mahardian rahmadi <mahardianr@ff.unair.ac.id>

[IJCP - Do Not Reply] Editorial Review

Editorial IJCP <jurnal@unpad.ac.id> Wed, Apr 8, 2020 at 10:57 AM
To: Mahardian Rahmadi <mahardianr@ff.unair.ac.id>, Indira Dhany Kharismawati <indiradhany08@gmail.com>

Dear Mrs./Ms. Indira Dhany Kharismawati,

Thank you for submitting your manuscript to Indonesian Journal of Clinical Pharmacy, entitled "Differential Effect of Timing of Antiemetic Premedication on Nausea and Vomiting after Chemotherapy for Breast Cancer".

Based on our initial editorial review, this manuscript needs some technical revising in order to conform with journal rules and guideline prior to the double blind peer-review process. Please find attached editorial review and guideline. Revised manuscript should be submitted on the website (http://jurnal.unpad.ac.id/ijcp). After logging into the site, head to your submission page (ID 26768) >> REVIEW >> Upload Author Version (at the bottom of the page), and upload your revision and other files required. Please do not making any new submission nor replying to this email to submit the revised version of this manuscript.

Please make sure that your manuscript follows our manuscript template before submitting your revised manuscript. Furthermore, your revised manuscript should be accompanied with 3 (three) administration forms (attached).

We are hoping to receive the revised manuscript and administration forms within 7 days. Should you have any questions/trouble in submitting your revised manuscript through the website, please contact us and send your manuscript via email to editorial@ijcp.or.id.

Thank you for your attention and cooperation.

Best Regards,
Managing Editor
Indonesian Journal of Clinical Pharmacy
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mahardian rahmadi <mahardianr@ff.unair.ac.id>

[IJCP - Do Not Reply] Informasi Manuskrip

1 message

Editorial IJCP <jurnal@unpad.ac.id> Tue, Apr 21, 2020 at 12:57 PM
To: Indira Dhany Kharismawati <indiradhany08@gmail.com>
Cc: Mahardian Rahmadi <mahardianr@ff.unair.ac.id>

Kepada Yth.
Ibu Indira Dhany Kharismawati

Terima kasih atas revisi manuskrip berjudul ““Differential Effect of Timing of Antiemetic Premedication on Nausea and Vomiting after Chemotherapy for Breast Cancer“ yang dikirimkan. Setelah mengevaluasi hasil revisi manuskrip ini, Editorial Team memutuskan bahwa manuskrip ini akan memasuki proses double blind peer-review. Kami akan menginformasikan kembali apabila telah terdapat hasil reviewnya, selain itu Ibu juga dapat mengetahui progres manuskrip ini melalui http://jurnal.unpad.ac.id/ijcp.
Atas perhatian dan kerjasamanya, kami ucapkan terima kasih.

Best Regards,
Managing Editor
Indonesian Journal of Clinical Pharmacy
editorial@ijcp.or.id

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Editor/Author Correspondence

Editor
2020-05-21 06:13 PM

Subject: [IJCP - Do Not Reply] Hasil Peer-Review Pertama DELETE

Kepada Yth.
Ibu Indira Dhany Kharismawati

Selamat sore,
Kami telah menerima hasil review artikel Ibu, IJCP-26768, berjudul Differential Effect of Timing of Antiemetic Premedication on Nausea and Vomiting after Chemotherapy for Breast Cancer. Dengan mempertimbangkan evaluasi Reviewer, Dewan Redaksi memutuskan bahwa artikel ini memerlukan revisi major terutama pada bagian metode. Berikut kami lampirkan poin evaluasi dari kedua reviewer dan manuskrip yang telah diberi komentar.

Hasil revisi wajib disertai dengan rebuttal letter untuk masing-masing Reviewer. Mohon hasil revisi dan rebuttal letter dapat disubmit pada website http://jurnal.unpad.ac.id/ijcp dengan cara:
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5. Selesai.

Mohon tidak membalas email ini untuk mengirimkan revisinya, sebab apabila membalas email ini secara langsung (direct reply), maka email balasan akan terkirim ke jurnal@unpad.ac.id sedangkan kami tidak dapat mengakses email tersebut. Apabila terdapat kesulitan dalam mengirimkan revisi melalui web, silakan kirimkan melalui email editorial@ijcp.or.id, atau login ke website IJCP dan klik logo surat untuk mengirimkan email melalui sistem OJS.

Demikian informasi ini kami sampaikan dan kami nantikan hasil revisi manuskrip ini.
Atas perhatian dan kerjasamanya, kami ucapkan terima kasih.

Best Regards,
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Indonesian Journal of Clinical Pharmacy

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Editor
2020-07-01 04:57 PM

Subject: [IJCP - Do Not Reply] Hasil Peer-Review Kedua DELETE

Kepada Yth.
Ibu Indira Dhany Kharismawati

Selamat sore,
Kami telah menerima hasil review kedua artikel Ibu, IJCP-26768, berjudul Differential Effect of Timing of Antiemetic Premedication on Nausea and Vomiting after Chemotherapy for Breast Cancer. Berdasarkan hasil review kedua, pada bagian Metode, Reviewer tetap menyarankan studi RCT merupakan yang paling tepat. Namun apabila penulis memutuskan untuk menggunakan studi observasional maka mohon untuk memberikan alasan yang jelas beserta referensi yang up-to-date mengenai studi tersebut. Berikut kami lampirkan poin evaluasi dari kedua reviewer dan manuskrip yang telah diberi komentar.

Hasil revisi wajib disertai dengan rebuttal letter untuk masing-masing Reviewer. Mohon hasil revisi dan rebuttal letter dapat disubmit pada website http://jurnal.unpad.ac.id/ijcp dengan cara:
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Demikian informasi ini kami sampaikan dan kami nantikan hasil revisi manuskrip ini.
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Best Regards,
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Editor
2020-10-05 10:18 AM

Subject: [IJCP - Do Not Reply] Hasil Peer-Review Ketiga DELETE

Kepada Yth.
Ibu Indira Dhany Kharismawati

Selamat pagi,
Kami telah menerima hasil review ketiga artikel Ibu, IJCP-26768, berjudul Differential Effect of Timing of Antiemetic Premedication on Nausea and Vomiting after Chemotherapy for Breast Cancer. Dengan mempertimbangkan evaluasi Reviewer, Dewan Redaksi memutuskan bahwa artikel ini dapat diterima dengan sedikit perbaikan minor (mohon meng-submit hasil revisinya). Berikut kami lampirkan poin evaluasi dari kedua reviewer dan manuskrip yang telah diberi komentar.

Mohon hasil revisi dan rebuttal letter dapat disubmit pada website

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Demikian informasi ini kami sampaikan dan kami nantikan hasil revisi manuskrip ini dalam waktu 10 hari.
Atas perhatian dan kerjasamanya, kami ucapkan terima kasih.

Best Regards,
Managing Editor
Indonesian Journal of Clinical Pharmacy

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Editor
2020-10-15 09:39 PM

Subject: [ijcp] Pemberitahuan Layak Terbit Artikel Jurnal Farmasi Klinik Indonesia DELETE

Kepada Yth.
Ibu Indira Dhany Kharismawati

Selamat malam,
Melalui email ini, kami informasikan bahwa artikel Ibu dengan nomor IJCP-26768, berjudul Differential Effect of Timing of Antiemetic Premedication on Nausea and Vomiting after Chemotherapy for Breast Cancer, telah diterima untuk dapat dipublikasikan di Jurnal Farmasi Klinik Indonesia/Indonesian Journal of Clinical Pharmacy (IJCP). Artikel Ibu selanjutnya akan memasuki proses layouting dan pemeriksaan pembuatan author proof. Kami akan segera mengirimkan author proof tersebut untuk Ibu periksa kembali.
Atas perhatian dan kerjasamanya, kami ucapkan terima kasih.

Best Regards,
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Submission

Authors	Mahardian Rahmadi, Indira D. Kharismawati, Heru Purwanto, Irvina Harini, Suharjono Suharjono, Chris Alderman
Title	Analysis of Antiemetic Premedication Administration Timing on Nausea and Vomiting Incidence among Breast Cancer Patients Receiving Chemotherapy
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Date submitted	March 31, 2020 - 04:13 PM
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Submission Metadata

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Title and Abstract

Title

Analysis of Antiemetic Premedication Administration Timing on Nausea and Vomiting Incidence among Breast Cancer Patients Receiving Chemotherapy

Abstract

The risk factors affecting chemotherapy-induced nausea and vomiting (CINV) includes antiemetic premedication time pattern, and this study investigates the capability of enhancing this in breast cancer patients receiving high emetogenic chemotherapy (HEC). Furthermore, this observational research was implemented at the oncology unit of Dr. Soetomo General Hospital Surabaya over a three-month period involving 69 female patients. The results showed unspecific antiemetic premedication timing in comparison to those with recommended timeframes, was connected with greater occurrence of both acute nausea in all cycles of chemotherapy ($p<0.05$), and acute vomiting in second and third cycles ($p<0.05$) but not in the first cycle ($p=0.49$). However, specific time administration of antiemetic treatment was linked with lower incidence of delayed nausea in all cycles ($p<0.05$), and less delayed vomiting in second and third cycles ($p<0.05$) but not in first cycle ($p=0.10$). These findings indicate specific time administration of antiemetic drugs causes significant advantages in mitigating CINV among breast cancer patients treated with emetogenic chemotherapy, and significantly lessened the occurrence of acute and delayed nausea and vomiting.

Keywords: Antiemetic premedication timing, breast cancer, CINV, nausea and vomiting

Analisis Waktu Pemberian Premedikasi Antiemetik terhadap Kejadian Mual Muntah pada Pasien Kanker Payudara yang Mendapatkan Kemoterapi

Abstrak

Kemoterapi dapat menginduksi mual muntah (*chemotherapy-induced nausea and vomiting*, CINV) yang dipengaruhi oleh beberapa faktor. Salah satu faktornya adalah waktu pemberian premedikasi antiemetik yang dapat meningkatkan kejadian CINV pada pasien kanker payudara yang menerima kemoterapi. Studi ini menganalisis waktu pemberian premedikasi antiemetik terhadap kejadian mual dan muntah yang terjadi pada pasien kanker payudara yang mendapatkan kemoterapi dengan tingkat emetogenik yang tinggi. Penelitian ini merupakan penelitian observasional prospektif dilakukan di Poli Onkologi Satu Atap RSUD Dr. Soetomo Surabaya selama periode pengambilan data tiga bulan dan melibatkan 69 wanita kanker payudara yang mendapat kemoterapi dengan tingkat emetogenik yang tinggi. Pemberian premedikasi antiemetik dengan waktu yang tidak spesifik, meningkatkan kejadian mual akut pada semua siklus dengan $p<0,05$ dan pada kejadian muntah akut pada siklus kedua dan ketiga ($p<0,05$), namun tidak pada siklus pertama kemoterapi ($p=0,49$). Pemberian premedikasi antiemetik dengan waktu spesifik dapat menurunkan kejadian mual tertunda di siklus pertama hingga ketiga ($p<0,05$) dan pada kejadian muntah tertunda pada siklus kedua dan ketiga ($p<0,05$), namun tidak pada siklus pertama ($p=0,10$). Penelitian ini memberikan bukti bahwa premedikasi antiemetik yang diberikan dengan waktu spesifik memberikan manfaat dalam mengurangi kejadian CINV yang berpotensi pada pasien kanker payudara yang mendapatkan kemoterapi dengan tingkat emetogenik tinggi.

Kata kunci: CINV, kanker payudara, mual dan muntah, waktu pemberian premedikasi antiemetik

Indexing

Keywords: Antiemetic premedication timing, breast cancer, CINV, nausea and vomiting

Language: english

Supporting Agencies

Agencies: —

References

References

Setiowati DAI, Tanggo EH, Soebijanto RI. Hubungan antara pemakaian KB hormonal dengan kejadian kanker payudara di poli onkologi satu atap RSUD Dr. Soetomo, Februari-April 2015. Indones J Cancer. 2016;10(1):11–7. doi: 10.33371/ijoc.v10i1.409

Lee HB, Han W. Unique features of young age breast cancer and its management. J Breast Cancer. 2014;17(4):301-7. doi: 10.4048/jbc.2014.17.4.301

Klein J, Tran W, Watkins E, Vesprini D, Wright FC, Hong NJL, et al. Locally advanced breast cancer treated with neoadjuvant chemotherapy and adjuvant radiotherapy: A retrospective cohort analysis. BMC Cancer. 2019;19(1):306. doi: 10.1186/s12885-019-5499-2

Rao KV, Faso A. Chemotherapy-induced nausea and vomiting: Optimizing prevention and management. Am Health Drug Benefits. 2012;5(4):232–40.

Dipiro J, Burns M, Scwinghammer T, Wells B, Malone P, Kolesar J. Pharmacotherapy principles and practice 4th Edition. New York: The McGraw-Hill Companies Inc; 2016.

Aapro M. CINV: Still troubling patients after all these years. Support Care Cancer. 2018;26(1):5–9. oi: 10.1007/s00520-018-4131-3

Hayashi T, Shimokawa M, Matsuo K, Miyoshi T, Toriyama Y, Yokota C, et al. Risk factors for delayed chemotherapy-induced nausea and vomiting with low-emetic-risk chemotherapy: A prospective, observational, multicenter study. Cancer Manag Res. 2018;10:4249–55. doi: 10.2147/CMAR.S176574

Pluzanski A, Kalinka E, Lacko A, Rubach M. Prevention of chemotherapy-induced nausea and vomiting—standards versus clinical practice. Oncol Clin Pract. 2016;12(4):153–7. doi: 10.5603/OCP.201 6.0002

Molassiotis A, Aapro M, Dicato M, Gascon P, Novoa SA, Isambert N, et al. Evaluation of risk factors predicting chemotherapy-related nausea and vomiting: Results from a European prospective observational study. J Pain Symptom Manage. 2014;47(5):839–48. doi: 10.1016/j.jpainsymman.2013.06.012

Kawazoe H, Murakami A, Yamashita M, Nishiyama K, Kobayashi K, Komatsu S, et al. Patient-related

risk factors for nausea and vomiting with standard antiemetics in patients with breast cancer receiving anthracycline-based chemotherapy: A retrospective observational study. Clin Ther. 2018;40(12):2170–9. doi: 10.1016/j.clinthera.2018.10.004

Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark RA, et al. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2017;35(28):3240–61. doi: 10.1200/JCO.2017.74.4789

Jordan K, Warr DG, Hinke A, Sun L, Hesketh PJ. Defining the efficacy of neurokinin-1 receptor antagonists in controlling chemotherapy-induced nausea and vomiting in different emetogenic settings—a meta-analysis. Support Care Cancer. 2016;24(5):1941–54. doi: 10.1007/s00520-015-2990-4

Zaidan M, Soufi L, Hafeez M, Abdelwahid M, Rasul KI. Assessing prescribing patterns for the prevention of chemotherapy-induced nausea and vomiting in the national center for cancer care and research. Saudi Pharm J. 2015;23(4):381–7. doi: 10.1016/j.jsps.2015.01.003

Bourdeanu L, Frankel P, Yu W, Hendrix G, Pal S, Badr L, et al. Chemotherapy-induced nausea and vomiting in Asian women with breast cancer receiving anthracycline-based adjuvant chemotherapy. J Support Oncol. 2012;10(4):149–54. doi: 10.1016/j.suponc.2011.10.007

Tageja N, Groninger H. Chemotherapy-induced nausea and vomiting #285. J Palliative Med. 2014;17(12):1400–2. doi: 10.1089/jpm.2014.9392

Costa AL, Abreu C, Pacheco TR, Macedo D, Sousa AR, Pulido C, et al. Prevention of nausea and vomiting in patients undergoing oral anticancer therapies for solid tumors. BioMed Res Int. 2015;2015:1–7. doi: 10.1155/2015/309601

Rapoport BL. Delayed chemotherapy-induced nausea and vomiting: pathogenesis, incidence, and current management. Frontiers Pharmacol. 2017;8:19. doi: 10.3389/fphar.2017.00019

Schwartzberg LS, McLaughlin T, Geller RB, Gabrail NY, Marks SM. Real-world efficacy: Intravenous palonosetron three-drug regimen for chemotherapy-induced nausea and vomiting with highly emetogenic chemotherapy. J Comp Eff Res. 2018;7(12):1161–70. doi: 10.2217/cer-2018-0089.

Berger MJ, Ettinger DS, Aston J, Barbour S, Bergsbaken J, Bierman PJ, et al. NCCN Guidelines Insights: Antiemesis, version 2.2017 featured updates to the NCCN guidelines. J Natl Compr Canc Netw. 2017;15(7):883–93. doi: 10.6004/jnccn.2017.0117

Corbett A, Dana W, Fuller M, Gallagher J, Golembiewski J, Gonzales J, et al. Drug information handbook with international trade names index twenty 3rd edition. United States: Wolters Kluwer Health; 2015.

Lilley L, Snyder J, Collins S. Pharmacology and the nursing process, 9th edition. USA: Elsevier Inc; 2020.

Ueda H, Shimono C, Nishimura T, Shimamoto M, Yamaue H. Palonosetron exhibits higher total control rate compared to first generation serotonin antagonists and improves appetite in delayed phase chemotherapy induced nausea and vomiting. Mol Clin Oncol. 2014;2(3):375–9. doi: 10.3892/mco.2014.263

National Cancer Institute. In: Agency BC cancer system management guidelines: Cancer Related Nausea and Vomiting 2010 [Accessed on: 12 Desember 2019]. Available at: http://www.bccancer.bc.ca/nursingsite/Documents/11.%20Nausea%20and%20Vomiting.pdf

Setyowibowo H, Purba FD, Hunfeld JA, Iskandarsyah A, Sadarjoen SS, Passchier J, et al. Quality of life and health status of Indonesian women with breast cancer symptoms before the definitive diagnosis: A comparison with Indonesian women in general. PLoS one. 2018;13(7):e0200966. doi: 10.1371/journal.pone.0200966

Phillips RS, Friend AJ, Gibson F, Houghton E, Gopaul S, Craig JV, et al. Antiemetic medication for prevention and treatment of chemotherapy-induced nausea and vomiting in childhood. Cochrane Database Syst Rev. 2016;2(2):1–100. doi: 10.1002/14651858.CD007786.pub3

Salihah N, Mazlan N, Lua PL. Chemotherapy-induced nausea and vomiting: Exploring patients' subjective experience. J Multidiscip Healthc. 2016;9:145–51. doi: 10.2147/JMDH.S97695

Lihara H, Fujii H, Yoshimi C, Yamada M, Suzuki A, Matsuhashi N, et al. Control of chemotherapy-induced nausea in patients receiving outpatient cancer chemotherapy. Int J Clin Oncol. 2016;21(2):409–18. doi: 10.1007/s10147-015-0908-2

Yap KYL, Low XH, Chan A. Exploring chemotherapy-induced toxicities through multivariate projection of risk factors: Prediction of nausea and vomiting. Toxicol Res. 2012;28(2):81–91. doi: 10.5487/TR.2012.28.2.081

Janicki P. Management of acute and delayed chemotherapy-induced nausea and vomiting: Role of netupitant–palonosetron combination. Ther Clin Risk Manag. 2016;12:693–9. doi: 10.2147/TCRM.S81126

Escobar Y, Cajaraville G, Virizuela J, Álvarez R, Muñoz A, Olariaga O, et al. Incidence of chemotherapy-induced nausea and vomiting with moderately emetogenic chemotherapy: ADVICE (Actual Data of Vomiting Incidence by Chemotherapy Evaluation) study. Support Care Cancer. 2015;23(9):2833–40. doi: 10.1007/s00520-015-2809-3

Dranitsaris G, Mazzarello S, Smith S, Vandermeer L, Bouganim N, Clemons M. Measuring the impact of guideline-based antiemetic therapy on nausea and vomiting control in breast cancer patients with multiple risk factors. Support Care Cancer. 2016;24(4):1563–9. doi: 10.1007/s00520-015-2944-x

Navari RM. Treatment of breakthrough and refractory chemotherapy-induced nausea and vomiting. Biomed Res Int. 2015;2015:595894. doi: 10.1155/2015/595894

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Terakreditasi KEMRISTEKDIKTI, SK Dirjen Penguatan Riset dan Pengembangan Kementerian Riset, Teknologi, dan Pendidikan Tinggi Republik Indonesia No.30/E/KPT/2019

Submission

Authors	Mahardian Rahmadi, Indira D. Kharismawati, Heru Purwanto, Irvina Harini, Suharjono Suharjono, Chris Alderman
Title	Analysis of Antiemetic Premedication Administration Timing on Nausea and Vomiting Incidence among Breast Cancer Patients Receiving Chemotherapy
Section	Original Research
Editor	Ajeng Diantini Editorial IJCP

Peer Review

Round 1

Review Version	26768-83773-2-RV.DOCX 2020-04-21
Initiated	2020-05-04
Last modified	2020-05-21
Uploaded file	None
Editor Version	26768-84348-1-ED.PDF 2020-04-08 26768-84348-2-ED.PDF 2020-04-14 26768-84348-3-ED.DOCX 2020-04-21 26768-84348-4-ED.PDF 2020-05-21 26768-84348-5-ED.PDF 2020-05-21 26768-84348-6-ED.PDF 2020-05-21 26768-84348-7-ED.DOCX 2020-06-12
Author Version	26768-84574-1-ED.DOCX 2020-04-11 26768-84574-2-ED.PDF 2020-04-11 26768-84574-3-ED.PDF 2020-04-11 26768-84574-4-ED.DOCX 2020-04-19 26768-84574-5-ED.PDF 2020-04-19 26768-84574-6-ED.PDF 2020-04-19 26768-84574-7-ED.DOCX 2020-06-11 26768-84574-8-ED.DOCX 2020-06-11

Round 2

Review Version	26768-83773-3-RV.DOCX 2020-06-12
Initiated	2020-06-12
Last modified	2020-06-30
Uploaded file	None
Editor Version	26768-84348-8-ED.DOCX 2020-06-12 26768-84348-9-ED.PDF 2020-07-01 26768-84348-10-ED.PDF 2020-07-01 26768-84348-11-ED.PDF 2020-07-01 26768-84348-12-ED.DOCX 2020-08-06
Author Version	26768-84574-9-ED.DOCX 2020-08-05 26768-84574-10-ED.DOCX 2020-08-05

Round 3

Review Version	26768-83773-4-RV.DOCX 2020-08-06
Initiated	2020-08-06
Last modified	2020-10-05
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Editor Decision

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SUMMARY REVIEW **EDITING**

Submission

Authors	Mahardian Rahmadi, Indira D. Kharismawati, Heru Purwanto, Irvina Harini, Suharjono Suharjono, Chris Alderman
Title	Analysis of Antiemetic Premedication Administration Timing on Nausea and Vomiting Incidence among Breast Cancer Patients Receiving Chemotherapy
Section	Original Research
Editor	Ajeng Diantini Editorial IJCP

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Poin Review Artikel

Nomor artikel	:	26768
Judul	:	Differential Effect of Timing of Antiemetic Premedication on Nausea and Vomiting after Chemotherapy for Breast Cancer

Poin Evaluasi Reviewer 1*:

Komentar umum	:	1. Studi prospektif ini sebetulnya sangat berpotensi mendapatkan informasi yang bermanfaat secara klinis, jika dilakukan dengan desain yang benar sedari awal, sebagai RCT. Karena yang akan dinilai adalah efek rentang waktu pemberian antiemetik terhadap kejadian *nausea-vomitus*, maka randomisasi dilakukan dengan mengalokasikan tiap-tiap pasien ke dalam kelompok-kelompok rentang waktu pemberian. Waktu pemberian bagi seorang pasien harus tetap sama sejak siklus 1 s/d siklus 3. Sayangnya, tidak dilakukan randomisasi dan protokol tidak dibuat secara cermat, sehingga nyata ada bias (lebih detil di Lain-lain). 2. Jenis antiemetik yang digunakan telah diketahui kurang efektif untuk HEC, padahal seluruh pasien studi ini menerima HEC. Maka, efek antiemetik yang diamati otomatis sangat rentan terhadap kesalahan interpretasi (karena efek yang kurang kuat). 3. Baseline pasien "tidak sama", karena *patient-related factors* (usia, riwayat *nausea-vomiting*, konsumsi alkohol) tidak dikontrol. 4. Dasar protokol pemberian antiemetik setidaknya mengacu tata laksana yang lazim digunakan (asosiasi dalam/luar negeri). 5. Setidaknya ada 4 jenis CINV, namun hanya *acute* & *delayed* saja yang dilaporkan (*breaktrough/anticipatory* CINV berpotensi bias). 6. Kualitas bahasa Inggris secara keseluruhan kurang baik. Hal ini akan sangat menyulitkan pembaca non-

		penutur Bahasa Indonesia, karena: a. ditulis dengan Bahasa Inggris dengan gaya tutur Bahasa Indonesia dan b. banyak kesalahan gramatikal.
Abstrak	:	-
Pendahuluan	:	Hipotesis dan tujuan studi kurang jelas.
Metode Penelitian	:	Tujuan studi seperti ini hanya dapat dicapai dengan RCT. Metode observasional saja rentan terpapar bias (lihat Lain-lain). Kriteria inklusi-eksklusi tidak jelas
Hasil	:	-
Pembahasan	:	-
Simpulan	:	-
Daftar Pustaka	:	-
Lain-lain	:	1. Fig. 1. ***Observer bias*** pada studi prospektif ini tampak jelas dari adanya perubahan bertahap (siklus 1 ke siklus 3) banyaknya pasien yang menerima antiemetik, yang bersesuaian pada rentang waktu 15-30 menit dan >120 menit. Sangat mungkin di awal studi (pasien2 masuk siklus 1), sebagian besar pasien menerima antiemetik pada >120 menit sebelum kemo. Seiring waktu (pasien masuk ke siklus 2 dan kemudian siklus 3), makin banyak pasien yang menerima antiemetik pada 15-30 menit sebelum kemo. Hal ini akan terhindarkan jika dari awal dilakukan randomisasi berdasarkan rentang waktu pemberian antiemetik, sehingga setiap pasien menerima antiemetik pada rentang waktu yang tetap sama sejak siklus 1. Kontrol terhadap faktor pasien (usia, riwayat emesis sebelumnya) juga harus dilakukan. 2. ***Recall bias***: studi ini mendasarkan informasi dari ingatan pasien. Tidak jelas kapan pasien diinterview (setiap siklus atau di akhir siklus 3 saja). Sangat mungkin pasien tidak akurat dalam informasi. 3. ***Interviewer bias***: *Interview* disebutkan dilakukan secara terstruktur, namun tidak ada informasi detil tentang bagaimana *interview* dilakukan. Terkait

	dengan *recall bias*, dapat pula terjadi *interviewer bias* karena kemungkinan pasien lupa (terutama jika baru ditanya setelah siklus 3) sangat tinggi. 4. Mengingat waktu yang diperlukan untuk studi ini <u>hanya 3 bulan dan kepentingan klinis yang tinggi,</u> sangat disarankan untuk mengulang studi ini dari awal dengan desain RCT. Konsultasi dengan pakar *clinical trial* dan komite etik yang mumpuni sangat disarankan. Konsultasi penulisan manuskrip dengan pakar bahasa Inggris klinis sangat disarankan.

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Poin Evaluasi Reviewer 2*:

Komentar umum	:	Please see comments below.
Abstrak	:	-
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Metode Penelitian	:	Method is still unclear. Please describe as e.g. ethical consideration, study design and setting, patient samples, data collection and study measure, statistical analysis
Hasil	:	Result is still unclear. 1. Please describe as patient characteristics, chemotherapy drugs vs nausea, simple or short grouping of premedication, pre-medication antiemetic timing vs emetic case. 2. The sample size in this study was small, table presentation is better than graphical presentation. 3. Please use statistical analysis for each variable or testing.
Pembahasan	:	Discussions and conclusion(s) must adjust to the method and results.
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Komentar umum	:	1. Mohon manuskrip diperbaiki sesuai saran dan komentar dari seluruh reviewer. Penulis **wajib melampirkan rebuttal letter**. Rebuttal letter berisi tanggapan (baik berupa persetujuan dari saran reviewer, jawaban atas pertanyaan reviewer, maupun sanggahan yang disertai dengan alasan mengapa penulis tidak melakukan saran perbaikan tersebut). Pada rebuttal letter dapat dibuat Tabel yg berisi 2 kolom; kolom sebelah kiri untuk pertanyaan/saran reviewer, dan kolom sebelah kanan untuk tanggapan/ sanggahan penulis disertai keterangan halaman dan baris berapa perbaikannya dilakukanpada manuskrip revisi. Rebuttal letter dibuat dalam format file **word** dan tidak disatukan dengan file word manuskrip. Mohon diperhatikan bahwa jawaban dari pertanyaan reviewer tidak hanya dibuat pada rebuttal letter saja, namun lakukan perbaikannya juga pada manuskrip. 2. Pada saat melakukan revisi pada manuskrip, bagian-bagian yang telah diperbaiki sesuai saran reviewer diberi **highlight** (dan bila perlu diberi **komentar**, contoh: “Bagian ini adalah perbaikan sesuai komentar reviewer mengenai ...”). Apabila hendak memberi komentar, sebelumnya mohon **tidak menggunakan nama asli** di username Microsoft Word (jika masih menggunakan nama asli, silakan **dihilangkan/diganti** terlebih dahulu dengan cara klik File > Options > ganti nama di Username). Mohon diperhatikan bahwa **komentar tidak digunakan** untuk menjawab pertanyaan reviewer, melainkan hanya keterangan seperti yang disebutkan di atas saja. Pertanyaan

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Research Article

DIFFERENTIAL EFFECT OF TIMING OF ANTIEMETIC PREMEDICATION ON NAUSEA AND VOMITING AFTER CHEMOTHERAPY FOR BREAST CANCER

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DIFFERENTIAL EFFECT OF TIMING OF ANTIEMETIC PREMEDICATION ON NAUSEA AND VOMITING AFTER CHEMOTHERAPY FOR BREAST CANCER

Abstract

~~Introduction:~~ Chemotherapy-induced nausea and vomiting (CINV) is influenced by risk factors; one of them is antiemetic premedication time pattern that can increase CINV incidence in breast cancer patients receiving chemotherapy. This study examined the influence of the timing of antiemetic premedication upon nausea and vomiting amongst women treated with highly emetogenic chemotherapy (HEC) for breast cancer.

Keywords: Antiemetic premedication timing, breast cancer, CINV, nausea and vomiting

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PENGARUH WAKTU PEMBERIAN PREMEDIKASI DAN KEJADIAN MUAL MUNTAH PADA PASIEN KANKER PAYUDARA YANG MENDAPATKAN KEMOTERAPI

Abstrak

~~Pendahuluan:~~ Kemoterapi dapat menginduksi mual muntah (CINV) dipengaruhi beberapa faktor. Salah satu faktornya adalah waktu pemberian premedikasi antiemetik yang dapat meningkatkan kejadian CINV pada pasien kanker payudara yang menerima kemoterapi. Studi ini menguji pengaruh waktu premedikasi antiemetik pada kejadian mual dan muntah yang terjadi pada pasien kanker payudara yang mendapatkan kemoterapi dengan tingkat emetogenik yang tinggi.

Kata kunci: Waktu pemberian premedikasi antiemetik, kanker payudara, CINV, mual dan muntah

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Introduction

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Breast cancer is one of the most common types of neoplasm affecting Indonesians, and up 50% of women affected in Indonesia have their disease diagnosed at an advanced stage[1,2]. The standard treatment for breast cancer involves the use of chemotherapy[3]. Combination chemotherapy regimens are associated with higher response rates compared to single-agent therapies but is often associated with Chemotherapy Induced Nausea and Vomiting (CINV), serious adverse effect that can negatively impact upon patients quality of life and their ability to tolerate and comply with therapy[4,5,6].Patient-related risk factors for CINV are known to include young age, female gender, a history of low alcohol intake, experience of emesis during pregnancy, previous adverse experience with chemotherapy[7,8,9.]Anthracycline-based chemotherapy is categorized as a highly emetogenic chemotherapy (HEC)[10].Some chemotherapy drugs are highly emetogenic (risk of 90% or more, such as cisplatin and doxorubicin), moderate emetic risk (30-90%, such as cyclophosphamide and epirubicin), low emetic risk (10-30%, such as paclitaxel) and minimal emetic risk (<10%, such as methotrexate)[11,12,13]. The c~~e~~ombinations of several chemotherapeutics agents can increase CINV activity. CINV prevention and treatment is prevention to against CINV and antiemetic given to patients receiving chemotherapy[7].

Chemotherapy-induced nausea and vomiting (CINV) are associated with significant deterioration in quality of life and are perceived by patients as one of the most important adverse effects associated with cancer treatment[6]. Risk factors for developing CINV can be categorized as patient or treatment-related. While there may be some variability in patient risk factors based on chemotherapy regimen, the common patient-related factors include younger age (<~~than~~ 50 years), female gender, history of motion sickness and/or pregnancy-related nausea and vomiting, lower history of alcohol use (<5 standard drinks per week), emesis with prior chemotherapy and a dosing schedule of premedication antiemetic that covers both acute and delayed emesis[7,8]. CINV can be subdivided as acute and delayed. Acute onset nausea and vomiting usually occur within a few minutes to several hours after drug administration and commonly resolves within the first 24 hours. The intensity of acute onset emesis generally peaks after 5 to 6 hours. The occurrence of acute emesis is high in younger (<50 years) women with lower ethanol use, history of motion sickness. Other factors that influence acute emesis include previous chemotherapy-related nausea and vomiting, the dosage of the emetogenic agent, and the efficacy of the antiemetic regimen. On the other hand, delayed nausea and vomiting usually occurs in the period 24 - 120 hoursafter chemotherapy[6,8].

National Comprehensive Cancer Network (NCCN) guidelines provide a classification that addresses the likelihood of CINV that is primarily related to the emetogenic potential of the specific chemotherapeutic agents used. The classification of chemotherapeutic agents is divided into 4 levels according to the percentage of patients who experience acute emesis when they do not receive antiemetic prophylaxis. These classifications include high emetic risk (more than 90% of patients experience acute emesis: e.g. anthracycline and cyclophosphamide combination, cisplatin, and cyclophosphamide ≥1500 mg/m$^{2)}$; moderate emetic risk (30-90% of patients experience acute emesis: e.g. bendamustine, carboplatin, cyclophosphamide <1500 mg/m^2, daunorubicin, doxorubicin, epirubicin, idarubicin, and ifosfamide); low emetic risk

(10-30% of patients experience acute emesis: e.g. cytarabine ≤1000 mg/m^2, docetaxel, etoposide, 5-fluorouracil, gemcitabine, methotrexate, and paclitaxel);and minimal emetic risk (fewer than 10% of patients experience acute emesis: e.g. bleomycin, fludarabine, vinblastine, vincristine, and vinorelbine)[8,13].In general, to provide maximal protection against chemotherapy induced nausea and vomiting, antiemetic therapy should be initiated before chemotherapy. The antiemetic therapy should also be continued for the same length of time as the duration of the emetic activity of the chemotherapeutic agent being used[21].The acute CINV occurs within 1 – 2 hours of chemotherapy administration and can last for up to 24 hours, the delayed CINV presents more than 24 hours until 120 hours periods after chemotherapy administration[14].The use of antiemetic premedication has reduced the incidence of vomiting substantially, but the evaluation shows that approximately 60.7% of patients still experience either acute or delayed nausea after chemotherapy[15].

In Oncolocy unit of dr. Soetomo hospital, antiemetic regimen used during highly emetogenic chemotherapy includes a 5-Hydroxytrptamine (5-HT3) receptor antagonist (ondansetron), a corticosteroid (dexamethasone), an antihistamine (diphenhydramine) and an H2 receptor antagonist (ranitidine) (Fig.1). Although this type of regimen is known to be effective in preventing nausea and vomiting induced by chemotherapy with low emetogenic potential, previous research suggests that this approach may not be effective for patients who received chemotherapy with moderate and high emetogenic levels[16]. It is known that appropriate timing of antiemetic premedication one variable that can impact upon increased occurrence of CINV. To maximize effectiveness, antiemetic administration must be timed properly and should be administered 15-30 minutes before chemotherapy[22]. The present research study has been undertaken to explore this variable.

Methods

This was a prospective observational research study investigating the effects of the timeliness of antiemetic premedication as a determinant of CINV amongst women treated for breast cancer patients with highly emetogenic chemotherapy in oncology unit in dr. Soetomo hospital Surabaya.

The participants were recruited from a convenience sample of women undergoing their first cycle of chemotherapy for breast cancer and who antiemetic premedication as antiemetic prophylaxis during the period spanning March to April 2016. The subjects were followed to the third chemotherapy cycle and underwent structured interview by a pharmacist to evaluate the response to antiemetic treatment.

Antiemetic premedication (ondansetron) was given 15-30 minutes (on time) before chemotherapy, while less than 15 minutes and more than 30 minutes was late of administration of antiemetic premedication. Then, the effect of antiemetic premedication time with incidence of nausea and vomiting was shown. It occurred during the acute and delayed using a modified form of *Morrow* assessment of nausea and emesis follow-up questionnaire[10].

The timing of the administration of antiemetic premedication was classified as on-time (15-30 minutes before chemotherapy), or late (< 15 minutes before to > 30 minutes). The incidence of nausea and vomiting that occurred during the acute and delayed time frames was assessed using a shortened Bahasa language version of the *Morrow* assessment of nausea and emesis follow-up questionnaire with NCI-CTCAE version 4.03 guideline to assess the grade of nausea and vomiting [17,18].

This study was declared ethical by the health research ethics committee of RSUD dr. Soetomo Surabaya with ethics number 100/Panke.KKE/II/2016.

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Results

During the data capture period, 72 women proceeded to receive chemotherapy, with three subjects who dropped out (one deceased, two declining interview) leaving 69 patients who proceeded to evaluation. All were women, with 17% <40 years old, 74% 40-60 years old, 9% >60 years old. A variety of chemotherapy regimens were used (refer table 1), all of which were classified as highly emetogenic. All patients received the same the same antiemetic premedication combination as shown in figure 1.

As shown in figure 2, the distribution of timing for the administration of antiemetic premedication was highly variable. The range of antiemetic premedication administration time was within 15 minutes until more than 2 hours before chemotherapy. Most of patient had late antiemetic administration, whereas only small amount of patients that had on-time administration of antiemetic premedication.

The incidence of acute and delayed CINV during cycles 1, 2 and 3-chemotherapy can be seen at figure 3 and 4. Those figure showed that with same regimen of antiemetic premedication, the antiemetic could reduce the incidence and severity of acute nausea but not delayed nausea. In the incidence of vomiting, the regimentation also could reduce the incidence and severity of both acute and delayed vomiting (the response is higher than in nausea).

The effect of antiemetic premedication timing on the incidence of acute nausea and vomiting at cycle 1, 2 and 3-chemotherapy could be seen at figure 5, 6, 7 and 8. Those figure showed that either in acute and delayed CINV, late-time administration of antiemetic premedication significantly increased the incidence of acute and delayed nausea and vomiting. Late administration of antiemetic treatment was associated with a greater prevalence of acute nausea all cycles of chemotherapy ($p < 0.05$) and with a greater prevalence of acute vomiting in cycles 2 and 3 ($p < 0.05$) but not in cycle one of chemotherapy ($p = 0.49$) . Timely administration of antiemetic treatment was associated with a lower prevalence of delayed nausea in cycles 1-3 ($p < 0.05$), as well as a lower prevalence of delayed vomiting in cycles 2-3 ($p < 0.05$) but not in cycle 1 ($p = 0.10$)

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Discussion

Breast cancer is a common malignancy in Indonesia and around the world[23]. CINV associated with cytotoxic chemotherapy in this context has a potentially major impact upon quality of life and treatment tolerability, and may impact overall treatment outcomes[6]. The use of chemotherapy that can produce nausea and vomiting, these extremely unpleasant sensations continue to be a problem despite better antiemetic [19,20]. This research has demonstrated that delayed administration of antiemetics treatment was associated with compromised antiemetic treatment efficacy, to some extent in the acute stage and more prominently in the latent phase. The effect was noted for both severity and incidence of both nausea and vomiting.These findings are similar to those seen in previous research. It has previously been observed that complete protection from acute and delayed nausea in the first cycle of chemotherapy were 60% and 45%, respectively, for high emetic risk chemotherapy and the rates were improved in the overall cycles[24].

The research findings here provide further evidence that timely administration of antiemetic drugs produces important benefits in reducing the impact of potentially debilitating CINV amongst people treated with emetogenic chemotherapy for breast cancer. The results emphasize the need to redesign workflows to improve the timeliness of antiemetic treatment provided in this setting. Possible approaches to explore could involve redesign of processes for dispensing and delivery of antiemetic drugs, more involvement from pharmacists in the processes of preparing the medications for administration (currently undertaken by nursing staff), greater education for nursing and medical staff about the importance of timely antiemetic treatment, and greater standardization of practices overall. The effects of process redesign and changes to practice should be re-assessed in future research. If more timely administration of the antiemetic drugs cannot produce a more robust response in reducing delayed phase CINV, especially in cycles after the initial treatment, it is also possible that changes to the antiemetic treatment regimen may need to be considered and evaluated.

This research study has a range of limitations. The sample size was small and some participants declined to participate. The study design did not explore or document the reasons for late or delayed administration of antiemetic treatments, and the protocol was not sufficiently powered to allow detailed exploration of the effects associated with different chemotherapy regimens. Future research studies could be designed to address these limitations and to provide additional data to explore these aspects of this clinically important issue.

Conclusions

The impact of antiemetic premedication timing is a significant influence upon the incidence of acute and delayed nausea and vomiting. This study suggests that process redesign and other approaches to increase the timeliness of antiemetic treatment may enhance protection against CINV for people treated with emetogenic chemotherapy for breast cancer, potentially improving quality of life and improving outcomes.

Acknowledgements (If any)

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Conflict of Interest

The authors did not have any conflict of interest in this research or publication.

References

1. Ministry of Health Indonesia. ***Hari Kanker Sedunia 2019***. Department of Health Indonesia. 2019.
2. American Cancer Society. *Breast Cancer Facts & Figures 2017-2018*. Atlanta: American Cancer Society, Inc. 2017.
3. Lundqvist EÅ, Fujiwara K, Seoud M. Principles of chemotherapy. International Journal of Gynecology & Obstetrics. 2015 Oct 1;131(S2).
4. Carrick S, Parker S, Thornton CE, Ghersi D, Simes J, Wilcken N. ***Single agent versus combination chemotherapy for metastatic breast cancer***. Cochrane Database of Systematic Reviews. 2009(2).
5. Chisholm-Burns MA. ***Pharmacotherapy principles & practice/editors***, Marie A. Chisholm-Burns, Terry L. Schwinghammer, Barbara G. Wells, Patrick M. Malone, Jill M. Kolesar, Joseph T. DiPiro.
6. Navari RM. ***Olanzapine for the prevention of chemotherapy-induced nausea and vomiting***. In Management of Chemotherapy-Induced Nausea and Vomiting 2016 (pp. 107-120). Adis, Cham
7. Hayashi T, Shimokawa M, Matsuo K, Miyoshi T, Toriyama Y, Yokota C, Taniguchi J, Hanada K, Tsumagari K, Okubo N, Koutake Y. ***Risk factors for delayed chemotherapy-induced nausea and vomiting with low-emetic-risk chemotherapy: a prospective, observational, multicenter study***. Cancer management and research. 2018;10:4249.
8. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology. Antiemesis. Version 2.2017. NCCN Web site http://www. nccn. org/professionals/physician_gls/pdf/antiemesis. pdf. Accessed April. 2017;14.
9. Sun YS, Zhao Z, Yang ZN, Xu F, Lu HJ, Zhu ZY, Shi W, Jiang J, Yao PP, Zhu HP. ***Risk factors and preventions of breast cancer.*** International journal of biological sciences. 2017;13(11):1387.
10. Kawazoe H, Murakami A, Yamashita M, Nishiyama K, Kobayashi-Taguchi K, Komatsu S, Aoki R, Kusakabe E, Yamasawa H, Yakushijin Y, Nakamura T. ***Patient-related Risk Factors for Nausea and Vomiting with Standard Antiemetics in Patients with Breast Cancer Receiving Anthracycline-based Chemotherapy: A Retrospective Observational Study***. Clinical therapeutics. 2018 Dec 1;40(12):2170-9.
11. Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark-Snow RA, Danso MA, Dennis K, Dupuis LL, Dusetzina SB, Eng C. ***Antiemetics: American Society of Clinical Oncology clinical practice guideline update***. Journal of Clinical Oncology. 2017 Jul 31;35(28):3240-61.

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-Online
Cashin RP, Yang M. Medications prescribed and occurrence of falls in general medicine inpatients [Accessed on: 12 Desember 2011]. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3203823/.

12. Jordan K, Warr DG, Hinke A, Sun L, Hesketh PJ. ***Defining the efficacy of neurokinin-1 receptor antagonists in controlling chemotherapy-induced nausea and vomiting in different emetogenic settings—a meta-analysis***. Supportive Care in Cancer. 2016 May 1;24(5):1941-54.
13. Roila F, Molassiotis A, Herrstedt J, Aapro M, Gralla RJ, Bruera E, Clark-Snow RA, Dupuis LL, Einhorn LH, Feyer P, Hesketh PJ. 2016. ***MASCC and ESMO guideline update for the prevention of chemotherapy-and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients***. Annals of Oncology. 2016 Sep 1;27(suppl_5):v119-33.
14. Rapoport BL. ***Delayed chemotherapy-induced nausea and vomiting: pathogenesis, incidence, and current management***. Frontiers in pharmacology. 2017 Jan 30;8:19.
15. Schwartzberg LS, McLaughlin T, Geller RB, Gabrail NY, Marks SM. ***Real-world efficacy: intravenous palonosetron three-drug regimen for chemotherapy-induced nausea and vomiting with highly emetogenic chemotherapy.*** Journal of comparative effectiveness research. 2018 Oct 11;7(12):1161-70.
16. Ranganath P, Einhorn L, Albany C. ***Management of chemotherapy induced nausea and vomiting in patients on multiday cisplatin based combination chemotherapy***. BioMed research international. 2015;2015
17. Morrow GR. ***A patient report measure for the quantification of chemotherapy induced nausea and emesis: psychometric properties of the Morrow assessment of nausea and emesis (MANE)***. The British journal of cancer. Supplement. 1992 Dec;19:S72.
18. National Cancer Institute.***CTCAE version 4.03***. In: Agency BC Cancer System Management Guidelines: Cancer Related Nausea and Vomiting 2010 (pp.3).
19. Phillips RS, Friend AJ, Gibson F, Houghton E, Gopaul S, Craig JV, Pizer B. ***Antiemetic medication for prevention and treatment of chemotherapy-induced nausea and vomiting in childhood***. Cochrane Database of Systematic Reviews. 2016(2).
20. Salihah N, Mazlan N, Lua PL. ***Chemotherapy-induced nausea and vomiting: exploring patients' subjective experience.*** Journal of multidisciplinary healthcare. 2016;9:145.
21. Costa AL, Abreu C, Pacheco TR, Macedo D, Sousa AR, Pulido C, Quintela A, Costa L. Prevention of nausea and vomiting in patients undergoing oral anticancer therapies for solid tumors. BioMed research international. 2015;2015
22. National Cancer Institute. Nausea and Vomiting (PDQ□)-Health Professional Version . 2016.http://www.cancer.gov/aboutcancer/treatment/side-effects/nausea/nausea-hp-pdq#link/_180_toc
23. Torre LA, Islami F, Siegel RL, Ward EM, Jemal A. Global cancer in women: burden and trends.
24. Lihara H, Fujii H, Yoshimi C, Yamada M, Suzuki A, Matsuhashi N, Takahashi T, Yoshida K, Itoh Y. **Control of chemotherapy-induced nausea in patients receiving outpatient cancer chemotherapy**. International journal of clinical oncology. 2016 Apr 1;21(2):409-18.

Table 1: Patient characteristics

Characteristics	Total	Percentage (%)
Age		
< 40 years	12	17
40-60 years	51	74
> 60 years	6	9
Gender		
Female	69	100
Male	0	0
Chemotherapy regimen *		
Cyclophospamide, Adriamycin, Fluorouracil	59	85
Cyclophospamide, Epirubicin, Fluorourcil	8	12
Cyclophospamide, Adriamycin	2	3
Level of emetogenic chemotherapy		
High Emetogenic Chemotherapy Moderate	69	100
Emetogenic Chemotherapy	0	0
Low Emetogenic Chemotherapy	0	0
Minimal Emetogenic Chemotherapy	0	0

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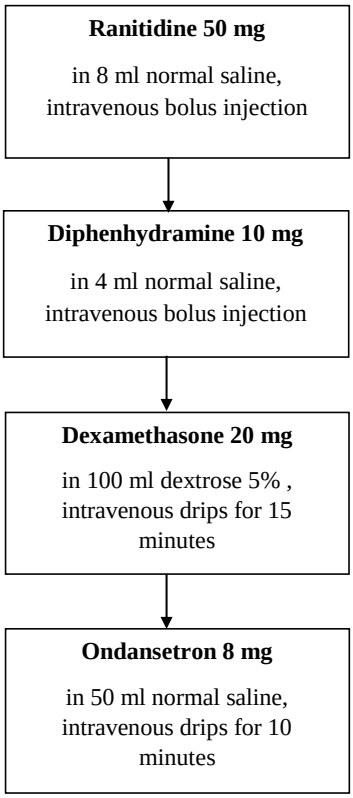

Figure 1: Antiemetic premedication Regimentation protocol in Oncology unit Dr. Sutomo Hospital

Figure 2:

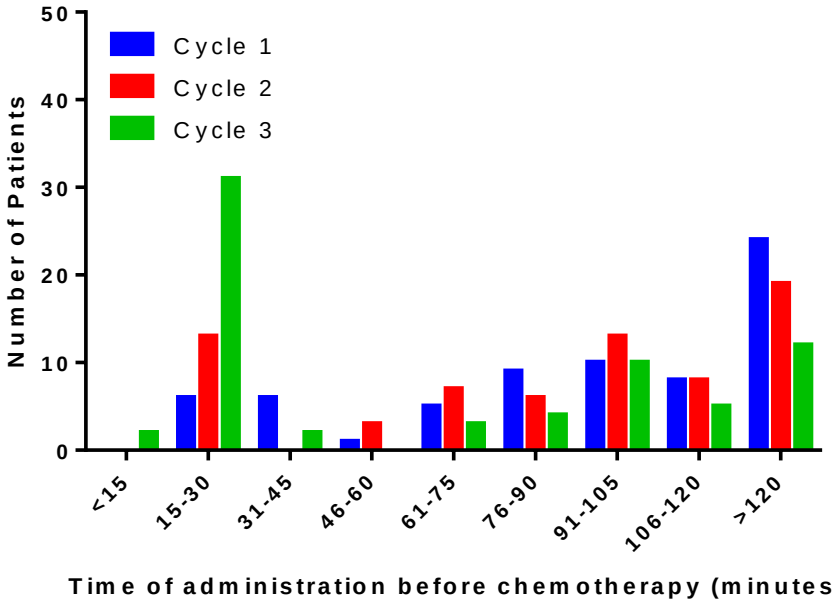

Figure 2. Profiles of antiemetic-premedication administration time among patients at chemotherapy cycle-1, -2 or -3. At cycle-1 and -2 most of the administration time were late (<15 or >30 minutes before chemotherapy), only 6 and 13 patients form 69 patients were administered on time. In addition, at cycle-3, there were 31 patients that had on time administration of antiemetic premedication.

Figure 3

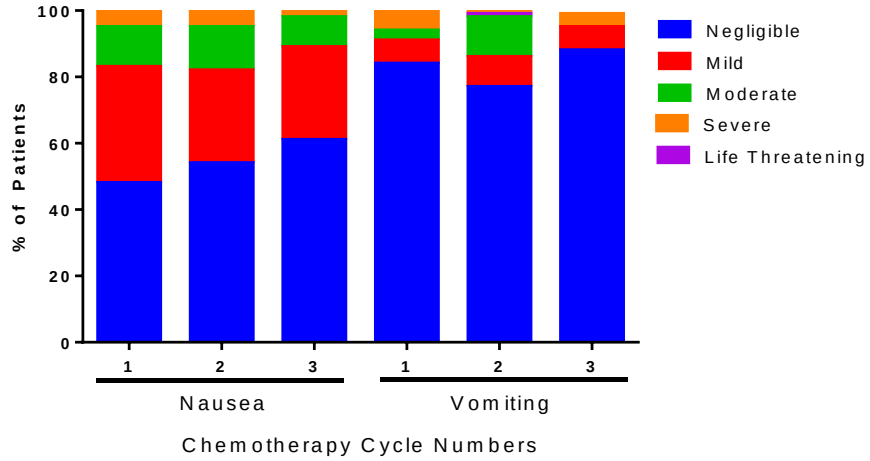

Figure 3 The incidence of acute CINV at the first, second and third cycle of chemotherapy. Among 69 patients that had high emetogenic chemotherapy procedure at cycles 1, 3 and 3, the antiemetic premedication could protect about 50 and 80 percent of the subject form acute nausea and vomiting (0-24 hours after chemotherapy), respectively. Most of incidence of nausea and vomiting were only mild and moderate. Some of patient had severe nausea and only one patient had live threatening vomiting

Figure 4

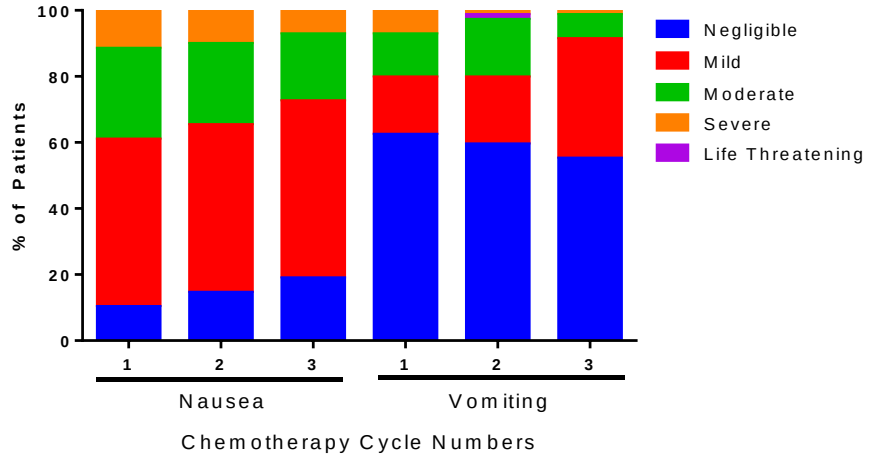

Figure 4 The incidence of delayed CINV at the first, second and third cycle of chemotherapy. Among 69 patients that had high emetogenic chemotherapy procedure at cycle one, two and three, the antiemetic premedication could protect about 15 and 55 percent of the subject form delayed nausea and vomiting (24 – 120 hours after chemotherapy), respectively. Most of incidences of nausea were mild and moderate, followed with negligible and severe nausea. Incidence of vomiting mostly negligible followed with mild and moderate.

Figure 5

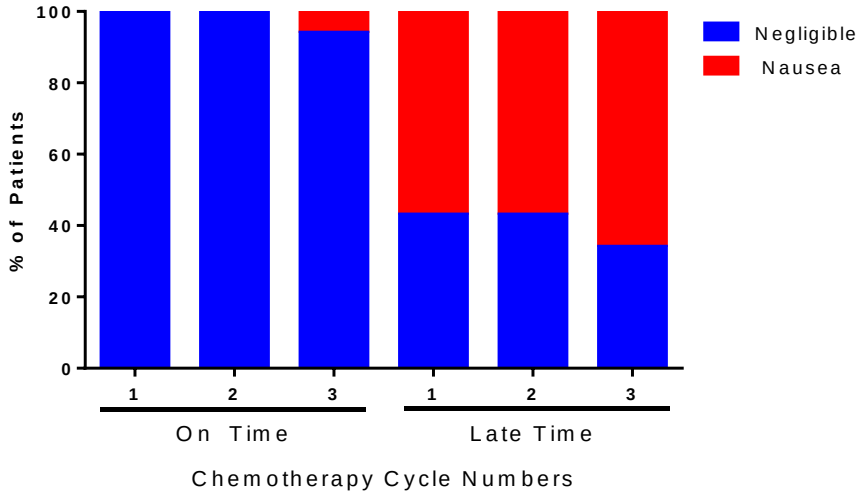

Figure 5. The Effect of Antiemetic Premedication Timing on Incident of Acute Nausea. On time administration of Antiemetic premedication (15-30 minutes before chemotherapy) could completely inhibit acute nausea (93-100%). In contrast, late administration of antiemetic premedication (>30 min or <15 min before chemotherapy) only partially inhibit (33-43%) the incidence of acute nausea.

Figure 6

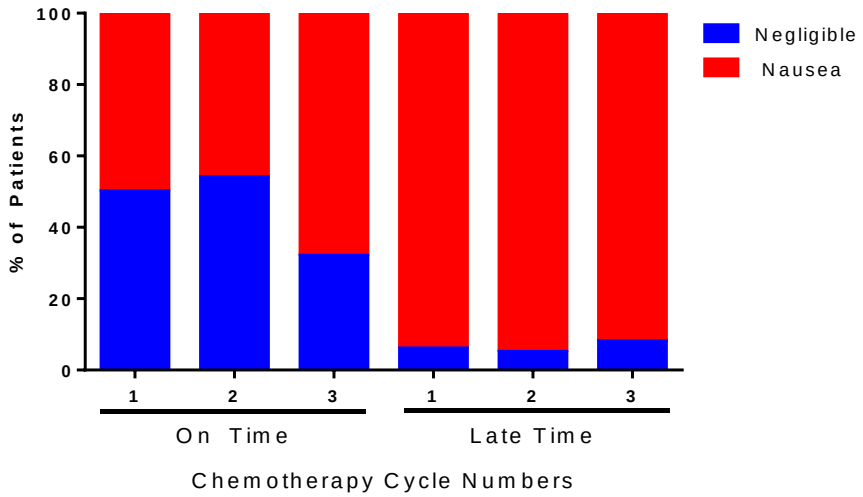

Figure 6. The Effect of Antiemetic Premedication Timing on Incident of delayed nausea. On time administration of Antiemetic premedication (15-30 minutes before chemotherapy) could partially inhibit delayed (32-52%). Moreover, late administration of antiemetic premedication (>30 min or <15 min before chemotherapy) only could inhibit small numbers of delayed nausea(< 8%).

Figure 7

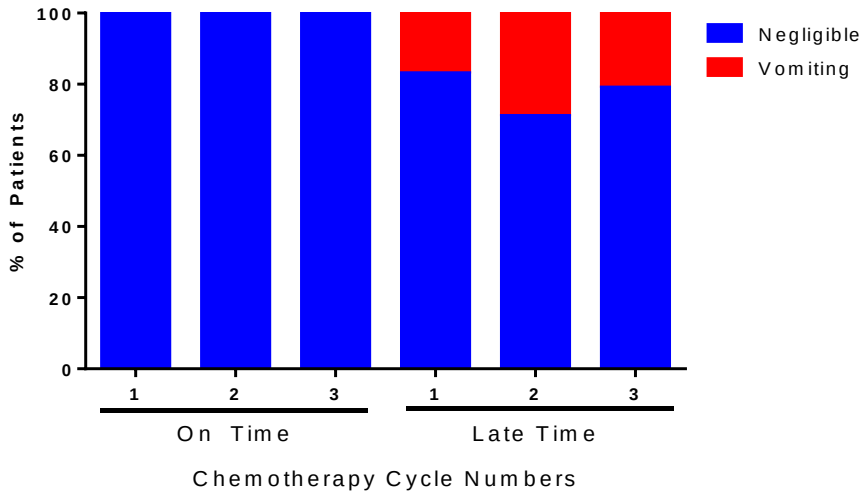

Figure 7. The Effect of Antiemetic Premedication Timing on Incident of Acute vomiting. On time administration of Antiemetic premedication (15-30 minutes before chemotherapy) could completely inhibit the incidence acute vomiting (100%). Furthermore, late administration of antiemetic premedication (>30 min or <15 min before chemotherapy) only had 72-85% protection on acute vomiting incidence.

Figure 8

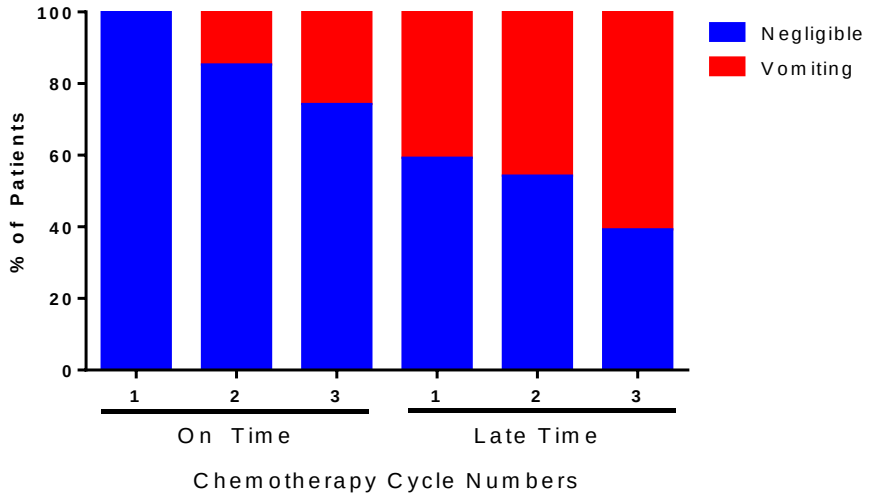

Figure 6. The Effect of Antiemetic Premedication Timing on Incident of delayed vomiting. On time administration of Antiemetic premedication (15-30 minutes before chemotherapy) could partially inhibit delayed (72-100%). Furthermore, late administration of antiemetic premedication (>30 min or <15 min before chemotherapy) only could inhibit smaller numbers of delayed vomiting (39-58%).