equal
153 means using an F test with a 0.05000 significance level. The size of the variation in the
154 means is represented by their standard deviation which is 30.0 the common standard
155 deviation within a group is assumed to be 1.13. Between group, one way analysis of variance
156 with multiple comparison test at 5% level. Sample size formula- used was:
157 $(Z_{\alpha} + Z_{\beta})^2 * \text{Sqrt}(n * \delta^2 / 2kS^2)$,
158 wWhere $Z_{\alpha}=1.96$, $Z_{\beta}=0.84$, $n=$ total number of groups=3, $\delta=$ mean
159 difference=30.0, $k=$ degrees of freedom= $n-1=2$, $S=$ Standard Deviation= 1.13.

160

161 —However number of patients enrolled in the study were 252 divided into in
162 following three groups: (A) preheated 2% lignocaine, ($n = 84$); (B) buffered local anesthesia,
163 ($n = 804$); and (C) conventional 2% lignocaine, ($n = 884$).

164

165 **Selection criteria.**

166 Patients were selected as per the *inclusion*: patients among 18 to 60 years of age with
167 mandibular hot teeth (Symptomatic irreversible pulpitis), having actively experienced
168 moderate to severe pain on a VAS scale of 5 or more were included in the study. *Exclusion*

169 *criteria:* Patients with known hypersensitivity to Lignocaine and sodium bicarbonates, who
170 had undergone cardiac surgery in the last 6 months, pregnant or lactating females, or with
171 necrosed teeth with sinus or swelling, severe periodontitis and poor oral hygiene, cracks,
172 fracture, and open apex were excluded from the study.

173

174 **Randomization and allocation concealment.**

175 A postgraduate student assessed the eligibility of five hundred and twenty-one
176 patients based on clinical examinations, radiographs, and pulp sensibility tests. Clinically
177 tooth having spontaneous/lingering pain/nocturnal pain with moderate to deep carious lesion
178 and absences of tenderness on percussion and delayed response to EPT were taken for further
179 radiographic examination. Tooth with radiolucency involving enamel, dentin, and
180 approaching pulp was selected. All the radiographs were taken with a long cone and
181 paralleling technique using a positioning indicator device. Two hundred and fifty-two
182 patients meet the selection criteria and agreed to participate in the trial. Co-investigator
183 implemented the random sequence generation and allocation concealment. Randomization
184 was done by computer randomization (<https://www.randomizer.org/>) and patients were
185 assigned into 3 groups.

186 The allocation concealment ratio was 1:1:1. This was done by inserting the LA
187 cartridges in sequentially numbered sealed opaque envelopes. The envelopes were marked
188 with the randomization code. As soon as the patient was placed in the intervention group, the
189 number was noted in the patient's case sheet and decoded at the end of the trial.

190

191 **Blinding.**

192 The entire procedure was double-blinded to avoid bias. The primary investigator and
193 the patient both were blinded to the groups allotted. The operator directly received an
194 aspirating metal syringe loaded with the cartridge of lignocaine; pre-heated lignocaine or
195 buffered lignocaine with a 27-gauge needle attached to the tip of the unit.

196

197

198

199 **Clinical procedure.**

200 Patients were sensitized to a (1 to 10-point) VAS scale. This scale was given to
201 the patient to choose thrice: the first time was before the injection,

202 second time after receiving the injection, and the third after entering the
203 pulp chamber and a pre-operative VAS score was recorded. Pre-operative pulp sensibility
204 test was recorded using EPT (Electric pulp test). The patient was explained about the test and
205 the tooth was checked first followed by the affected tooth. Patients were asked to indicate
206 when a tingling sensation occurs to him/her, and the response of the affected tooth was noted
207 down in numbers.

208 For group A – The preparation of preheated local anesthesia was done according to
209 method described by [Allen et al., \(2008\)](#); [Davidson & Boom, \(1992\)](#). A 1.8 ml cartridge of
210 commercially accessible 2% lignocaine hydrochloride with 1:80,000 adrenaline (Lignospan
211 special, Septodont Healthcare India) was placed in an (AR Heat) Composite warmer (12
212 VDC, 2000Mpa, 24W0 power supply), for 4 minutes. Two cartridges were placed in the
213 heating slot of the warmer and the thermostat is set in such a way that a temperature of 42°C
214 was obtained for the anesthetic liquid. The rubber cap of the second cartridge was removed
215 and a thermometer was used to check the temperature of the anesthetic solution, as it is
216 ascertained at 37°C (Body temp), the first 1.8 ml cartridge was administered to the patient.

217 For group B – The preparation of Buffered local anesthesia was done according to a
218 previous study ([Saatchi et al., 2015](#)). The buffered local anesthetic solution has a shelf-life of
219 one week, but it was prepared fresh once every two days for maximum efficacy. Under sterile
220 conditions, 0.18 ml from a 1.8-ml cartridge of 2% Lignocaine with 1:80,000 adrenaline was
221 drawn and replaced with 0.18 ml 8.4% sodium bicarbonate using a 1 ml plastic syringe and
222 stored in the refrigerator. The cartridge was inverted five times to mix the solution. As a
223 result, no precipitation was formed. It was shaken until the solution was clear; this ensured
224 that the sodium bicarbonate was completely dissolved. The cartridge was then loaded into a
225 metal syringe and injected.

226 For group C- Preparation of conventional *group* – Conventional nerve block with
227 1.8ml of 2% lignocaine with 1:80,000 adrenaline was injected. IANB in all the three
228 experimental groups was given with a metal syringe with 27-G, a 1.5-inch needle attached to
229 a standard aspirating dental injection syringe about 1mm, and 1.8ml of the solution was
230 deposited slowly (2 minutes). Immediately after injection, VAS was used to evaluate the
231 injection pain for all the experimental groups.

232 All the patients were asked to wait for 15 minutes for the profound anesthesia to be
233 achieved. Subjective symptoms like tingling sensation, numbness of lower lip, buccal and
234 lingual periosteum on the respective side of jaw were considered, whereas objective
235 symptoms like EPT (Parkell gentel pulse vitality tester) of concerned tooth was done,

236 negative response to EPT was considered as effective anesthesia. Those patients who do not
237 showed subjective and objective symptoms were given supplementary intra-ligamentary
238 injections and were excluded from the study (Consort Flow chart).

239

240 — Isolation was performed with the help of a rubber dam fifteen minutes after the
241 injection. Excavation of caries was done along the walls of the tooth and lastly, the pulpal
242 roof was prepared. Access cavity preparation was done with help of endo access bur to design
243 the access cavity. After entering the pulp chamber and intra-operative VAS score was
244 recorded as intra-operative reading. Further, the endodontic treatment was performed as per
245 the standard methods and protocol by the primary investigator.

246

247 **Statistical methods.**

248 The obtained data were tabulated and statistically analyzed using SPSS version 21 and
249 p-value and Chi-square Value, One Way ANOVA with Tukey's Post Hoc Test, and Paired T-
250 Test were applied. For the statistical test between the group, a one-way analysis of variance
251 with multiple comparison tests at the level of significance was set as 5%.

252

253 **Results**

254 **Demographic data.**

255 The patients enrolled in the clinical trial are presented on the CONSORT 2010 flow
256 diagram (Figure 1). Total of 252 patients were included in present study of which 11 patients
257 were dropped out as lip numbness was not achieved after 15 minutes of INAB and considered
258 as failure due to the wrong technique. So, 241 patients were included for final evaluation. Out
259 of the total enrolled patients, 119 were male, while 122 were female. The age of 416 patients
260 was between (18-25) years of age, 825 patients were between (26-36) years, 669 patients
261 were between (37- 46) years of age and the remaining 522 patients were between (47- 60)
262 years of age.

263

264

265

266 **Pre-Intra operative VAS score.**

267 The mean pre-operative pain using a 10-mm Visual Analog Scale (VAS) was 7.28
268 mm \pm 1.26 mm, for Group A. For Group B mean VAS score was 6.88 mm \pm 1.23 mm, and

269 for Group C score was $6.88 \text{ mm} \pm 1.24 \text{ mm}$ (Table 1). On comparing the means of all three
270 groups no statistical difference was found in the pre-operative pain values. While the mean of
271 Intra-operative pain for Group A was $1.59 \text{ mm} \pm 1.03 \text{ mm}$, for Group B $1.69 \text{ mm} \pm 1.07 \text{ mm}$,
272 and Group C was $3.54 \text{ mm} \pm 2.34 \text{ mm}$. This shows that all three local anesthetic agents were
273 highly effective in reducing pain (P value <0.001).

274 Table 2 shows an inter-group comparison between all the three experimental groups
275 for the reduction in intra-operative pain, there was no statistically significant difference
276 (P=0.183) between Group A (Preheated LA) and Group B (Buffered LA). Whereas there was
277 a highly significant difference (P <0.001) between Group A (Preheated LA) - Group C
278 (Conventional LA) and between Group B (buffered LA) – Group C (Conventional LA). This
279 indicates that buffered and preheated local anesthetic solutions are more efficient in reducing
280 pain in patients with symptomatic irreversible pulpitis in comparison to conventional 2%
281 local anesthetic agents.

282

283 **Pain on injection.**

284 The mean pain on LA administration using VAS (Visual Analog Scale) for Group A
285 was $1.35 \text{ mm} \pm 1.09 \text{ mm}$, Group B was $2.08 \text{ mm} \pm 1.27 \text{ mm}$, and Group C was $3.19 \text{ mm} \pm$
286 0.93 mm . Table 3 shows the mean difference between Group A and Group B was $-0.73 \text{ mm} \pm$
287 0.17 mm and between Group A and Group C was $-1.84 \text{ mm} \pm 0.17 \text{ mm}$ stating that there
288 statistically significant difference between the groups (P value <0.001). Correspondingly
289 comparing Group B with Group C showed a mean difference of $-1.11 \text{ mm} \pm 0.17 \text{ mm}$ and a p-
290 value of <0.001 thus indicating there was a statistically significant difference between them
291 concerning pain on injection. This shows that preheated LA showed the least pain on
292 injection followed by buffered and conventional LA.

293

294 **Discussion**

295 In the current clinical exploration, patients with symptomatic irreversible pulpitis
296 were evaluated to determine the effectiveness of inferior alveolar nerve block in relieving
297 pain using pre-heated, buffered, and standard 2% lignocaine. The study's null hypothesis was
298 rejected in light of the findings. The present clinical study was conducted to evaluate the
299 efficacy of inferior alveolar nerve block in reducing pain with pre-heated, buffered, and
300 conventional 2% lignocaine in patients with symptomatic irreversible pulpitis. Based on the
301 results the null hypothesis for this study was rejected.

302

303 Clinical dentistry has changed from being an unpleasant and traumatic experience to
304 one that is substantially less uncomfortable and more satisfying because to the efficacious use
305 of LA. Profound anaesthesia during root canal therapy not only helps the patient but also
306 frees the dentist from worrying about unanticipated movements or reactions from the patient.
307 Patients with symptomatic irreversible pulpitis (hot tooth) and challenges with mandibular
308 teeth sometimes have trouble achieving enough anaesthetic effect (Sahu et al., 2019).
309 Therefore, amendments are suggested to increase efficacy. The successful use of LA has
310 transformed clinical dentistry from being an unpleasant and frightful experience to one that is
311 much less unpleasant and more satisfying. In addition to benefiting the patient, profound
312 anaesthesia during root canal therapy will relieve the dentist from worrying about sudden
313 movements or reactions of the patients. Routinely, it is difficult to achieve adequate
314 anaesthesia in patients with symptomatic irreversible pulpitis (hot tooth) and challenges
315 multiply increases in in mandibular teeth_ (Sahu et al., 2019). So, modifications are proposed
316 to improve efficacy.

317

318 Changing the pH and temperature of the anaesthetic solution is the most productive
319 technique to improve efficacy and lessen pain during injection, according to a clinical trial on
320 minors (Kurien et al., 2018). Warming the local anaesthetic solution to body temperature
321 (37°C) before administration seemed to lessen pain during intraoral local anaesthesia
322 administration (Aravena et al., 2018; Tirupathi & Rajasekhar, 2020) and buffered local
323 anaesthetic (Kattan et al., 2019) solutions in adult patients, according to a number of
324 randomised clinical studies and systematic reviews on prewarmed and unwarmed LA
325 solution. However, there is scant information comparing preheated, buf. So the current study
326 was created. A clinical study on children has shown that changing the pH and temperature of
327 the anesthetic solution is the most effective way of increasing efficacy and reducing pain
328 during injection (Kurien et al., 2018). There are various randomized clinical studies and
329 systematic reviews on prewarmed and unwarmed LA solution and concluded that warming
330 the local anesthesia solution to body temperature (37°C) before administration seemed to
331 reduce the discomfort during intraoral local anesthesia administration (Aravena et al., 2018;
332 Tirupathi & Rajasekhar, 2020) and buffered local anesthetic (Kattan et al., 2019) solutions in
333 adult patients but scarce information on comparing preheated, buffered, and conventional 2%
334 lignocaine. So present study was designed.

335

336 Visual Analog Score was used to assess the decrease in intra-operative pain and pre-
337 operative discomfort. Because the VAS is dependable, repeatable, and simpler for patients to
338 comprehend and record, we chose to utilise it (Hawker et al., 2011). Pre-operative pain and
339 reduction in Intra-operative pain were evaluated with Visual Analog Score. We opted to use
340 the VAS, as it is reliable, reproducible, and easier for patients to understand and document
341 (Hawker et al., 2011).

342

343 The effectiveness of IANB is often assessed by the subjective and objective
344 symptoms that patients experience after being under anaesthesia, however an electric pulp
345 tester (EPT) is a more accurate way to assess pulpal anaesthesia (Warren et al., 2017).
346 Progressive pulpal anaesthesia is defined as no response to EPT. Contrasted with the study by
347 Certosimo & Archer (1996), which demonstrated that a "no reaction" at an 80-reading
348 guaranteed pulpal anaesthesia in crucial asymptomatic teeth For a longer shelf life,
349 anaesthetic solutions sold commercially are acidic (Malamed et al., 2013). Efficacy of IANB-
350 is normally evaluated by subjective and objective symptoms patients develop after anesthesia-
351 however more reliable method to evaluate pulpal anesthesia is by using an electric pulp tester
352 (EPT) (Warren et al., 2017). No response to EPT is considered profound pulpal anesthesia-
353 As compared to the study by Certosimo and Archer (1996) that showed that a "no response"
354 at an 80-reading ensured pulpal anesthesia in vital asymptomatic teeth. Commercially-
355 available anesthetic solutions are acidic for longer shelf life (Malamed et al., 2013).
356 Unfortunately, the LA solution's acidity has several drawbacks that affect how well it works
357 in clinical settings, so we need to modify it. Buffering local anaesthesia is one such
358 improvement. It is made by mixing 1.8ml of LA with 0.18ml of sodium bicarbonate, 8.4%,
359 which results in the creation of carbon dioxide and water (Afsal et al., 2019). Since carbon
360 dioxide directly depresses the axon, concentrates LA into the nerve trunk (ion trapping), and
361 changes LA into an active cationic state, it helps buffered LA work more
362 effectively. However acidity of the LA solution has certain demerits, due to which its clinical
363 performance is compromised, hence we require modification in LA solution. One such
364 modification is buffered Local anesthesia. Which is prepared by adding 0.18 ml of 8.4%
365 sodium bicarbonate to 1.8ml of LA, which leads to the formation of carbon dioxide and water
366 (Afsal et al., 2019). Carbon dioxide is beneficial in improving the efficacy of buffered LA

367 since it has a direct depressant effect on the axon, by concentrating LA into the nerve trunk
368 (ion-trapping) and by converting LA into an active cationic form.

369

370 In patients with a hot tooth, buffering LA enhances the chance of effective anaesthesia
371 by 2.29 times, according to a systematic review by Kattan et al., (2019), Kurien et al. (2018),
372 and Saatchi et al. (2018) both endorse the same (2016). But Schellenberg et al. (2015) and
373 Hobeich et al. (2015) reported dissenting findings (2013). Different populations involved,
374 non-standard buffering approaches, varying injection methodologies, and various assessment
375 techniques can all lead to variances (Palanivel et al., 2020). A Systematic review by Kattan et
376 al., (2019)) concluded buffering LA increases the likelihood of achieving successful
377 anesthesia by 2.29 times in patients with a hot tooth. The same is approved by Kurien et al.,
378 (2018) and Saatchi et al., (2016). But contradictory results were reported by Schellenberg et
379 al., (2015) and Hobeich et al., (2013). Differences may occur due to different populations
380 involved, non-standardized buffering methods, and differences in injection techniques and
381 evaluation methods (Palanivel et al., 2020).

382

383 Pre-heating local anaesthetic at 42 °C is another method for increasing LA
384 effectiveness in inflamed pulp (Afsal et al., 2019). By blocking sodium channels,
385 conventional LA prevents a change in the nerve impulse's course of propagation. By
386 increasing membrane fluidity, which makes it easier for lignocaine to pass and reach the
387 effective concentration faster, and by densely expressing TRPV1 channels in trigeminal
388 tissue, warming at 42°C aids in faster blockage of the sodium channels (Afsal et al., 2019).
389 Another way to improve LA efficacy in inflamed pulp is pre-heating local anesthesia at 42°C.
390 (Afsal MM 2019) Conventional LA acts by preventing a change in the propagation of the
391 nerve impulse by blocking sodium channels. Warming at 42°C help the in faster blocking of
392 the sodium channels by increasing the membrane fluidity allowing lignocaine to cross more
393 easily and reach the effective concentration more quickly and by densely expressed TRPV1
394 channels in trigeminal tissue (Afsal et al., 2019). According to Alonso et al. (1993), there was
395 a negative correlation between temperature and pain, with 10°C having the greatest mean
396 pain level and the following temperatures: 18°C, 37°C, and 42°C. In order to prevent any
397 negative reactions from happening to the oral tissue, pre-heated LA was administered at
398 37°C, or at the physiological tissue pH. According to Davidson & Boom (1992),

399 subcutaneous infusion of LA at body temperature (37°C) lowers pain severity after minor
400 oral surgery. Alonso et al (1993) found an inverse relationship between temperature and pain,
401 with 10°C having the highest mean pain level, followed by 18°C, 37°C, and 42°C. Pre-heated
402 LA was administrated at 37°C i.e., at physiological tissue pH so that no harmful reaction
403 occurred to oral tissue. Davidson et al., (1992) concluded that use of LA at body temperature
404 (37°C) reduces pain intensity during subcutaneous administration for minor oral surgery.

405

406 In this investigation, the warmed group's intra-operative agony was much lower than
407 it was in the traditional LA group. There were no significant differences between pre-warmed
408 and traditional LA, which was in contrast to Ram et al. (2002) but in conformity with
409 Tirupathi & Rajasekhar (2020) and Aravena et al. (2018). The modified Behavioral Pain
410 Scale (BPS), which is difficult to comprehend, was employed as the evaluation criterion,
411 which may have contributed to the disparity between the research populations. In this study,
412 intra-operative pain was significantly reduced in the preheated group compared with
413 conventional LA. This was consistent with Tirupathi et al., (2019) and Aravena et al., (2018)
414 but contrary to Ram et al., (2002) were no significant differences between pre-warmed and
415 conventional LA. The difference may be due to different study populations and the evaluation
416 criteria used was the modified Behavioral Pain Scale (BPS) which is complex to understand.

417 The secondary result of pain during injection was investigated, and preheated and
418 buffered 2% lignocaine was shown to cause the least discomfort. This finding was consistent
419 with a clinical investigation by Gümüş & Aydınbelge (2020). Pain on injection was evaluated
420 as a secondary outcome where the least pain on administration was between Preheated and
421 buffered 2 % lignocaine which was similar to a clinical study conducted by Gümüş et al.,
422 (2020).

423

424 The study's shortcoming is that just one concentration of sodium bicarbonate (8.4%)
425 was utilised to buffer LA; more research carried out using different concentrations is
426 warranted. The same research design must be used to analyse patients with systemic disorders
427 (such as hypertension, diabetes mellitus, and other systemic illnesses). The limitation of the
428 study includes only one concentration of sodium bicarbonate (8.4%) was used for buffering
429 LA; further studies with different concentrations should be carried out. Patient with systemic

430 ~~conditions (Hypertension, Diabetes mellitus) and other systemic illness needs to be evaluated~~
431 ~~using the same study design.~~

432

433

434 **Conclusions**

435 Considering the limitations of the study, we would like to conclude that preheated,
436 buffered, and conventional local anesthesia was effective in reducing pain in symptomatic
437 irreversible pulpitis. When compared to standard LA, warmed and buffered LA was more
438 successful in reducing intraoperative discomfort. Preheated local anaesthetics and buffered
439 local anaesthetics caused the least amount of discomfort during administration, but the
440 standard group caused higher pain. Future RCTs with a larger sample size will be beneficial
441 to confirm the findings.~~In comparison preheated and buffered proved more effective in the~~
442 ~~reduction of intra-operative pain compared with conventional LA. The pain on administration~~
443 ~~was found least in Preheated followed by buffered local anesthetics, whereas more pain was~~
444 ~~felt in the conventional group. More RCT with an increased sample size will be helpful in the~~
445 ~~future to validate the results.~~

446

447 **Acknowledgments**

448 The authors extend their appreciation to the Deanship of Scientific research at King Khalid
449 University, Abha, Saudi Arabia for their support through the Short Research Project under
450 grant number (RGP-1/347/43).

451

452 **ADDITIONAL INFORMATION AND DECLARATIONS**

453 **Funding**

454 The authors received no funding for this work.

455

456 **Competing Interests**

457 The authors deny any conflict of interest.

458

459 **Author Contributions**

460 Namita Gandhi and Nimisha Shah conceived and designed the experiments, performed the
461 experiments, analyzed the data, prepared figures and/or tables, prepared the draft of the
462 manuscript, and approved the final draft.

463 Dian Agustin Wahjuningrun, Sweetly Purnomo, Suraj Arora, and Ajinkya M. Pawar
464 performed a pre-proof reading and editing of the manuscript.

465 Riana S. Nooshian helped in formatting the manuscript according to the journal style.

466

467 **Data Availability Statement**

468 The data of study can be obtained at clinical trial registry of India (www.ctri.nic.in/,

469 [CTRI/2020/09/027796](https://ctri.nic.in/Clinicaltrials/showbrief.aspx?CTRI/2020/09/027796)).

470

471 **References**

472 [Afsal MM., Khatri A., Kalra N., Tyagi R., Khandelwal D. 2019. Pain perception and efficacy
473 of local analgesia using 2% lignocaine, buffered lignocaine, and 4% articaine in
474 pediatric dental procedures. *Journal of Dental Anesthesia and Pain Medicine* 19:101.
475 DOI: \[10.17245/jdapm.2019.19.2.101\]\(https://doi.org/10.17245/jdapm.2019.19.2.101\).](#)

476 [Allen MJ., Bunce C., Presland AH. 2008. The effect of warming local anaesthetic on the pain
477 of injection during sub-tenon's anaesthesia for cataract surgery. *Anaesthesia* 63:276–
478 278. DOI: \[10.1111/j.1365-2044.2007.05351.x\]\(https://doi.org/10.1111/j.1365-2044.2007.05351.x\).](#)

479 [Alonso PE., Perula LA., Rioja LF. 1993. Pain-temperature relation in the application of local
480 anaesthesia. *British Journal of Plastic Surgery* 46:76–78. DOI: \[10.1016/0007-
1226\\(93\\)90070-r\]\(https://doi.org/10.1016/0007-
481 1226\(93\)90070-r\).](#)

482 [Aravena PC., Barrientos C., Troncoso C., Coronado C., Sotelo-Hitschfeld P. 2018. Effect of
483 warming anesthetic on pain perception during dental injection: A split-mouth
484 randomized clinical trial. *Local and Regional Anesthesia* Volume 11:9–13. DOI:
485 \[10.2147/lra.s147288\]\(https://doi.org/10.2147/lra.s147288\).](#)

486 [Aulestia-Viera PV., Braga MM., Borsatti MA. 2018. The effect of adjusting the ph of local
487 anaesthetics in Dentistry: A systematic review and meta-analysis. *International
488 Endodontic Journal* 51:862–876. DOI: \[10.1111/iej.12899\]\(https://doi.org/10.1111/iej.12899\).](#)

489 [Badrian H., Modaresi J., Davoudi A., Sabzian R. 2016. Irreversible pulpitis and achieving
490 profound anesthesia: Complexities and managements. *Anesthesia: Essays and
491 Researches* 10:3. DOI: \[10.4103/0259-1162.164675\]\(https://doi.org/10.4103/0259-1162.164675\).](#)

492 [Bhalla VK., Taneja S., Chockattu SJ. 2021. Failure of molar anesthesia in endodontics: A
493 systematic review. *Saudi Endodontic Journal* 11:283–291.](#)

- 494 [Certosimo AJ, Archer RD. 1996. A clinical evaluation of the electric pulp tester as an](#)
495 [indicator of local anesthesia. . *Operative Dentistry* 21:25–30.](#)
- 496 [CLAFFEY E., READER A., NUSSTEIN J, BECK M., WEAVER J. 2004. Anesthetic](#)
497 [efficacy of articaine for inferior alveolar nerve blocks in patients with irreversible](#)
498 [pulpitis. *Journal of Endodontics* 30:568–571. DOI:](#)
499 [10.1097/01.don.0000125317.21892.8f.](#)
- 500 [Davidson JA., Boom SJ. 1992. Warming lignocaine to reduce pain associated with](#)
501 [injection. *BMJ* 305:617–618. DOI: 10.1136/bmj.305.6854.617.](#)
- 502 [Gümüş H., Aydinbelge M. 2019. Evaluation of effect of warm local anesthetics on pain](#)
503 [perception during dental injections in children: A split-mouth randomized clinical](#)
504 [trial. *Clinical Oral Investigations* 24:2315–2319. DOI: 10.1007/s00784-019-03086-6.](#)
- 505 [Hawker GA., Mian S., Kendzerska T., French M. 2011. Measures of adult pain: Visual](#)
506 [Analog Scale for pain \(Vas Pain\), numeric rating scale for pain \(NRS Pain\), McGill](#)
507 [Pain Questionnaire \(MPO\), short-form mcgill pain questionnaire \(SF-MPQ\), chronic](#)
508 [pain grade scale \(CPGS\), short form-36 bodily pain scale \(SF. *Arthritis Care &*](#)
509 [*Research* 63. DOI: 10.1002/acr.20543.](#)
- 510 [Hobeich P., Simon S., Schneiderman E., He J. 2013. A prospective, randomized, double-](#)
511 [blind comparison of the injection pain and anesthetic onset of 2% lidocaine with](#)
512 [1:100,000 epinephrine buffered with 5% and 10% sodium bicarbonate in maxillary](#)
513 [infiltrations. *Journal of Endodontics* 39:597–599. DOI: 10.1016/j.joen.2013.01.008.](#)
- 514 [Hogan M-E., vanderVaart S., Perampaladas K., Machado M., Einarson TR., Taddio A. 2011.](#)
515 [Systematic Review and meta-analysis of the effect of warming local anesthetics on](#)
516 [injection pain. *Annals of Emergency Medicine* 58. DOI:](#)
517 [10.1016/j.annemergmed.2010.12.001.](#)
- 518 [Kattan S., Lee S-M., Hersh EV., Karabucak B. 2019. DO buffered local anesthetics provide](#)
519 [more successful anesthesia than nonbuffered solutions in patients with pulpally](#)
520 [involved teeth requiring dental therapy? *The Journal of the American Dental*](#)
521 [*Association* 150:165–177. DOI: 10.1016/j.adaj.2018.11.007.](#)
- 522 [Kurien RS., Goswami M., Singh S. 2018. Comparative evaluation of anesthetic efficacy of](#)
523 [warm, buffered and conventional 2% lignocaine for the success of inferior alveolar](#)
524 [nerve block \(IANB\) in mandibular primary molars: A randomized controlled clinical](#)
525 [trial. *Journal of Dental Research, Dental Clinics, Dental Prospects* 12:102–109. DOI:](#)
526 [10.15171/joddd.2018.016.](#)
- 527 [Malamed SF., Tavara S., Falkel M. 2013. Faster onset and more comfortable injection with](#)
528 [alkalinized 2% lignocaine with adrenaline 1:100,000. *Compendium of Continuing*](#)
529 [*Education in Dentistry* 34:10–20.](#)
- 530 [Meechan JG. 1999. How to overcome failed local anaesthesia. *British Dental*](#)
531 [*Journal* 186:15–20. DOI: 10.1038/sj.bdj.4800006.](#)

- 532 [Nagendrababu V., Duncan HF., Whitworth J., Nekoofar MH., Pulikkotil SJ., Veettil SK.,](#)
533 [Dummer PM. 2019. Is articaine more effective than lidocaine in patients with](#)
534 [irreversible pulpitis? an Umbrella Review. *International Endodontic Journal* 53:200–](#)
535 [213. DOI: 10.1111/iej.13215.](#)
- 536 [Palanivel I., Ramakrishnan K., Narayanan V., Gurram P. 2020. A prospective, randomized,](#)
537 [double-blinded, cross over comparison of buffered versus non-buffered 2% lidocaine](#)
538 [with 1:80,000 adrenaline for dental extraction. . *International Journal of Applied*](#)
539 [Dental Sciences 6:35–38.](#)
- 540 [Potočnik I., Bajrović F. 1999. Failure of inferior alveolar nerve block in endodontics. *Dental*
541 \[Traumatology\]\(#\) 15:247–251. DOI: 10.1111/j.1600-9657.1999.tb00782.x.](#)
- 542 [Powell MF. 1987. *Pharmaceutical Research* 04:42–45. DOI: 10.1023/a:1016477810629.](#)
- 543 [Queiroz AM., Carvalho AB., Censi LL., Cardoso CL., Leite-Panissi CR., Silva RA.,](#)
544 [Carvalho FK., Nelson-Filho P., Silva LA. 2015. Stress and anxiety in children after the](#)
545 [use of computerized dental anesthesia. *Brazilian Dental Journal*26:303–307. DOI:](#)
546 [10.1590/0103-6440201300211.](#)
- 547 [Ram D., Hermida LB., Peretz B. 2002. A comparison of warmed and room-temperature](#)
548 [anesthetic for local anesthesia in children. *Pediatric Dentistry* 24:333–336.](#)
- 549 [Saatchi M., Khademi A., Baghaei B., Noormohammadi H. 2015. Effect of sodium](#)
550 [bicarbonate-buffered lidocaine on the success of inferior alveolar nerve block for teeth](#)
551 [with symptomatic irreversible pulpitis: A prospective, randomized double-blind](#)
552 [study. *Journal of Endodontics* 41:33–35. DOI: 10.1016/j.joen.2014.09.011.](#)
- 553 [Sahu S., Kabra P., Choudhary E. 2019. Hot Tooth - A Challenge to](#)
554 [Endodontists. *International Journal of Science and Research* 8:106–109.](#)
- 555 [Schellenberg J., Drum M., Reader A., Nusstein J., Fowler S., Beck M. 2015. Effect of](#)
556 [buffered 4% lidocaine on the success of the inferior alveolar nerve block in patients](#)
557 [with symptomatic irreversible pulpitis: A prospective, randomized, double-blind](#)
558 [study. *Journal of Endodontics* 41:791–796. DOI: 10.1016/j.joen.2015.02.022.](#)
- 559 [Schulz KF., Altman DG., Moher D. 2010. Consort 2010 statement: Updated guidelines for](#)
560 [reporting parallel group randomised trials. *Journal of Pharmacology and*](#)
561 [Pharmacotherapeutics](#) 1:100–107. DOI: 10.4103/0976-500x.72352.
- 562 [Tirupathi SP., Rajasekhar S. 2020. Effect of warming local anesthesia solutions before](#)
563 [Intraoral Administration in dentistry: A systematic review. *Journal of Dental*](#)
564 [Anesthesia and Pain Medicine](#) 20:187. DOI: 10.17245/jdapm.2020.20.4.187.
- 565 [Warren VT., Fisher AG., Rivera EM., Saha PT., Turner B., Reside G., Phillips C., White RP.](#)
566 [2017. Buffered 1% lidocaine with epinephrine is as effective as non-buffered 2%](#)
567 [lidocaine with epinephrine for mandibular nerve block. *Journal of Oral and*](#)
568 [Maxillofacial Surgery](#) 75:1363–1366. DOI: 10.1016/j.joms.2016.12.045.

569 [Wells JE., Bingham V., Rowland KC., Hatton J. 2007. Expression of nav1.9 channels in](#)
570 [human dental pulp and trigeminal ganglion. *Journal of Endodontics* 33:1172–1176.](#)
571 [DOI: 10.1016/j.joen.2007.05.023.](#)

572 [Yadav S. 2015. Anesthetic success of supplemental infiltration in mandibular molars with](#)
573 [irreversible pulpitis: A systematic review. *Journal of Conservative Dentistry* 18:182.](#)
574 [DOI: 10.4103/0972-0707.157238.](#)

575 [Queiroz A, Carvalho A, Censi L et al. Stress and Anxiety in Children After the Use of Computerized Dental](#)
576 [Anesthesia. *Braz Dent J*. 2015;26\(3\):303-307. doi:10.1590/0103-6440201300211.](#)

577 [CLAFFEY E, READER A, NUSSTEIN J, BECK M, WEAVER J. Anesthetic Efficacy of Articaine for Inferior](#)
578 [Alveolar Nerve Blocks in Patients with Irreversible Pulpitis. *J Endod*. 2004;30\(8\):568-571.](#)
579 [doi:10.1097/01.don.0000125317.21892.8f](#)

580 [Potočnik I, Bajrovič F. Failure of inferior alveolar nerve block in endodontics. *Dental Traumatology*.](#)
581 [1999;15\(6\):247-251. doi:10.1111/j.1600-9657.1999.tb00782.x](#)

582 [Wells J, Bingham V, Rowland K, Hatton J. Expression of Nav1.9 Channels in Human Dental Pulp and](#)
583 [Trigeminal Ganglion. *J Endod*. 2007;33\(10\):1172-1176. doi:10.1016/j.joen.2007.05.023](#)

584 [Modaresi J, Davoudi A, Badrian H, Sabzian R. Irreversible pulpitis and achieving—profound anesthesia—](#)
585 [Complexities and managements. *Anesthesia, Essays and Research* 2016;10:3-6. DOI: 10.4103/0259-](#)
586 [1162.164675.](#)

587 [Meechan JG. How to overcome failed local anaesthesia. *Br Dent J* 1999;186:15–20. DOI:](#)
588 [10.1038/sj.bdj.4800006.](#)

589 [Yadav S. Anesthetic success of supplemental infiltration in mandibular molars with irreversible pulpitis: A](#)
590 [systematic review. *J Conserv Dent* 2015;18:182–6. DOI: 10.4103/0972-0707.157238.](#)

591 [Bhalla VK, Taneja S, Chockattu SJ. Failure of molar anesthesia in endodontics: A systematic review. *Saudi*](#)
592 [Endod J. 2021;11:283-291.](#)

593 [Nagendrababu V, Duncan HF, Whitworth J, Nekoofar MH, Pulikkotil SJ, Vccttil SK, Dummer PM. Is articaine](#)
594 [more effective than lignocaine in patients with irreversible pulpitis? An umbrella review. *Int Endod J*.](#)
595 [2020;53:200-213. DOI: 10.1111/iej.13215.](#)

596 [Malamed SF, Tavara S, Falkel M. Faster onset and more comfortable injection with alkalized 2% lignocaine](#)
597 [with adrenaline 1:100,000. *Compend contin. educ. dent*. 2013;34:10-20.](#)

598 [Kattan S, Lee SM, Hersh EV, Karabueak B. Do buffered local anesthetics provide more successful anesthesia](#)
599 [than nonbuffered solutions in patients with pulpally involved teeth requiring dental therapy?: a systematic](#)
600 [review. *J Am Dent Assoc*. 2019;150:165-77. DOI: 10.1016/j.adaj.2018.11.007.](#)

601 [Aravena P, Barrientos C, Troncoso C, Coronado C, Hirschfeld PS. Effect of warming anesthetic on pain](#)
602 [perception during dental injection: A split-mouth randomized clinical trial. *Local Reg. Anesth*. 2018;11:9–13.](#)
603 [DOI: 10.2147/LRA.S147288.](#)

604 [Tirupathi SP, Rajasekhar S. Effect of warming local anesthesia solutions before intraoral administration in](#)
605 [dentistry: a systematic review. *J Dent Anesth Pain Med; JDAPM*. 2020;20:187–94. DOI:](#)
606 [10.17245/jdapm.2020.20.4.187.](#)

607 Hogan ME, vanderVaart S, Perampaladas K, Machado M, Einarson TR, Taddio A. Systematic review and meta-
608 analysis of the effect of warming local anesthetics on injection pain. *Ann Emerg Med*. 2011;58:86-98. DOI:
609 10.1016/j.annemergmed.2010.12.001.

610 Gümüş H, Aydınbelge M. Evaluation of effect of warm local anesthetics on pain perception during dental
611 injections in children: a split-mouth randomized clinical trial. *Clin Oral Investig*. 2020;24:2315-9. DOI:
612 10.1007/s00784-019-03086-6.

613 Allen MJ, Bunce C, Presland AH. The effect of warming local anesthetic on the pain of injection during sub-
614 Tenon's anesthesia for cataract surgery. *Anaesthesia*. 2008;63:276-8. DOI: 10.1111/j.1365-2044.2007.05351.x.

615 Powell MF. Stability of lidocaine in aqueous solution: effect of temperature, pH, buffer, and metal ions on
616 amide hydrolysis. *Pharm. Res*. 1987;4:42-5. DOI: 10.1023/a:1016477810629.

617 Palanivel I, Ramakrishnan K, Narayanan V, Gurram P. A prospective, randomized, double-blinded, cross-over
618 comparison of buffered versus non-buffered 2% lidocaine with 1:80,000 adrenaline for dental extraction. *Int J*
619 *Appl Dent Sci*. 2020; 6:35-38.

620 Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel-group
621 randomised trials. *Trials*. 2010;11:100-7. DOI: 10.4103/0976-500X.72352.

622 Davidson JA, Boom SJ. Warming lignocaine to reduce pain associated with injection. *Br. Med. J*.
623 1992;305:617-8. DOI: 10.1136/bmj.305.6854.617.

624 Saatchi M, Khademi A, Baghaei B, Noormohammadi H. Effect of sodium bicarbonate-buffered lidocaine on the
625 success of inferior alveolar nerve block for teeth with symptomatic irreversible pulpitis: a prospective,
626 randomized double-blind study. *J Endod*. 2015;41:33-5. DOI: 10.1016/j.joen.2014.09.011.

627 Sahu S, Kabra P, Choudhary E. Hot Tooth – A Challenge to Endodontists. *Int. J. Sci. Res*. 201;8:106-9.

628 Kurien RS, Goswami M, Singh S. Comparative evaluation of anesthetic efficacy of warm, buffered and
629 conventional 2% lignocaine for the success of inferior alveolar nerve block (IANB) in mandibular primary
630 molars: A randomized controlled clinical trial. *J. Dent. Res. Dent. Clin. Dent. Prospects*. 2018;12:102-9. DOI:
631 10.15171/joddd.2018.016.

632 Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS-
633 Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain
634 Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short-Form-36 Bodily Pain Scale (SF-36 BPS),
635 and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res*. 2011;63:S240-52.
636 DOI: 10.1002/aer.20543.

637 Warren VT, Fisher AG, Rivera EM, Saha PT, Turner B, Reside G, Phillips C, White Jr RP. Buffered 1%
638 lidocaine with epinephrine is as effective as non-buffered 2% lidocaine with epinephrine for mandibular nerve
639 block. *Int J Oral Maxillofac Surg*. 2017;75:1363-6. DOI: 10.1016/j.joms.2016.12.045.

640 Certosimo AJ, Archer RD. A clinical evaluation of the electric pulp tester as an indicator of
641 local anesthesia. *Oper Dent*. 1996;21:25-30.

642 Afzal MM, Khatri A, Kabra N, Tyagi R, Khandelwal D. Pain perception and efficacy of local analgesia using
643 2% lignocaine, buffered lignocaine, and 4% articaine in pediatric dental procedures. *J Dent Anesth Pain Med*.
644 2019;19:101-9. DOI: 10.17245/jdapm.2019.19.2.101.

645 Alonso P, Perula L, Rioja L. Pain-temperature relation in the application of local anaesthesia. *Br J Plast Surg*.
646 1993;46(1):76-78. doi:10.1016/0007-1226(93)90070-r

- 647 Schellenberg J, Drum M, Reader A, Nusstein J, Fowler S, Beck M. Effect of buffered 4% lidocaine on the
648 success of the inferior alveolar nerve block in patients with symptomatic irreversible pulpitis: a prospective,
649 randomized, double-blind study. *J Endod.* 2015;41:791-6. DOI: 10.1016/j.joen.2015.02.022.
- 650 Hobcich P, Simon S, Schneiderman E, He J. A Prospective, Randomized, Double-blind Comparison of the
651 Injection Pain and Anesthetic Onset of 2% Lidocaine with 1:100,000 epinephrine Buffered with 5% and 10%
652 Sodium Bicarbonate in Maxillary Infiltrations. *J Endod.* 2013;39:597-599. DOI: 10.1016/j.joen.2013.01.008.
- 653 Aulestia-Viera PV, Braga MM, Borsatti MA. The effect of adjusting the pH of local anesthetics in dentistry: a
654 systematic review and meta-analysis. *Int Endod J.* 2018;51:862-76. DOI: 10.1111/iej.12899.
- 655 Ram D, Hermida LB, Peretz B. A comparison of warmed and room-temperature anesthetic for local anesthesia
656 in children. *Pediatr Dent.* 2002;24:333-6.

1 **Evaluation of pulpal anesthesia and injection pain**
2 **using IANB with pre-heated, buffered and**
3 **conventional 2% lignocaine in teeth with**
4 **symptomatic irreversible pulpitis- A Randomized**
5 **Clinical Study.**

6
7 Namita Gandhi¹, Nimisha Shah¹, Dian Agustin Wahjuningrum^{2,*}, Sweetly Purnomo², Riana
8 S. Nooshian⁴, Suraj Arora³, Ajinkya M. Pawar^{4,*}

9
10 ¹Department of Conservative Dentistry and Endodontics, K M Shah Dental College and
11 Hospital, Sumandeeep Vidyapeeth, Vadodara, Gujarat, India.

12 ²Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga,
13 Surabaya City, East Java 60132, Indonesia.

14 ³Department of Restorative Dental Sciences, College of Dentistry, King Khalid University,
15 Abha, P.O. Box 960, Postal Code: 61421, Saudi Arabia.

16 ⁴Department of Conservative Dentistry and Endodontics, Nair Hospital Dental College,
17 Mumbai 400008, Maharashtra, India.

18
19 ***Corresponding Authors**

20 **Ajinkya M. Pawar**

21 Department of Conservative Dentistry and Endodontics, Nair Hospital Dental College,
22 Mumbai, Maharashtra, India

23 Email address: ajinkya@drpawars.com

24
25 **Dian Agustin Wahjuningrum**

26 Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga,
27 Surabaya City, East Java, Indonesia

28 Email address: dian-agustin-w@fkg.unair.ac.id

31 **Abstract**

32

33 **Background.** Efficacy of 2% Lignocaine is reduced in a hot tooth. Local aesthetic agents can
34 be preheated and buffered to increase their effectiveness. The present investigation was
35 carried out due to a limited information concerning adult patients with symptomatic
36 irreversible pulpitis in mandibular teeth.

37 **Methods.** A total of 252 individuals were included in the clinical trial in accordance with the
38 selection criteria only after clinical study was registered with the Clinical Trial Registry of
39 India (CTRI/2020/09/027796). Scores on the VAS and EPT on a 1–10 scale were recorded
40 prior to the commencement of therapy. In this double-blinded study, patients were randomly
41 divided by a Co-investigator using computer randomisation (www.randomizer.org) into three
42 groups, Group A: IANB with 2% lignocaine preheated at 42° c (injected at 37 ° c) (N=84),
43 group B: IANB of 2 % lignocaine buffered with 0.18ml of 8.4% sodium bicarbonate (N=80)
44 and group C: 2 % lignocaine (N=88). Excluding the dropouts of individuals (n=11), where in
45 the anaesthesia failed, a total of 241 people were finally assessed 15 minutes after profound
46 anaesthesia, endodontic access, and intraoperative pain were quantified using VAS. Pain on
47 injection for all three groups was recorded immediately after IANB with VAS. The analysis
48 was performed using One Way ANOVA with Tukey's Post Hoc Test and Paired T-Test using
49 SPSS version 21.

50 **Results.** Preheated, Buffered, and conventional 2% lignocaine showed statistically significant
51 reduction in intraoperative pain ($P < 0.001$) compared to pre-operative but on inter-group
52 comparison preheated and buffered showed highly significant pain reduction compared with
53 conventional 2% lignocaine ($P < 0.001$).

54 **Conclusions.** Warm and buffered LA were effective in reducing intraoperative discomfort
55 than conventional LA. Preheated local anesthetics caused the least pain, followed by buffered
56 local anesthetics, while conventional local anesthetics caused the most pain. (Sumandeep
57 Vidyapeeth Institutional Ethics Committee) SVIEC/ON/DentBNPG18/D19047; date of
58 approval 22/11/2019 and the clinical trial registry of India no.: CTRI/2020/09/027796).

59

60 **Keywords.** Buffered; Endodontics; Irreversible Pulpitis; local anesthesia; pre-warm

61 **Introduction**

62 In order to minimise discomfort during different dental, endodontic, and minor
63 surgical treatments, local anaesthetic (LA) is necessary (Queiroz et al., 2015). In the majority
64 of patients, it is challenging to achieve enough anaesthetic success for a "hot" tooth.

65 According to the literature, inferior alveolar nerve blocks (IANB) using lignocaine in
66 mandibular posterior teeth had a failure rate of 44%–81% (Claffey et al., 2004; Potocnik et
67 al., 2000). There are a number of causes, including local tissue acidosis brought on by the
68 production of lactic acid and its by-products, hyperalgesia offered on by inflamed pulp, and a
69 lower resting membrane potential, but the most widely accepted theory is that tetrodotoxin-
70 resistant sodium channels are to penalise (TTXr). Lignocaine makes it four times harder for
71 these channels to close, and inflammation doubles the production of these molecules (Wells
72 et al., 2007; Badrian et al., 2016).

73 Changes in injection method (Meechan, 1999), supplemental anaesthesia techniques
74 (Yadav, 2005; Bhalla et al., 2021), changes in anaesthetic liquid, etc. (Nagendrababu et al.,
75 2020) are a few of the approaches utilised to increase the success rate of IANB in hot teeth.
76 Lignocaine containing adrenaline usually have a pH range between 2.9 - 4.4 (Malamed et al.,
77 2013). This pH is recommended to prolong the shelf life and to prevent oxidation of LA, but
78 at the same time it shows reduction in its efficacy, burning sensation, slow anesthesia onset.

79 When used for mandibular or maxillary anaesthesia, elevating the pH of lignocaine by
80 neutralising it with 8.4% sodium bicarbonate accelerates the dissociation rate and increases
81 the concentration of uncharged base ions crossing the nerve membrane (Kattan et al., 2019).

82 Warming LA to 42°C is another effective way to boost its effectiveness (Aravena et
83 al., 2018; Tirupathi & Rajasekhar, 2020; Hogan et al. 2011). The LA molecule may infiltrate
84 the nociceptor, causing sodium channels to block more promptly. This could be the result of
85 local anaesthetics' temperature-dependent, decreasing pKa (dissociation constant) value
86 (Allen et al., 2008). According to Powell (1987), lignocaine has a pKa of 7.57 at 40°C and
87 7.92 at 25°C. As a result, warming lignocaine may expedite the initiation of local anaesthetic
88 and enhance its effectiveness.

89 The speed, location, and pH of the anaesthetic solution are only a few of the many
90 aspects of local anaesthesia delivery that might induce pain. As a result, patients get anxious
91 and postpone away necessary surgeries. A research by Gümüş & Aydinbelge (2020)
92 demonstrated that pre-warming LA decreases injection discomfort. In a similar context,

93 Palanivel et al., (2020) revealed that buffered LA caused the least discomfort during
94 administration.

95 Since there is sporadic literature comparing the efficacy of preheated, buffered, and
96 conventional LA on adult population, the present double-blinded randomized clinical study
97 was designed aiming to evaluate the pulpal anesthesia and injection pain using IANB with
98 pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible
99 pulpitis. The null hypothesis was that there is no difference in efficacy of pulpal anesthesia
100 and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in
101 teeth with symptomatic irreversible pulpitis

102

103 **Materials and Method**

104 **Study design, Ethical Approval, and Clinical Trial Registry.**

105 This double-blind randomized clinical study was approved by the Sumandeep Vidyapeeth
106 Institutional Ethics Committee (SVIEC/ON/DentBNPG18/D19047; date of approval
107 22/11/2019), India. The protocol was developed and registered at the clinical trial registry of
108 India (CTRI/2020/09/027796). The current superiority trial was reported according to
109 Consolidated Standards of Reporting Trials (CONSORT) guidelines (Schulz et al., 2010).
110 Written informed consent was obtained from all participants in this study.

111

112 **Sample size.**

113 In a one-way ANOVA study, sample sizes of minimum 60, 60 and 60 were obtained
114 from the 3 groups whose means were compared. The total sample of 180 subjects achieves
115 80% power to detect differences among the means versus the alternative of equal means
116 using an F test with a 0.05000 significance level. The size of the variation in the means is
117 represented by their standard deviation which is 30.0 the common standard deviation within a
118 group is assumed to be 1.13. Between group, one way analysis of variance with multiple
119 comparison test at 5% level. Sample size formula used was:

120 $(Z_{\alpha} + Z_{\beta})^2 \cdot \text{Sqrt}(n \cdot \delta^2 / 2kS^2)$,

121 where $Z_{\alpha}=1.96$, $Z_{\beta}=0.84$, $n=$ total number of groups=3, $\delta=$ mean difference=30.0,
122 $k=$ degrees of freedom= $n-1=2$, $S=$ Standard Deviation= 1.13.

123 However number of patients enrolled in the study were 252 divided into in following
124 three groups: (A) preheated 2% lignocaine, (n = 84); (B) buffered local anesthesia, (n = 80);
125 and (C) conventional 2% lignocaine, (n = 88).

126 **Selection criteria.**

127 Patients were selected as per the *inclusion*: patients among 18 to 60 years of age with
128 mandibular hot teeth (Symptomatic irreversible pulpitis), having actively experienced
129 moderate to severe pain on a VAS scale of 5 or more were included in the study. *Exclusion*
130 *criteria*: Patients with known hypersensitivity to Lignocaine and sodium bicarbonates, who
131 had undergone cardiac surgery in the last 6 months, pregnant or lactating females, or with
132 necrosed teeth with sinus or swelling, severe periodontitis and poor oral hygiene, cracks,
133 fracture, and open apex were excluded from the study.

134

135 **Randomization and allocation concealment.**

136 A postgraduate student assessed the eligibility of five hundred and twenty-one
137 patients based on clinical examinations, radiographs, and pulp sensibility tests. Clinically
138 tooth having spontaneous/lingering pain/nocturnal pain with moderate to deep carious lesion
139 and absences of tenderness on percussion and delayed response to EPT were taken for further
140 radiographic examination. Tooth with radiolucency involving enamel, dentin, and
141 approaching pulp was selected. All the radiographs were taken with a long cone and
142 paralleling technique using a positioning indicator device. Two hundred and fifty-two
143 patients meet the selection criteria and agreed to participate in the trial. Co-investigator
144 implemented the random sequence generation and allocation concealment. Randomization
145 was done by computer randomization (<https://www.randomizer.org/>) and patients were
146 assigned into 3 groups.

147 The allocation concealment ratio was 1:1:1. This was done by inserting the LA
148 cartridges in sequentially numbered sealed opaque envelopes. The envelopes were marked
149 with the randomization code. As soon as the patient was placed in the intervention group, the
150 number was noted in the patient's case sheet and decoded at the end of the trial.

151

152 **Blinding.**

153 The entire procedure was double-blinded to avoid bias. The primary investigator and
154 the patient both were blinded to the groups allotted. The operator directly received an
155 aspirating metal syringe loaded with the cartridge of lignocaine; pre-heated lignocaine or
156 buffered lignocaine with a 27-gauge needle attached to the tip of the unit.

157

158

160 Clinical procedure.

161 Patients were sensitized to a (1 to 10-point) VAS scale. This scale was given to
162 the patient to choose thrice: the first time was before the injection,
163 second time after receiving the injection, and the third after entering the
164 pulp chamber and a pre-operative VAS score was recorded. Pre-operative pulp sensibility
165 test was recorded using EPT (Electric pulp test). The patient was explained about the test and
166 the tooth was checked first followed by the affected tooth. Patients were asked to indicate
167 when a tingling sensation occurs to him/her, and the response of the affected tooth was noted
168 down in numbers.

169 For group A – The preparation of preheated local anesthesia was done according to
170 method described by Allen *et al.*, (2008); Davidson & Boom, (1992). A 1.8 ml cartridge of
171 commercially accessible 2% lignocaine hydrochloride with 1:80,000 adrenaline (Lignospan
172 special, Septodont Healthcare India) was placed in an (AR Heat) Composite warmer (12
173 VDC, 2000Mpa, 24W0 power supply), for 4 minutes. Two cartridges were placed in the
174 heating slot of the warmer and the thermostat is set in such a way that a temperature of 42°C
175 was obtained for the anesthetic liquid. The rubber cap of the second cartridge was removed
176 and a thermometer was used to check the temperature of the anesthetic solution, as it is
177 ascertained at 37°C (Body temp), the first 1.8 ml cartridge was administered to the patient.

178 For group B – The preparation of Buffered local anesthesia was done according to a
179 previous study (*Saatchi et al.*, 2015). The buffered local anesthetic solution has a shelf-life of
180 one week, but it was prepared fresh once every two days for maximum efficacy. Under sterile
181 conditions, 0.18 ml from a 1.8-ml cartridge of 2% Lignocaine with 1:80,000 adrenaline was
182 drawn and replaced with 0.18 ml 8.4% sodium bicarbonate using a 1 ml plastic syringe and
183 stored in the refrigerator. The cartridge was inverted five times to mix the solution. As a
184 result, no precipitation was formed. It was shaken until the solution was clear; this ensured
185 that the sodium bicarbonate was completely dissolved. The cartridge was then loaded into a
186 metal syringe and injected.

187 For group C- Preparation of conventional *group* – Conventional nerve block with
188 1.8ml of 2% lignocaine with 1:80,000 adrenaline was injected. IANB in all the three
189 experimental groups was given with a metal syringe with 27-G, a 1.5-inch needle attached to
190 a standard aspirating dental injection syringe about 1mm, and 1.8ml of the solution was

191 deposited slowly (2 minutes). Immediately after injection, VAS was used to evaluate the
192 injection pain for all the experimental groups.

193 All the patients were asked to wait for 15 minutes for the profound anesthesia to be
194 achieved. Subjective symptoms like tingling sensation, numbness of lower lip, buccal and
195 lingual periosteum on the respective side of jaw were considered, whereas objective
196 symptoms like EPT (Parkell gentel pulse vitality tester) of concerned tooth was done,
197 negative response to EPT was considered as effective anesthesia. Those patients who do not
198 showed subjective and objective symptoms were given supplementary intra-ligamentary
199 injections and were excluded from the study (Consort Flow chart).

200 Isolation was performed with the help of a rubber dam fifteen minutes after the
201 injection. Excavation of caries was done along the walls of the tooth and lastly, the pulpal
202 roof was prepared. Access cavity preparation was done with help of endo access bur to design
203 the access cavity. After entering the pulp chamber and intra-operative VAS score was
204 recorded as intra-operative reading. Further, the endodontic treatment was performed as per
205 the standard methods and protocol by the primary investigator.

206

207 **Statistical methods.**

208 The obtained data were tabulated and statistically analyzed using SPSS version 21 and
209 p-value and Chi-square Value, One Way ANOVA with Tukey's Post Hoc Test, and Paired T-
210 Test were applied. For the statistical test between the group, a one-way analysis of variance
211 with multiple comparison tests at the level of significance was set as 5%.

212

213 **Results**

214 **Demographic data.**

215 The patients enrolled in the clinical trial are presented on the CONSORT 2010 flow
216 diagram (Figure 1). Total of 252 patients were included in present study of which 11 patients
217 were dropped out as lip numbness was not achieved after 15 minutes of INAB and considered
218 as failure due to the wrong technique. So, 241 patients were included for final evaluation. Out
219 of the total enrolled patients, 119 were male, while 122 were female. The age of 41 patients
220 was between (18-25) years of age, 82 patients were between (26-36) years, 66 patients were
221 between (37- 46) years of age and the remaining 52 patients were between (47- 60) years of
222 age.

223

224

225

226 **Pre-Intra operative VAS score.**

227 The mean pre-operative pain using a 10-mm Visual Analog Scale (VAS) was 7.28
228 mm \pm 1.26 mm, for Group A. For Group B mean VAS score was 6.88 mm \pm 1.23 mm, and
229 for Group C score was 6.88 mm \pm 1.24 mm (Table 1). On comparing the means of all three
230 groups no statistical difference was found in the pre-operative pain values. While the mean of
231 Intra-operative pain for Group A was 1.59 mm \pm 1.03 mm, for Group B 1.69 mm \pm 1.07mm,
232 and Group C was 3.54 mm \pm 2.34 mm. This shows that all three local anesthetic agents were
233 highly effective in reducing pain (P value $<$ 0.001).

234 Table 2 shows an inter-group comparison between all the three experimental groups
235 for the reduction in intra-operative pain, there was no statistically significant difference
236 (P=0.183) between Group A (Preheated LA) and Group B (Buffered LA). Whereas there was
237 a highly significant difference (P $<$ 0.001) between Group A (Preheated LA) - Group C
238 (Conventional LA) and between Group B (buffered LA) – Group C (Conventional LA). This
239 indicates that buffered and preheated local anesthetic solutions are more efficient in reducing
240 pain in patients with symptomatic irreversible pulpitis in comparison to conventional 2%
241 local anesthetic agents.

242

243 **Pain on injection.**

244 The mean pain on LA administration using VAS (Visual Analog Scale) for Group A
245 was 1.35 mm \pm 1.09 mm, Group B was 2.08 mm \pm 1.27 mm, and Group C was 3.19mm \pm
246 0.93 mm. Table 3 shows the mean difference between Group A and Group B was -0.73mm \pm
247 0.17mm and between Group A and Group C was -1.84mm \pm 0.17mm stating that there
248 statistically significant difference between the groups (P value $<$ 0.001). Correspondingly
249 comparing Group B with Group C showed a mean difference of -1.11 mm \pm 0.17mm and a p-
250 value of $<$ 0.001 thus indicating there was a statistically significant difference between them
251 concerning pain on injection. This shows that preheated LA showed the least pain on
252 injection followed by buffered and conventional LA.

253

254 **Discussion**

255 In the current clinical exploration, patients with symptomatic irreversible pulpitis
256 were evaluated to determine the effectiveness of inferior alveolar nerve block in relieving

257 pain using pre-heated, buffered, and standard 2% lignocaine. The study's null hypothesis was
258 rejected in light of the findings.

259 Clinical dentistry has changed from being an unpleasant and traumatic experience to
260 one that is substantially less uncomfortable and more satisfying because to the efficacious use
261 of LA. Profound anaesthesia during root canal therapy not only helps the patient but also
262 frees the dentist from worrying about unanticipated movements or reactions from the patient.
263 Patients with symptomatic irreversible pulpitis (hot tooth) and challenges with mandibular
264 teeth sometimes have trouble achieving enough anaesthetic effect (Sahu et al., 2019).
265 Therefore, amendments are suggested to increase efficacy.

266 Changing the pH and temperature of the anaesthetic solution is the most productive
267 technique to improve efficacy and lessen pain during injection, according to a clinical trial on
268 minors (Kurien et al., 2018). Warming the local anaesthetic solution to body temperature
269 (37°C) before administration seemed to lessen pain during intraoral local anaesthesia
270 administration (Aravena et al., 2018; Tirupathi & Rajasekhar, 2020) and buffered local
271 anaesthetic (Kattan et al., 2019) solutions in adult patients, according to a number of
272 randomised clinical studies and systematic reviews on prewarmed and unwarmed LA
273 solution. However, there is scant information comparing preheated, buf. So the current study
274 was created.

275 Visual Analog Score was used to assess the decrease in intra-operative pain and pre-
276 operative discomfort. Because the VAS is dependable, repeatable, and simpler for patients to
277 comprehend and record, we chose to utilise it (Hawker et al., 2011).

278 The effectiveness of IANB is often assessed by the subjective and objective
279 symptoms that patients experience after being under anaesthesia, however an electric pulp
280 tester (EPT) is a more accurate way to assess pulpal anaesthesia (Warren et al., 2017).
281 Progressive pulpal anaesthesia is defined as no response to EPT. Contrasted with the study by
282 Certosimo & Archer (1996), which demonstrated that a "no reaction" at an 80-reading
283 guaranteed pulpal anaesthesia in crucial asymptomatic teeth For a longer shelf life,
284 anaesthetic solutions sold commercially are acidic (Malamed et al., 2013). Unfortunately, the
285 LA solution's acidity has several drawbacks that affect how well it works in clinical settings,
286 so we need to modify it. Buffering local anaesthesia is one such improvement. It is made by
287 mixing 1.8ml of LA with 0.18ml of sodium bicarbonate, 8.4%, which results in the creation
288 of carbon dioxide and water (Afsal et al., 2019). Since carbon dioxide directly depresses the

289 axon, concentrates LA into the nerve trunk (ion trapping), and changes LA into an active
290 cationic state, it helps buffered LA work more effectively.

291 In patients with a hot tooth, buffering LA enhances the chance of effective anaesthesia
292 by 2.29 times, according to a systematic review by Kattan et al., (2019). Kurien et al. (2018)
293 and Saatchi et al. (2018) both endorse the same (2016). But Schellenberg et al. (2015) and
294 Hobeich et al. (2015) reported dissenting findings (2013). Different populations involved,
295 non-standard buffering approaches, varying injection methodologies, and various assessment
296 techniques can all lead to variances (Palanivel et al., 2020).

297 Pre-heating local anaesthetic at 42 °C is another method for increasing LA
298 effectiveness in inflamed pulp (Afsal et al., 2019). By blocking sodium channels,
299 conventional LA prevents a change in the nerve impulse's course of propagation. By
300 increasing membrane fluidity, which makes it easier for lignocaine to pass and reach the
301 effective concentration faster, and by densely expressing TRPV1 channels in trigeminal
302 tissue, warming at 42°C aids in faster blockage of the sodium channels (Afsal et al., 2019).
303 According to Alonso et al. (1993), there was a negative correlation between temperature and
304 pain, with 10°C having the greatest mean pain level and the following temperatures: 18°C,
305 37°C, and 42°C. In order to prevent any negative reactions from happening to the oral tissue,
306 pre-heated LA was administered at 37°C, or at the physiological tissue pH. According to
307 Davidson & Boom (1992), subcutaneous infusion of LA at body temperature (37°C) lowers
308 pain severity after minor oral surgery.

309 In this investigation, the warmed group's intra-operative agony was much lower than
310 it was in the traditional LA group. There were no significant differences between pre-warmed
311 and traditional LA, which was in contrast to Ram et al. (2002) but in conformity with
312 Tirupathi & Rajasekhar (2020) and Aravena et al. (2018). The modified Behavioral Pain
313 Scale (BPS), which is difficult to comprehend, was employed as the evaluation criterion,
314 which may have contributed to the disparity between the research populations. The secondary
315 result of pain during injection was investigated, and preheated and buffered 2% lignocaine
316 was shown to cause the least discomfort. This finding was consistent with a clinical
317 investigation by Gümüş & Aydinbelge (2020).

318 The study's shortcoming is that just one concentration of sodium bicarbonate (8.4%)
319 was utilised to buffer LA; more research carried out using different concentrations is

320 warranted. The same research design must be used to analyse patients with systemic disorders
321 (such as hypertension, diabetes mellitus, and other systemic illnesses).

322

323 **Conclusions**

324 Considering the limitations of the study, we would like to conclude that preheated,
325 buffered, and conventional local anesthesia was effective in reducing pain in symptomatic
326 irreversible pulpitis. When compared to standard LA, warmed and buffered LA was more
327 successful in reducing intraoperative discomfort. Preheated local anaesthetics and buffered
328 local anaesthetics caused the least amount of discomfort during administration, but the
329 standard group caused higher pain. Future RCTs with a larger sample size will be beneficial
330 to confirm the findings.

331

332 **Acknowledgments**

333 The authors extend their appreciation to the Deanship of Scientific research at King Khalid
334 University, Abha, Saudi Arabia for their support through the Short Research Project under
335 grant number (RGP-1/347/43).

336

337 **ADDITIONAL INFORMATION AND DECLARATIONS**

338 **Funding**

339 The authors received no funding for this work.

340

341 **Competing Interests**

342 The authors deny any conflict of interest.

343

344 **Author Contributions**

345 Namita Gandhi and Nimisha Shah conceived and designed the experiments, performed the
346 experiments, analyzed the data, prepared figures and/or tables, prepared the draft of the
347 manuscript, and approved the final draft.

348 Dian Agustin Wahjuningrun, Sweetly Purnomo, Suraj Arora, and Ajinkya M. Pawar
349 performed a pre-proof reading and editing of the manuscript.

350 Riana S. Nooshian helped in formatting the manuscript according to the journal style.

351

352 **Data Availability Statement**

353 The data of study can be obtained at clinical trial registry of India (www.ctri.nic.in/
354 CTRI/2020/09/027796).

355 **References**

- 356 Afsal MM., Khatri A., Kalra N., Tyagi R., Khandelwal D. 2019. Pain perception and efficacy
357 of local analgesia using 2% lignocaine, buffered lignocaine, and 4% articaine in
358 pediatric dental procedures. *Journal of Dental Anesthesia and Pain Medicine* 19:101.
359 DOI: 10.17245/jdapm.2019.19.2.101.
- 360 Allen MJ., Bunce C., Presland AH. 2008. The effect of warming local anaesthetic on the pain
361 of injection during sub-tenon's anaesthesia for cataract surgery. *Anaesthesia* 63:276–
362 278. DOI: 10.1111/j.1365-2044.2007.05351.x.
- 363 Alonso PE., Perula LA., Rioja LF. 1993. Pain-temperature relation in the application of local
364 anaesthesia. *British Journal of Plastic Surgery* 46:76–78. DOI: 10.1016/0007-
365 1226(93)90070-r.
- 366 Aravena PC., Barrientos C., Troncoso C., Coronado C., Sotelo-Hitschfeld P. 2018. Effect of
367 warming anesthetic on pain perception during dental injection: A split-mouth
368 randomized clinical trial. *Local and Regional Anesthesia* Volume 11:9–13. DOI:
369 10.2147/lra.s147288.
- 370 Aulestia-Viera PV., Braga MM., Borsatti MA. 2018. The effect of adjusting the ph of local
371 anaesthetics in Dentistry: A systematic review and meta-analysis. *International*
372 *Endodontic Journal* 51:862–876. DOI: 10.1111/iej.12899.
- 373 Badrian H., Modaresi J., Davoudi A., Sabzian R. 2016. Irreversible pulpitis and achieving
374 profound anesthesia: Complexities and managements. *Anesthesia: Essays and*
375 *Researches* 10:3. DOI: 10.4103/0259-1162.164675.
- 376 Bhalla VK., Taneja S., Chockattu SJ. 2021. Failure of molar anesthesia in endodontics: A
377 systematic review. . *Saudi Endodontic Journal* 11:283–291.
- 378 Certosimo AJ., Archer RD. 1996. A clinical evaluation of the electric pulp tester as an
379 indicator of local anesthesia. . *Operative Dentistry* 21:25–30.
- 380 CLAFFEY E., READER A., NUSSTEIN J., BECK M., WEAVER J. 2004. Anesthetic
381 efficacy of articaine for inferior alveolar nerve blocks in patients with irreversible
382 pulpitis. *Journal of Endodontics* 30:568–571. DOI:
383 10.1097/01.don.0000125317.21892.8f.
- 384 Davidson JA., Boom SJ. 1992. Warming lignocaine to reduce pain associated with
385 injection. *BMJ* 305:617–618. DOI: 10.1136/bmj.305.6854.617.

- 386 Gümüş H., Aydinbelge M. 2019. Evaluation of effect of warm local anesthetics on pain
387 perception during dental injections in children: A split-mouth randomized clinical
388 trial. *Clinical Oral Investigations* 24:2315–2319. DOI: 10.1007/s00784-019-03086-6.
- 389 Hawker GA., Mian S., Kendzerska T., French M. 2011. Measures of adult pain: Visual
390 Analog Scale for pain (Vas Pain), numeric rating scale for pain (NRS Pain), McGill
391 Pain Questionnaire (MPQ), short-form mcgill pain questionnaire (SF-MPQ), chronic
392 pain grade scale (CPGS), short form-36 bodily pain scale (SF. *Arthritis Care &*
393 *Research* 63. DOI: 10.1002/acr.20543.
- 394 Hobeich P., Simon S., Schneiderman E., He J. 2013. A prospective, randomized, double-
395 blind comparison of the injection pain and anesthetic onset of 2% lidocaine with
396 1:100,000 epinephrine buffered with 5% and 10% sodium bicarbonate in maxillary
397 infiltrations. *Journal of Endodontics* 39:597–599. DOI: 10.1016/j.joen.2013.01.008.
- 398 Hogan M-E., vanderVaart S., Perampaladas K., Machado M., Einarson TR., Taddio A. 2011.
399 Systematic Review and meta-analysis of the effect of warming local anesthetics on
400 injection pain. *Annals of Emergency Medicine* 58. DOI:
401 10.1016/j.annemergmed.2010.12.001.
- 402 Kattan S., Lee S-M., Hersh EV., Karabucak B. 2019. DO buffered local anesthetics provide
403 more successful anesthesia than nonbuffered solutions in patients with pulpally
404 involved teeth requiring dental therapy? *The Journal of the American Dental*
405 *Association* 150:165–177. DOI: 10.1016/j.adaj.2018.11.007.
- 406 Kurien RS., Goswami M., singh S. 2018. Comparative evaluation of anesthetic efficacy of
407 warm, buffered and conventional 2% lignocaine for the success of inferior alveolar
408 nerve block (IANB) in mandibular primary molars: A randomized controlled clinical
409 trial. *Journal of Dental Research, Dental Clinics, Dental Prospects* 12:102–109. DOI:
410 10.15171/joddd.2018.016.
- 411 Malamed SF., Tavana S., Falkel M. 2013. Faster onset and more comfortable injection with
412 alkalized 2% lignocaine with adrenaline 1:100,000. *Compendium of Continuing*
413 *Education in Dentistry* 34:10–20.
- 414 Meechan JG. 1999. How to overcome failed local anaesthesia. *British Dental*
415 *Journal* 186:15–20. DOI: 10.1038/sj.bdj.4800006.
- 416 Nagendrababu V., Duncan HF., Whitworth J., Nekoofar MH., Pulikkotil SJ., Veettil SK.,
417 Dummer PM. 2019. Is articaine more effective than lidocaine in patients with
418 irreversible pulpitis? an Umbrella Review. *International Endodontic Journal* 53:200–
419 213. DOI: 10.1111/iej.13215.
- 420 Palanivel I., Ramakrishnan K., Narayanan V., Gurram P. 2020. A prospective, randomized,
421 double-blinded, cross over comparison of buffered versus non-buffered 2% lidocaine
422 with 1:80,000 adrenaline for dental extraction. *International Journal of Applied*
423 *Dental Sciences* 6:35–38.
- 424 Potočnik I., Bajrović F. 1999. Failure of inferior alveolar nerve block in endodontics. *Dental*
425 *Traumatology* 15:247–251. DOI: 10.1111/j.1600-9657.1999.tb00782.x.

- 426 Powell MF. 1987. *Pharmaceutical Research* 04:42–45. DOI: 10.1023/a:1016477810629.
- 427 Queiroz AM., Carvalho AB., Censi LL., Cardoso CL., Leite-Panissi CR., Silva RA.,
 428 Carvalho FK., Nelson-Filho P., Silva LA. 2015. Stress and anxiety in children after the
 429 use of computerized dental anesthesia. *Brazilian Dental Journal* 26:303–307. DOI:
 430 10.1590/0103-6440201300211.
- 431 Ram D., Hermida LB., Peretz B. 2002. A comparison of warmed and room-temperature
 432 anesthetic for local anesthesia in children. *Pediatric Dentistry* 24:333–336.
- 433 Saatchi M., Khademi A., Baghaei B., Noormohammadi H. 2015. Effect of sodium
 434 bicarbonate-buffered lidocaine on the success of inferior alveolar nerve block for teeth
 435 with symptomatic irreversible pulpitis: A prospective, randomized double-blind
 436 study. *Journal of Endodontics* 41:33–35. DOI: 10.1016/j.joen.2014.09.011.
- 437 Sahu S., Kabra P., Choudhary E. 2019. Hot Tooth - A Challenge to
 438 Endodontists. *International Journal of Science and Research* 8:106–109.
- 439 Schellenberg J., Drum M., Reader A., Nusstein J., Fowler S., Beck M. 2015. Effect of
 440 buffered 4% lidocaine on the success of the inferior alveolar nerve block in patients
 441 with symptomatic irreversible pulpitis: A prospective, randomized, double-blind
 442 study. *Journal of Endodontics* 41:791–796. DOI: 10.1016/j.joen.2015.02.022.
- 443 Schulz KF., Altman DG., Moher D. 2010. Consort 2010 statement: Updated guidelines for
 444 reporting parallel group randomised trials. *Journal of Pharmacology and*
 445 *Pharmacotherapeutics* 1:100–107. DOI: 10.4103/0976-500x.72352.
- 446 Tirupathi SP., Rajasekhar S. 2020. Effect of warming local anesthesia solutions before
 447 Intraoral Administration in dentistry: A systematic review. *Journal of Dental*
 448 *Anesthesia and Pain Medicine* 20:187. DOI: 10.17245/jdapm.2020.20.4.187.
- 449 Warren VT., Fisher AG., Rivera EM., Saha PT., Turner B., Reside G., Phillips C., White RP.
 450 2017. Buffered 1% lidocaine with epinephrine is as effective as non-buffered 2%
 451 lidocaine with epinephrine for mandibular nerve block. *Journal of Oral and*
 452 *Maxillofacial Surgery* 75:1363–1366. DOI: 10.1016/j.joms.2016.12.045.
- 453 Wells JE., Bingham V., Rowland KC., Hatton J. 2007. Expression of nav1.9 channels in
 454 human dental pulp and trigeminal ganglion. *Journal of Endodontics* 33:1172–1176.
 455 DOI: 10.1016/j.joen.2007.05.023.
- 456 Yadav S. 2015. Anesthetic success of supplemental infiltration in mandibular molars with
 457 irreversible pulpitis: A systematic review. *Journal of Conservative Dentistry* 18:182.
 458 DOI: 10.4103/0972-0707.157238.
- 459

Evaluation of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis—a randomized clinical study

Namita Gandhi¹, Nimisha Shah¹, Dian Agustin Wahjuningrum², Sweetly Purnomo², Riana Nooshian³, Suraj Arora⁴ and Ajinkya M. Pawar³

¹ Department of Conservative Dentistry and Endodontics, K M Shah Dental College and Hospital, Sumandeep Vidyapeeth, Vadodara, Gujarat, India

² Department of Conservative Dentistry, Faculty of Dental Medicine, Universitas Airlangga, Surabaya City, East Java, Indonesia

³ Department of Conservative Dentistry and Endodontics, Nair Hospital Dental College, Mumbai, Maharashtra, India

⁴ Department of Restorative Dental Sciences, College of Dentistry, King Khalid University, Abha, Saudi Arabia

ABSTRACT

Background. The efficacy of 2% lignocaine is reduced in a hot tooth. Local aesthetic agents can be preheated and buffered to increase their effectiveness. The present investigation was carried out due to limited information concerning adult patients with symptomatic irreversible pulpitis in mandibular teeth.

Methods. A total of 252 individuals were included in the clinical trial in accordance with the selection criteria only after clinical study was registered with the Clinical Trial Registry of India (CTRI/2020/09/027796). Scores on the visual analog scale (VAS) and electric pulp test (EPT) on a 1–10 scale were recorded prior to the commencement of therapy. In this double-blinded study, patients were randomly divided by a co-investigator using computer randomisation (www.randomizer.org) into three groups, group A: inferior alveolar nerve blocks (IANB) with 2% lignocaine preheated at 42 °C (injected at 37 °C) ($N = 84$), group B: IANB of 2% lignocaine buffered with 0.18 ml of 8.4% sodium bicarbonate ($N = 80$) and group C: 2% lignocaine ($N = 88$). Excluding the dropouts of individuals ($n = 11$), wherein the anaesthesia failed, a total of 241 people were finally assessed 15 minutes after profound anaesthesia, endodontic access, and intraoperative pain were quantified using VAS. Pain on injection for all three groups was recorded immediately after IANB with VAS. The analysis was performed using one way ANOVA with Tukey's post hoc test and Paired T-Test using SPSS version 21.

Results. Preheated, Buffered, and conventional 2% lignocaine showed statistically significant reduction in intraoperative pain ($P < 0.001$) compared to pre-operative but on inter-group comparison preheated and buffered showed highly significant pain reduction compared with conventional 2% lignocaine ($P < 0.001$).

Conclusions. Warm and buffered local anaesthetic (LA) were effective in reducing intraoperative discomfort than conventional LA. Preheated local anesthetics caused the

Submitted 16 May 2022
Accepted 14 September 2022
Published 19 October 2022

Corresponding authors
Dian Agustin Wahjuningrum, dian-agustin-w@fkg.unair.ac.id
Ajinkya M. Pawar, ajinkya@drpawars.com

Academic editor
Luca Testarelli

Additional Information and
Declarations can be found on
page 10

DOI 10.7717/peerj.14187

© Copyright
2022 Gandhi et al.

Distributed under
Creative Commons CC-BY 4.0

OPEN ACCESS

least pain, followed by buffered local anesthetics, while conventional local anesthetics caused the most pain.

Subjects Anesthesiology and Pain Management, Clinical Trials, Dentistry, Drugs and Devices

Keywords Buffered, Local anesthesia, Pre-warm, Irreversible pulpitis, Endodontics

INTRODUCTION

In order to minimise discomfort during different dental, endodontic, and minor surgical treatments, local anaesthetic (LA) is necessary (Queiroz *et al.*, 2015). In the majority of patients, it is challenging to achieve enough anaesthetic success for a “hot” tooth. According to the literature, inferior alveolar nerve blocks (IANB) using lignocaine in mandibular posterior teeth had a failure rate of 44%–81% (Claffey *et al.*, 2004; Potočnik & Bajrović, 1999). There are a number of causes, including local tissue acidosis brought on by the production of lactic acid and its by-products, hyperalgesia offered on by inflamed pulp, and a lower resting membrane potential, but the most widely accepted theory is that tetrodotoxin-resistant sodium channels are to penalise (TTXr). Lignocaine makes it four times harder for these channels to close, and inflammation doubles the production of these molecules (Wells *et al.*, 2007; Badrian *et al.*, 2016).

Changes in injection method (Meechan, 1999), supplemental anaesthesia techniques (Yadav, 2015; Bhalla, Taneja & Chockattu, 2021), changes in anaesthetic liquid, etc. (Nagendrababu *et al.*, 2019) are a few of the approaches utilised to increase the success rate of IANB in hot teeth. Lignocaine containing adrenaline usually have a pH range between 2.9–4.4 (Malamed, Tavana & Falkel, 2013). This pH is recommended to prolong the shelf life and to prevent oxidation of LA, but at the same time it shows reduction in its efficacy, burning sensation, slow anesthesia onset.

When used for mandibular or maxillary anaesthesia, elevating the pH of lignocaine by neutralising it with 8.4% sodium bicarbonate accelerates the dissociation rate and increases the concentration of uncharged base ions crossing the nerve membrane (Kattan *et al.*, 2019).

Warming LA to 42 °C is another effective way to boost its effectiveness (Aravena *et al.*, 2018; Tirupathi & Rajasekhar, 2020; Hogan *et al.*, 2011). The LA molecule may infiltrate the nociceptor, causing sodium channels to block more promptly. This could be the result of local anaesthetics' temperature-dependent, decreasing pKa (dissociation constant) value (Allen, Bunce & Presland, 2008). According to Powell (1987), lignocaine has a pKa of 7.57 at 40 °C and 7.92 at 25 °C. As a result, warming lignocaine may expedite the initiation of local anaesthetic and enhance its effectiveness.

The speed, location, and pH of the anaesthetic solution are only a few of the many aspects of local anaesthesia delivery that might induce pain. As a result, patients get anxious and postpone away necessary surgeries. A research by Gümüş & Aydınbelge (2019) demonstrated that pre-warming LA decreases injection discomfort. In a similar context, Palanivel *et al.* (2020) revealed that buffered LA caused the least discomfort during administration.

Since there is sporadic literature comparing the efficacy of preheated, buffered, and conventional LA on adult population, the present double-blinded randomized clinical study was designed aiming to evaluate the pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis. The null hypothesis was that there is no difference in efficacy of pulpal anesthesia and injection pain using IANB with pre-heated, buffered and conventional 2% lignocaine in teeth with symptomatic irreversible pulpitis.

MATERIALS AND METHOD

Study design, ethical approval, and clinical trial registry

This double-blind randomized clinical study was approved by the Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC/ON/DentBNPG18/D19047; date of approval 22/11/2019), India. The protocol was developed and registered at the clinical trial registry of India (CTRI/2020/09/027796). The current superiority trial was reported according to Consolidated Standards of Reporting Trials (CONSORT) guidelines (Schulz, Altman & Moher, 2010). Written informed consent was obtained from all participants in this study.

Sample size

In a one-way ANOVA study, sample sizes of minimum 60, 60 and 60 were obtained from the three groups whose means were compared. The total sample of 180 subjects achieves 80% power to detect differences among the means *versus* the alternative of equal means using an F test with a 0.05 significance level. The size of the variation in the means is represented by their standard deviation which is 30.0 the common standard deviation within a group is assumed to be 1.13. Between groups, the one way analysis of variance with multiple comparison tested at 5% level. The sample size formula used was: $(Z_{\alpha} + Z_{\beta})^2 \cdot \frac{\sigma^2}{\Delta^2} \cdot \frac{1}{k}$, where $Z_{\alpha} = 1.96$; $Z_{\beta} = 0.84$; $n =$ total number of groups = 3; $\Delta =$ mean difference = 30.0; $k =$ degrees of freedom = $n - 1 = 2$; $S =$ standard deviation = 1.13.

However number of patients enrolled in the study were 252 divided into in following three groups: (A) preheated 2% lignocaine, ($n = 84$); (B) buffered local anesthesia, ($n = 80$); and (C) conventional 2% lignocaine, ($n = 88$).

Selection criteria

Patients were selected as per the inclusion: patients among 18 to 60 years of age with mandibular hot teeth (Symptomatic irreversible pulpitis), having actively experienced moderate to severe pain on a visual analog scale (VAS) scale of five or more were included in the study. Exclusion criteria: Patients with known hypersensitivity to Lignocaine and sodium bicarbonates, who had undergone cardiac surgery in the last six months, pregnant or lactating females, or with necrosed teeth with sinus or swelling, severe periodontitis and poor oral hygiene, cracks, fracture, and open apex were excluded from the study.

Randomization and allocation concealment

A postgraduate student assessed the eligibility of five hundred and twenty-one patients based on clinical examinations, radiographs, and pulp sensibility tests. Clinically tooth

having spontaneous/lingering pain/nocturnal pain with moderate to deep carious lesion and absences of tenderness on percussion and delayed response to the electric pulp test (EPT) were taken for further radiographic examination. Tooth with radiolucency involving enamel, dentin, and approaching pulp was selected. All the radiographs were taken with a long cone and paralleling technique using a positioning indicator device. Two hundred and fifty-two patients meet the selection criteria and agreed to participate in the trial. Co-investigator implemented the random sequence generation and allocation concealment. Randomization was done by computer randomization (<https://www.randomizer.org>) and patients were assigned into three groups.

The allocation concealment ratio was 1:1:1. This was done by inserting the LA cartridges in sequentially numbered sealed opaque envelopes. The envelopes were marked with the randomization code. As soon as the patient was placed in the intervention group, the number was noted in the patient's case sheet and decoded at the end of the trial.

Blinding

The entire procedure was double-blinded to avoid bias. The primary investigator and the patient both were blinded to the groups allotted. The operator directly received an aspirating metal syringe loaded with the cartridge of lignocaine; pre-heated lignocaine or buffered lignocaine with a 27-gauge needle attached to the tip of the unit.

Clinical procedure

Patients were sensitized to a (1 to 10-point) VAS scale. This scale was given to the patient to choose thrice: the first time was before the injection, second time after receiving the injection, and the third after entering the pulp chamber and a pre-operative VAS score was recorded. Pre-operative pulp sensibility test was recorded using the electric pulp test (EPT). The patient was explained about the test and the tooth was checked first followed by the affected tooth. Patients were asked to indicate when a tingling sensation occurs to him/her, and the response of the affected tooth was noted down in numbers.

For group A—The preparation of preheated local anesthesia was done according to method described by *Allen, Bunce & Presland (2008)* and *Davidson & Boom (1992)*. A 1.8 ml cartridge of commercially accessible 2% lignocaine hydrochloride with 1:80,000 adrenaline (Lignospan special, Septodont Healthcare India) was placed in a composite warmer (12 VDC, 2000Mpa, 24W0 power supply; AR Heat), for 4 min. Two cartridges were placed in the heating slot of the warmer and the thermostat is set in such a way that a temperature of 42 °C was obtained for the anesthetic liquid. The rubber cap of the second cartridge was removed and a thermometer was used to check the temperature of the anesthetic solution, as it is ascertained at 37 °C (body temp), the first 1.8 ml cartridge was administered to the patient.

For group B—The preparation of buffered local anesthesia was done according to a previous study (*Saatchi et al., 2015*). The buffered local anesthetic solution has a shelf-life of one week, but it was prepared fresh once every two days for maximum efficacy. Under sterile conditions, 0.18 ml from a 1.8-ml cartridge of 2% Lignocaine with 1:80,000 adrenaline was drawn and replaced with 0.18 ml 8.4% sodium bicarbonate using a 1 ml plastic syringe and

stored in the refrigerator. The cartridge was inverted five times to mix the solution. As a result, no precipitation was formed. It was shaken until the solution was clear; this ensured that the sodium bicarbonate was completely dissolved. The cartridge was then loaded into a metal syringe and injected.

For group C—Preparation of conventional group – Conventional nerve block with 1.8ml of 2% lignocaine with 1:80,000 adrenaline was injected. IANB in all the three experimental groups was given with a metal syringe with 27-G, a 1.5-inch needle attached to a standard aspirating dental injection syringe about 1 mm, and 1.8 ml of the solution was deposited slowly (2 min). Immediately after injection, VAS was used to evaluate the injection pain for all the experimental groups.

All the patients were asked to wait for 15 min for the profound anesthesia to be achieved. Subjective symptoms like tingling sensation, numbness of lower lip, buccal and lingual periosteum on the respective side of jaw were considered, whereas objective symptoms like EPT (Parkell Gentel Pulse vitality tester) of concerned tooth was done, negative response to EPT was considered as effective anesthesia. Those patients who do not showed subjective and objective symptoms were given supplementary intra-ligamentary injections and were excluded from the study (consort flow chart).

Isolation was performed with the help of a rubber dam fifteen minutes after the injection. Excavation of caries was done along the walls of the tooth and lastly, the pulpal roof was prepared. Access cavity preparation was done with help of endo access bur to design the access cavity. After entering the pulp chamber and intra-operative VAS score was recorded as intra-operative reading. Further, the endodontic treatment was performed as per the standard methods and protocol by the primary investigator.

Statistical methods

The obtained data were tabulated and statistically analyzed using SPSS version 21 and *p*-value and Chi-square Value, one way ANOVA with Tukey's post hoc test, and paired *t*-test were applied. For the statistical test between the group, a one-way analysis of variance with multiple comparison tests at the level of significance was set as 5%.

RESULTS

Demographic data

The patients enrolled in the clinical trial are presented on the CONSORT 2010 flow diagram (Fig. 1). Total of 252 patients were included in present study of which 11 patients were dropped out as lip numbness was not achieved after 15 min of INAB and considered as failure due to the wrong technique. So, 241 patients were included for final evaluation. Out of the total enrolled patients, 119 were male, while 122 were female. The age of 41 patients was between (18–25) years of age, 82 patients were between (26–36) years, 66 patients were between (37–46) years of age and the remaining 52 patients were between (47–60) years of age.

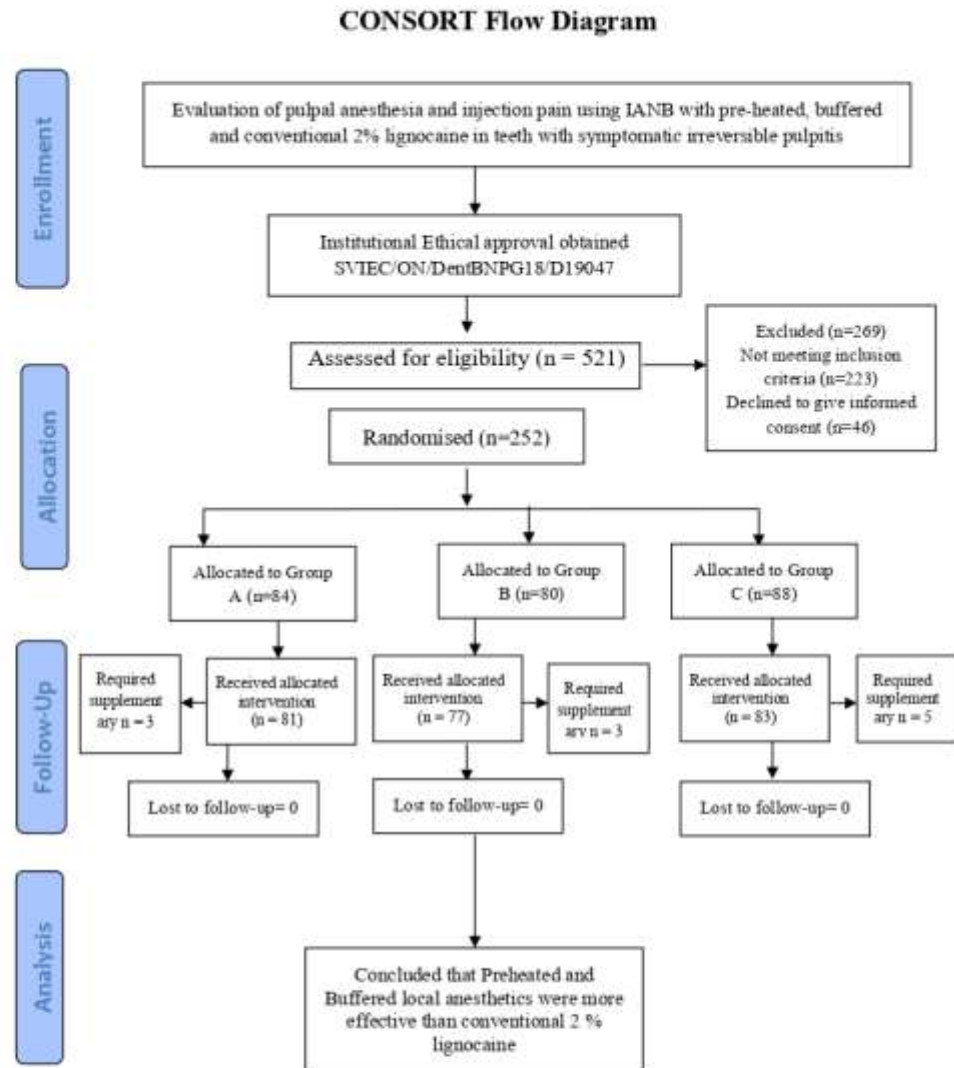


Figure 1 CONSORT 2010 flow diagram.

Full-size [DOI: 10.7717/peerj.14187/fig-1](https://doi.org/10.7717/peerj.14187/fig-1)

Pre-Intra operative VAS score

The mean pre-operative pain using a 10-mm Visual Analog Scale (VAS) was $7.28 \text{ mm} \pm 1.26 \text{ mm}$, for Group A. For Group B mean VAS score was $6.88 \text{ mm} \pm 1.23 \text{ mm}$, and for Group C score was $6.88 \text{ mm} \pm 1.24 \text{ mm}$ (Table 1). On comparing the means of all three groups no statistical difference was found in the pre-operative pain values. While the mean of Intra-operative pain for Group A was $1.59 \text{ mm} \pm 1.03 \text{ mm}$, for Group B $1.69 \text{ mm} \pm 1.07 \text{ mm}$, and Group C was $3.54 \text{ mm} \pm 2.34 \text{ mm}$. This shows that all three local anesthetic agents were highly effective in reducing pain (P value < 0.001).

Table 1 Comparison of visual analog scale (VAS) pre and post with paired *t*-test for groups after excluding the drop-outs during the clinical trial.

Groups		N = 241	Mean	Std. deviation	Mean difference	<i>t</i> -value	<i>p</i> -value
Group A	VAS Pre	81	7.28	1.26	5.69	36.075	<0.001
	VAS Post	81	1.59	1.03			
Group B	VAS Pre	77	6.88	1.23	5.18	38.120	<0.001
	VAS Post	77	1.69	1.07			
Group C	VAS Pre	83	6.88	1.24	3.34	12.331	<0.001
	VAS Post	83	3.54	2.34			

Table 2 Comparison between the groups for vas score (pre-intra) by Tukey's post hoc test.

Dependent variable	Group	Mean difference	Std. Error	<i>p</i> -value	
VAS Difference (pre-intra)	Group-A	Group-B	0.51	0.28	0.183
		Group-C	2.35	0.28	<0.001*
	Group-B	Group-C	1.84	0.28	<0.001**

Notes.

The values marked with (* and **) exhibited significant difference.

Table 2 shows an inter-group comparison between all the three experimental groups for the reduction in intra-operative pain, there was no statistically significant difference ($P = 0.183$) between Group A (Preheated LA) and Group B (Buffered LA). Whereas there was a highly significant difference ($P < 0.001$) between Group A (Preheated LA)—Group C (Conventional LA) and between Group B (buffered LA)—Group C (Conventional LA). This indicates that buffered and preheated local anesthetic solutions are more efficient in reducing pain in patients with symptomatic irreversible pulpitis in comparison to conventional 2% local anesthetic agents.

Pain on injection

The mean pain on LA administration using VAS (Visual Analog Scale) for Group A was $1.35 \text{ mm} \pm 1.09 \text{ mm}$, Group B was $2.08 \text{ mm} \pm 1.27 \text{ mm}$, and Group C was $3.19 \text{ mm} \pm 0.93 \text{ mm}$. **Table 3** shows the mean difference between Group A and Group B was $-0.73 \text{ mm} \pm 0.17 \text{ mm}$ and between Group A and Group C was $-1.84 \text{ mm} \pm 0.17 \text{ mm}$ stating that there statistically significant difference between the groups (P value < 0.001). Correspondingly comparing Group B with Group C showed a mean difference of $-1.11 \text{ mm} \pm 0.17 \text{ mm}$ and a p -value of < 0.001 thus indicating there was a statistically significant difference between them concerning pain on injection. This shows that preheated LA showed the least pain on injection followed by buffered and conventional LA.

DISCUSSION

In the current clinical exploration, patients with symptomatic irreversible pulpitis were evaluated to determine the effectiveness of inferior alveolar nerve block in relieving pain

Table 3 Comparison between the groups for pain on injection (VAS SCORE).

Dependent variable	Group		Mean difference	Std. Error	p-value
Pain on injection	Group-A	Group-B	-0.73	0.17	<0.001
		Group-C	-1.84	0.17	<0.001
	Group-B	Group-C	-1.11	0.17	<0.001

Notes.

P values 0.05 are correlated with significant difference.

using pre-heated, buffered, and standard 2% lignocaine. The study's null hypothesis was rejected in light of the findings.

Clinical dentistry has changed from being an unpleasant and traumatic experience to one that is substantially less uncomfortable and more satisfying because to the efficacious use of LA. Profound anaesthesia during root canal therapy not only helps the patient but also frees the dentist from worrying about unanticipated movements or reactions from the patient. Patients with symptomatic irreversible pulpitis (hot tooth) and challenges with mandibular teeth sometimes have trouble achieving enough anaesthetic effect (Sahu, Kabra & Choudhary, 2019). Therefore, amendments are suggested to increase efficacy.

Changing the pH and temperature of the anaesthetic solution is the most productive technique to improve efficacy and lessen pain during injection, according to a clinical trial on minors (Kurien, Goswami & Singh, 2018). Warming the local anaesthetic solution to body temperature (37 °C) before administration seemed to lessen pain during intraoral local anaesthesia administration (Aravena et al., 2018; Tirupathi & Rajasekhar, 2020) and buffered local anaesthetic (Kattan et al., 2019) solutions in adult patients, according to a number of randomised clinical studies and systematic reviews on prewarmed and unwarmed LA solution. However, there is scant information comparing preheated, buf. So the current study was created.

The Visual Analog Score was used to assess the decrease in intra-operative pain and pre-operative discomfort. Because the VAS is dependable, repeatable, and simpler for patients to comprehend and record, we chose to utilise it (Hawker et al., 2011).

The effectiveness of IANB is often assessed by the subjective and objective symptoms that patients experience after being under anaesthesia, however an electric pulp tester (EPT) is a more accurate way to assess pulpal anaesthesia (Warren et al., 2017). Progressive pulpal anaesthesia is defined as no response to EPT. Contrasted with the study by Certosimo & Archer (1996), which demonstrated that a "no reaction" at an 80-reading guaranteed pulpal anaesthesia in crucial asymptomatic teeth For a longer shelf life, anaesthetic solutions sold commercially are acidic (Malamed, Tavana & Falke, 2013). Unfortunately, the LA solution's acidity has several drawbacks that affect how well it works in clinical settings, so we need to modify it. Buffering local anaesthesia is one such improvement. It is made by mixing 1.8 ml of LA with 0.18 ml of sodium bicarbonate, 8.4%, which results in the creation of carbon dioxide and water (Afsal et al., 2019). Since carbon dioxide directly depresses the axon, concentrates LA into the nerve trunk (ion trapping), and changes LA into an active cationic state, it helps buffered LA work more effectively.

In patients with a hot tooth, buffering LA enhances the chance of effective anaesthesia by 2.29 times, according to a systematic review by *Kattan et al. (2019)*. *Kurien, Goswami & Singh (2018)* and *Saatchi et al. (2018)* both endorse the same. However, *Schellenberg et al. (2015)* and *Hobeich et al. (2013)* reported dissenting findings. Different populations involved, non-standard buffering approaches, varying injection methodologies, and various assessment techniques can all lead to variances (*Palanivel et al., 2020*).

Pre-heating local anaesthetic at 42 °C is another method for increasing LA effectiveness in inflamed pulp (*Afsal et al., 2019*). By blocking sodium channels, conventional LA prevents a change in the nerve impulse's course of propagation. By increasing membrane fluidity, which makes it easier for lignocaine to pass and reach the effective concentration faster, and by densely expressing TRPV1 channels in trigeminal tissue, warming at 42 °C aids in faster blockage of the sodium channels (*Afsal et al., 2019*). According to *Alonso, Perula & Rioja (1993)*, there was a negative correlation between temperature and pain, with 10 °C having the greatest mean pain level and the following temperatures: 18 °C, 37 °C, and 42 °C. In order to prevent any negative reactions from happening to the oral tissue, pre-heated LA was administered at 37 °C, or at the physiological tissue pH. According to *Davidson & Boom (1992)*, subcutaneous infusion of LA at body temperature (37 °C) lowers pain severity after minor oral surgery.

In this investigation, the warmed group's intra-operative agony was much lower than it was in the traditional LA group. There were no significant differences between pre-warmed and traditional LA, which was in contrast to *Ram, Hermida & Peretz (2002)* but in conformity with *Tirupathi & Rajasekhar (2020)* and *Aravena et al. (2018)*. The modified Behavioral Pain Scale (BPS), which is difficult to comprehend, was employed as the evaluation criterion, which may have contributed to the disparity between the research populations. The secondary result of pain during injection was investigated, and preheated and buffered 2% lignocaine was shown to cause the least discomfort. This finding was consistent with a clinical investigation by *Gümüş & Aydınbelge (2019)*.

The study's shortcoming is that just one concentration of sodium bicarbonate (8.4%) was utilised to buffer LA; more research carried out using different concentrations is warranted. The same research design must be used to analyse patients with systemic disorders (such as hypertension, diabetes mellitus, and other systemic illnesses).

CONCLUSIONS

Considering the limitations of the study, we would like to conclude that preheated, buffered, and conventional local anesthesia was effective in reducing pain in symptomatic irreversible pulpitis. When compared to standard LA, the warmed and buffered LA was more successful in reducing intraoperative discomfort. Preheated local anaesthetics and buffered local anaesthetics caused the least amount of discomfort during administration, but the standard group caused higher pain. Future RCTs with a larger sample size will be beneficial to confirm the findings.

ADDITIONAL INFORMATION AND DECLARATIONS

Funding

The authors received support from the Deanship of Scientific research at King Khalid University, Abha, Saudi Arabia through the Short Research Project under grant number (RGP-1/347/43). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Grant Disclosures

The following grant information was disclosed by the authors:

The Deanship of Scientific research at King Khalid University, Abha, Saudi Arabia through the Short Research Project: RGP-1/347/43.

Competing Interests

Ajinkya M. Pawar is an Academic Editor for PeerJ.

Author Contributions

- Namita Gandhi conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Nimisha Shah conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Dian Agustin Wahjuningrum performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Sweetly Purnomo performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Riana Nooshian performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, formatting the manuscript according to the journal format, and approved the final draft.
- Suraj Arora performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Ajinkya M. Pawar performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.

Human Ethics

The following information was supplied relating to ethical approvals (i.e., approving body and any reference numbers):

This double-blind randomized clinical study was approved by the Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC/ON/DentBNPG18/D19047; date of approval 22/11/2019), India.

Clinical Trial Ethics

The following information was supplied relating to ethical approvals (i.e., approving body and any reference numbers):

This double-blind randomized clinical study was approved by the Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC/ON/DentBNPG18/D19047; date of approval 22/11/2019), India.

Data Availability

The following information was supplied regarding data availability:

The raw measurements are available as a [Supplemental File](#).

Clinical Trial Registration

The following information was supplied regarding Clinical Trial registration:

CTRI/2020/09/027796.

Supplemental Information

Supplemental information for this article can be found online at <http://dx.doi.org/10.7717/peerj.14187#supplemental-information>.

REFERENCES

- Afsal MM, Khatri A, Kalra N, Tyagi R, Khandelwal D. 2019. Pain perception and efficacy of local analgesia using 2% lignocaine, buffered lignocaine, and 4% articaine in pediatric dental procedures. *Journal of Dental Anesthesia and Pain Medicine* 19:101–109 DOI 10.17245/jdapm.2019.19.2.101.
- Allen MJ, Bunce C, Presland AH. 2008. The effect of warming local anaesthetic on the pain of injection during sub-tenon's anaesthesia for cataract surgery. *Anaesthesia* 63:276–278 DOI 10.1111/j.1365-2044.2007.05351.x.
- Alonso PE, Perula LA, Rioja LF. 1993. Pain-temperature relation in the application of local anaesthesia. *British Journal of Plastic Surgery* 46:76–78 DOI 10.1016/0007-1226(93)90070-r.
- Aravena PC, Barrientos C, Troncoso C, Coronado C, Sotelo-Hitschfeld P. 2018. Effect of warming anesthetic on pain perception during dental injection: a split-mouth randomized clinical trial. *Local and Regional Anesthesia Volume* 11:9–13 DOI 10.2147/lra.s147288.
- Badrian H, Modaresi J, Davoudi A, Sabzian R. 2016. Irreversible pulpitis and achieving profound anesthesia: complexities and managements. *Anesthesia: Essays and Researches* 10:3–6 DOI 10.4103/0259-1162.164675.
- Bhalla VK, Taneja S, Chockattu SJ. 2021. Failure of molar anesthesia in endodontics: a systematic review. *Saudi Endodontic Journal* 11:283–291.
- Certosimo AJ, Archer RD. 1996. A clinical evaluation of the electric pulp tester as an indicator of local anesthesia. *Operative Dentistry* 21:25–30.
- Claffey E, Reader A, Nusstein J, Beck M, Weaver J. 2004. Anesthetic efficacy of articaine for inferior alveolar nerve blocks in patients with irreversible pulpitis. *Journal of Endodontics* 30:568–571 DOI 10.1097/01.don.0000125317.21892.8f.

- Davidson JA, Boom SJ. 1992.** Warming lignocaine to reduce pain associated with injection. *BMJ* 305:617–618 DOI 10.1136/bmj.305.6854.617.
- Gümüş H, Aydınbelge M. 2019.** Evaluation of effect of warm local anesthetics on pain perception during dental injections in children: a split-mouth randomized clinical trial. *Clinical Oral Investigations* 24:2315–2319 DOI 10.1007/s00784-019-03086-6.
- Hawker GA, Mian S, Kendzerska T, French M. 2011.** Measures of adult pain: visual Analog Scale for pain (Vas Pain), numeric rating scale for pain (NRS Pain), McGill Pain Questionnaire (MPQ), short-form mcgill pain questionnaire (SF-MPQ), chronic pain grade scale (CPGS), short form-36 bodily pain scale (SF.). *Arthritis Care & Research* 63:S240–S252 DOI 10.1002/acr.20543.
- Hobeich P, Simon S, Schneiderman E, He J. 2013.** A prospective, randomized, double-blind comparison of the injection pain and anesthetic onset of 2% lidocaine with 1:100,000 epinephrine buffered with 5% and 10% sodium bicarbonate in maxillary infiltrations. *Journal of Endodontics* 39:597–599 DOI 10.1016/j.joen.2013.01.008.
- Hogan M-E, vanderVaart S, Perampaladas K, Machado M, Einarson TR, Tad-dio A. 2011.** Systematic review and meta-analysis of the effect of warming local anesthetics on injection pain. *Annals of Emergency Medicine* 58:86–98.e1 DOI 10.1016/j.annemergmed.2010.12.001.
- Kattan S, Lee S-M, Hersh EV, Karabucak B. 2019.** DO buffered local anesthetics provide more successful anesthesia than nonbuffered solutions in patients with pulpally involved teeth requiring dental therapy? *The Journal of the American Dental Association* 150:165–177 DOI 10.1016/j.adaj.2018.11.007.
- Kurien RS, Goswami M, Singh S. 2018.** Comparative evaluation of anesthetic efficacy of warm, buffered and conventional 2% lignocaine for the success of inferior alveolar nerve block (IANB) in mandibular primary molars: a randomized controlled clinical trial. *Journal of Dental Research, Dental Clinics, Dental Prospects* 12:102–109 DOI 10.15171/joddd.2018.016.
- Malamed SF, Tavana S, Falkel M. 2013.** Faster onset and more comfortable injection with alkalized 2% lignocaine with adrenaline 1:100,000. *Compendium of Continuing Education in Dentistry* 34:10–20.
- Meehan JG. 1999.** How to overcome failed local anaesthesia. *British Dental Journal* 186:15–20 DOI 10.1038/sj.bdj.4800006.
- Nagendrababu V, Duncan HF, Whitworth J, Nekoofar MH, Pulikkotil SJ, Veettil SK, Dummer PM. 2019.** Is articaine more effective than lidocaine in patients with irreversible pulpitis? an umbrella review. *International Endodontic Journal* 53:200–213 DOI 10.1111/iej.13215.
- Palanivel I, Ramakrishnan K, Narayanan V, Gurram P. 2020.** A prospective, randomized, double-blinded, cross over comparison of buffered versus non-buffered 2% lidocaine with 1:80,000 adrenaline for dental extraction. *International Journal of Applied Dental Sciences* 6:35–38.
- Potočnik I, Bajrović F. 1999.** Failure of inferior alveolar nerve block in endodontics. *Dental Traumatology* 15:247–251 DOI 10.1111/j.1600-9657.1999.tb00782.x.
- Powell MF. 1987.** *Pharmaceutical Research* 04:42–45 DOI 10.1023/a:1016477810629.

- Queiroz AM, Carvalho AB, Censi LL, Cardoso CL, Leite-Panissi CR, Silva RA, Carvalho FK, Nelson-Filho P, Silva LA. 2015. Stress and anxiety in children after the use of computerized dental anesthesia. *Brazilian Dental Journal* 26:303–307 DOI 10.1590/0103-6440201300211.
- Ram D, Hermida LB, Peretz B. 2002. A comparison of warmed and room-temperature anesthetic for local anesthesia in children. *Pediatric Dentistry* 24:333–336.
- Saatchi M, Khademi A, Baghaei B, Noormohammadi H. 2015. Effect of sodium bicarbonate-buffered lidocaine on the success of inferior alveolar nerve block for teeth with symptomatic irreversible pulpitis: a prospective, randomized double-blind study. *Journal of Endodontics* 41:33–35 DOI 10.1016/j.joen.2014.09.011.
- Sahu S, Kabra P, Choudhary E. 2019. Hot tooth—a challenge to endodontists. *International Journal of Science and Research* 8:106–109.
- Saatchi M, Shafiee M, Khademi A, Memarzadeh B. 2018. Anesthetic efficacy of Gow-gates nerve block, inferior alveolar nerve block, and their combination in mandibular molars with symptomatic irreversible pulpitis: a prospective, randomized clinical trial. *Journal of Endodontics* 44:384–388 DOI 10.1016/j.joen.2017.10.008.
- Schellenberg J, Drum M, Reader A, Nusstein J, Fowler S, Beck M. 2015. Effect of buffered 4% lidocaine on the success of the inferior alveolar nerve block in patients with symptomatic irreversible pulpitis: a prospective, randomized, double-blind study. *Journal of Endodontics* 41:791–796 DOI 10.1016/j.joen.2015.02.022.
- Schulz KF, Altman DG, Moher D. 2010. Consort 2010 statement: updated guidelines for reporting parallel group randomised trials. *Journal of Pharmacology and Pharmacotherapeutics* 1:100–107 DOI 10.4103/0976-500x.72352.
- Tirupathi SP, Rajasekhar S. 2020. Effect of warming local anesthesia solutions before Intraoral Administration in dentistry: a systematic review. *Journal of Dental Anesthesia and Pain Medicine* 20:187–194 DOI 10.17245/jdapm.2020.20.4.187.
- Warren VT, Fisher AG, Rivera EM, Saha PT, Turner B, Reside G, Phillips C, White RP. 2017. Buffered 1% lidocaine with epinephrine is as effective as non-buffered 2% lidocaine with epinephrine for mandibular nerve block. *Journal of Oral and Maxillofacial Surgery* 75:1363–1366 DOI 10.1016/j.joms.2016.12.045.
- Wells JE, Bingham V, Rowland KC, Hatton J. 2007. Expression of nav1.9 channels in human dental pulp and trigeminal ganglion. *Journal of Endodontics* 33:1172–1176 DOI 10.1016/j.joen.2007.05.023.
- Yadav S. 2015. Anesthetic success of supplemental infiltration in mandibular molars with irreversible pulpitis: a systematic review. *Journal of Conservative Dentistry* 18:182–186 DOI 10.4103/0972-0707.157238.