Available online on 20.05.2021 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

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Research Article

Regenerative Medicine in Urogynecological Services: Opportunities in Cases of Stress Urinary Incontinence

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Article Info

Article History:

Received 03 April 2021
Reviewed 08 May 2021
Accepted 14 May 2021
Published 20 May 2021

Cite this article as:

Kurniawati EM, Rahmawati NA, Regenerative Medicine in Urogynecological Services: Opportunities in Cases of Stress Urinary Incontinence, Journal of Drug Delivery and Therapeutics. 2021; 11(3):86-88
DOI: http://dx.doi.org/10.22270/jddt.v11i3.4807

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Abstract

Stress urinary incontinence (SUI) is a case that often occurs in women. The handling of this case is not yet fully effective, even though the challenge of health care is to provide quality services and adjust to the needs of the patient. The purpose of this study was to examine the effectiveness of regenerative medicine applied in urogynecology especially in stress urinary incontinence cases as a preliminary study. A selective database search of PubMed, and Google Scholar was conducted to validate the effectiveness of regenerative medicine in urogynecology especially urinary stress incontinence. The search included experimental research, written in English, and has Leak Point Pressure assessment data in the results analysis. Research involves both animals and humans. The search used the following keywords in various combinations: 'stem cell therapy', 'cell-based therapy for SUI', 'regenerative medicine for SUI', and 'tissue engineering'. LPP is an assessor of the success of SUI's services. Most of the studies explored the success and potential of stem cell utilization in cases of stress urinary incontinence even with different types of stem cells. Future studies need to test or experiment the manufacture of stem cell products that can be applied more easily and in the long term.

Keywords: Stress urinary incontinence, stem cell, regenerative medicine

INTRODUCTION

The medical world faces challenges in administering the services and treatment provided to patients. Services are provided by paying attention to the quality of treatment and the needs of the patient. Over time, the challenges to provide health services and improve the quality of life are getting bigger. This is marked by the emergence of research on 'regenerative medicine'. Regenerative medicine is a distinct major advance in medical care based on the principles of stem cell technology and tissue engineering to replace or regenerate human tissues and organs and restore their function. After years of basic research, this approach is starting to show a valuable treatment option for acute injuries, chronic diseases, and congenital disorders [1] (Gianluca, 2015).

The field of research related to regenerative medicine is still less well known (Gianluca, 2015) [1]. In regenerative medicine research involves aspects of biomaterials. These biomaterials are of substantial value in tissue engineering and regenerative medicine, but translating advances in biomaterials science into products with clinical applications involves many challenges, which are usually overlooked when proof of concept is the primary objective. The main problems encountered during research and development include unexpected technical challenges for manufacturing, limited commercialization expertise, and inadequate preclinical safety / risk assessment (Prafulla 2015)[2].

Services that require advancement of treatment include urogynecological care. Uroginecology is an important service related to the long-term health function of women. Uroginecology offers a mixture of problems affecting the pelvic floor in women. This involves treating women with urinary and / or anal symptoms (urgency, incontinence, and incomplete emptying), pelvic organ prolapse (POP), and the impact of these symptoms on sexual function. It is a relatively new subspecialty that requires a holistic approach to patient symptoms and expert skills to address the problems of an aging female population that meets patient expectations (Lone, 2019) [3]. Pelvic floor disorders, including urinary incontinence, pelvic organ prolapse (POP), and bowel dysfunction, affect millions of women worldwide resulting in significant cost and quality of life impacts (Lowenstein et al, 2012) [4].

One of the urogynecology services is a service on urinary stress incontinence. SUI has a significant impact on the quality of life of many women, although estimates of its prevalence vary widely due to inconsistencies in the definition of SUI and differences in the populations studied (Magon, 2011) [5]. Stress urinary incontinence is common and affects many women around the world. About 50% of women with urinary incontinence report symptoms of stress

incontinence, but estimates of prevalence and incidence based on measurement methods are inconsistent between epidemiological studies in different populations. Estimates are also based on fundamental observations in ethnic data. Longitudinal studies assessing the incidence and natural history of stress incontinence estimate an annual incidence of 4% to 10% (Reynolds et al, 2011) [6].

Stem cell research and regenerative medicine are integral parts of the field of Obstetrics and Gynecology. In particular, there is great interest in the regeneration of old or damaged tissue specific to female anatomy and the lower urinary tract through stem cell-based technology. In humans, damaged tissue is generally replaced by the continuous recruitment and differentiation of stem cells in the body. However, the body's ability to regenerate diminishes with age. Examples of conditions requiring regenerative therapy are urinary and fecal incontinence due to sphincter deficiency and pelvic organ prolapse. This condition is common in elderly women and greatly affects the quality of life and represents a huge health cost (Bertha Cen). This study aims to examine the effectiveness of regenerative medicine applied in urogynecology, especially related to stress urinary incontinence as a preliminary study.

METHODS

A systematic review examines several scientific articles related to recommendation systems. This literature review is conducted by digging up the qualified articles found through Pubmed, Google Scholar, and the SCOPUS database. The literature search is carried out using boolean logic including (AND, OR, NOT, or AND NOT) which is used to specify searches, making it easier to determine articles or journals that match the research topic. The keywords in this literature review are adjusted to the Medical Subject Heading (MeSH). The search used the following keywords in various combinations: 'stem cell therapy', 'cell-based therapy for SUI', 'regenerative medicine for SUI', and 'tissue engineering'. Duplicate articles are removed. We screened potentially eligible articles by article titles and abstracts obtained from extensive searches, and then, the full text of this screened trial was assessed for eligibility according to inclusion and exclusion criteria. The study data includes Leak Point Pressure (LPP) data or Urethral Pressure Profile (UPP) data as a clinical and research tool to evaluate stress urinary incontinence in women.

RESULTS AND DISCUSSION

Table 1: Previous studies that examined the use of stem cells in the treatment of stress urine incontinence

S.N.	Author, year	Stem Cell Type	Model	Finding
1	Jiang M, Liu J, Liu W, et al. 2021 [7]	Bone marrow stem cell BMSC-conditioned medium (BMSC-CM) and concentrated conditioned medium (CCM	Rats	LPP was decreased in mice with vaginal distension (VD) compared to the sham VD group (50.82 ± 6.45 cmH2O vs 33.84 ± 3.46 cmH2O), indicating that the VD model was successful. However, treatment with conditioned concentrated medium (CCM) reversed the decrease in LPP in the VD group (45.80 ± 6.42 cmH2O vs 33.84 ± 3.46 cmH2O). In addition, no differences were found in the LPP between the sham VD and VD + CCM groups, revealing that BMSC-CM facilitates functional recovery of the urethra. Moreover, no unstable contraction waves were observed in all three groups.
2	Jalali Tehrani H, et al, 2020 [8]	Adipose-derived, ADSCs, muscle-derived MDSCs,, and co-cultured stem cells	Rats	The mean difference in UPP values before and after cell injection in the ADSCs, MDSCs, and culture groups was calculated as 2.00,9.66, and 15.66 cmH2O, respectively, with an empty bladder, and 5.66, 8. , 33, and 11.66 cmH2O, respectively, with a full bladder. The mean UPP SUI group values were 1.66 cmH2O for an empty bladder and 2.66 cmH2O for a full bladder. The mean difference in UPP values before and after Ringer's injection was calculated as 2.66 with an empty bladder and 3.66 with a full bladder in the control group. One-way ANOVA followed by Tukey's post hoc test showed that the mean UPP score in the ADSCs / MDSCs group with the bladder was 1.399-fold compared with the MDSCs and 2.06-fold compared to the ADSCs group. The difference in mean UPPs in the culture group together with the empty bladder increased by 1.62-fold compared with MDSCs and was significantly increased compared to the ADSCs, SUI, and control groups (P <.01). In addition, the MDSCs group showed significant improvement (P <0.05) compared to the ADSCs group. Overall, the highest mean value of ure-thral pressure difference was observed in the culture group, reflecting increased urethral pressure post transplantation. These findings suggest a higher efficacy of applying co-culture cells for SUI treatment compared to other groups.
3	Wang Y, et al, 2020 [9]	bioactive extracellular matrix fragments	Mouse	One week post-injection, LPP in the ADSCECM group (37.8 ± 2.9cmH2O) restored to normal levels (40.8 ± 2.0cmH2O), which was higher than that observed in the (22.0 ± 4.2) group (P <0.05). Four weeks after injection, the LPP significantly lowered the in-group (23.8 ± 3.8 cmH2O) group compared with the normal group (22.0 ± 4.2) (P <0.05). , and there was an insignificant difference compared to the normal group. Injection of ECM fragments may be a promising minimally invasive approach to treating SUI.
4	Zhuang G, et al, 2021 [10]	human pluripotent stem cell-derived smooth muscle cell progenitors	Rats	Stress urinary incontinence (SUI) was induced in rats by surgical urethrolysis. Leak point pressure of the urethra (LPP) was used to evaluate in vivo urethral function after peri-urethral injection of the SUI rats with pSMC-CM derived from three human pluripotent stem lines: two iPSC lines (Huf5, BIR) and one embryonic stem cell line (H9). Compared with pure control rats (no surgery and no pSMC-CM treatment), the mean LPP was significantly lower in the SUI rats treated SMGS (sham controls) 8 weeks after urethrolysis (17.59 ± 3.18 cm H_2O vs. 36.51 ± 9.58 cm H_2O, $p < 0.05$), indicative of persistent decreased urethral function in the sham controls. Two out of three SUI rat groups treated with pSMC-CM (H9-pSMC-CM and BIR-pSMC-CM) showed significantly higher LPP compared to sham-SMGS rats (26.5 ± 6.85 cm H_2O vs. 17.59 ± 3.18 cm H_2O, 27.5 ± 9.50 cm H_2O vs. 17.59 ± 3.18 cm H_2O,

The results showed a positive effect of regeneration medicine in the field of urogynecology. Research in Indonesia needs to be developed because the number of studies is still rare. In fact, this field promises a quality journey of treatment in Indonesia, especially in the field of urogynecology. Current approaches to tissue regeneration include transplantation of adult mesenchymal cells or their derivatives and implantation of scaffold engineered with these cells. Induced pluripotent stem cells are a promising source of autologous cells. Due to their self-renewing nature, large numbers of cells can be produced for transplantation. In addition, its pluripotent status allows for the reduction of several cell types thereby facilitating the gradual implementation of simple cell injections to more complex matrices with multiple cell types with the potential for full regeneration (Bertha Cen) [11].

Things that need to be considered and emphasized are increasing the role of academic institutions in the translation process, connecting research scientists with experts in process development and commercialization, and building academic-industry partnerships, in order to encourage the successful translation of biomaterials into clinical applications. Incorporating quality with a design approach and process analytics technology into the biomaterial manufacturing process can improve quality, efficiency and cost effectiveness. In addition, the establishment of consistent guidelines and regulatory standards for manufacturing, quality control, and post-market assessment will be critical to the successful translation of new biomaterials in regenerative medicine (Prafula 2015) [2]. The effectiveness of regenerative medicine and reporting of side effects need to be developed. Even though most of the impacts are positive, it still needs further research that can be applied as well as a comparison of suitable ingredients as stem cells based on the results achieved and to carry out product development and multiplication of research in humans.

In this study, the research emphasizes the leak point pressure. LPP is not consistently defined and the technique is not standardized, leading to variations in test results. LPP reproducibility is poor, both due to biological variations and variations in the testing procedure itself (partly due to a lack of standardization). Although not well studied, LPP values correspond to the severity of incontinence symptoms, as a quantitative indication of the degree of urethral dysfunction. However, there is no prospective evidence to support the commonly used 60 cm H2O cutoff as an indication of intrinsic sphincter deficiency. LPP is potentially useful as a clinical and research tool for evaluating stress urinary incontinence in women. However, its use in clinical management is not well supported by evidence and further research is essential to determine its role (Weber et al, 2001) [12].

CONCLUSION

Previous studies have shown positive effects even with different types of stem cells. Future studies need to test or experiment the manufacture of stem cell products that can be applied more easily and in the long term.

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