SYSTEMATIC REVIEW

The role of stem cells in obstetrics and gynecology: A systematic review

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Article Info
Received May 2, 2023
Revised Jun 8, 2023
Accepted Jun 16, 2023
Published Dec 1, 2023

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Keywords:
Amniotic fluid stem cells
Gynecology
Bone marrow stem cells
Mesenchymal stem cells
Obstetrics
Stem cells
Maternal health

ABSTRACT

Objective: This study aimed to review the role of stem cells in obstetrics and gynecology.

Materials and Methods: This review used several databases, the PubMed, Wiley Online Library, and ScienceDirect to search open access original and review articles in English related to stem cells, obstetrics, and gynecology in the last 10 years. The results were analyzed qualitatively.

Results: Out of 1,016 records identified through database searching, fifteen articles were eligible for review. Several articles reported the role of stem cells in endometrium repair. Stem cell can also increase endometrial thickness and increase the likelihood of pregnancy. In the field of gynecology, stem cells can be used as potential treatment for stress urinary incontinence and anal incontinence. Despite of all those abilities, stem cells might have errors, such as chromosomal abnormalities, epigenetic and genetic defect, which could potentially turn the stem cells into tumor initiating cells (TICs), thus can contribute to ectopic growth of endometrium (endometriosis), leiomyoma, leiomyosarcomas, and adeno-myosis.

Conclusion: Stem cell technology has various roles in the field of obstetrics and gynecology, including fertility study as well as tissue damage repair. However, in-depth research to ensure the safety profile of stem cells technology use in human is necessary.

How to cite: Mirani P, Legiran, Kesty C, et al. The role of stem cells in obstetrics and gynecology: A systematic review. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2023;31(3):129-138. doi: 10.20473/mog.V31I32023.129-138.

Highlights:

1. Stem cell technology has various roles in the field of obstetrics and gynecology, including fertility study as well as tissue damage repair.
2. Safety profile of stem cells technology use in human still need to be assessed.

INTRODUCTION

Stem cells are a type of undifferentiated cell that can multiply indefinitely (self-renewal), starting from a single cell (clonal), and differentiate into a variety of cells and organs (potent).[1,2] Stem cells are unique to a particular variety of cell or tissue because they have not yet formed specific structures or proteins.[3] Stem cells have the capacity to differentiate while still having the capacity for self-replication and keeping the properties of progenitor cells. A cell is referred to as totipotent if it has the ability to split and develop into any embryonic cell as well as any extraembryonic cell, according to the spectrum of cell potential. For instance, a totipotent cell in human growth develops from an embryo, which is also a totipotent cell. With fertilization, the zygote splits, and the identical daughter cells maintain their totipotency up until the blastocyst is created. The bulk of the cell starts to divide at this point, and the cells that follow are categorized as pluripotent cells.[4]

Stem cells derived from the ever-increasing requirement to replace or regenerate damaged tissue caused by age-associated or degenerative conditions, trauma, tumors, and birth defects. Reconstructing damaged tissues with differentiated cells collected from biopsy, expanded in vitro, and implanted on artificial and/or natural scaffolds is the primary choice in regenerative therapy. The differentiated cells have the appropriate phenotype to carry out the desired biological functions. In spite of that, its use for tissue engineering is frequently constrained by the small number of harvested cells as well as their low proliferative capacity in vitro. Following this, advanced regenerative therapies concentrate on stem cells can be used for direct application to injured sites for tissue engineering, using appropriate scaffolds to transport these cells.[5]

Embryonic stem cells (ESCs) as well as tissue-derived (somatic) stem cells are the two principal cell types based on origin. Further classifications of tissue-derived stem cells include fetal stem cells, adult stem cells, as well as induced pluripotent stem cells.[4,6,7]

In obstetrics and gynecology, stem cell research has been conducted under various conditions. The treatment of pelvic floor prolapse, stress urinary incontinence, as well as vaginal and uterine reconstruction are these conditions. Other research has examined stem cell therapy for primary ovarian insufficiency.[8,9] In addition, there are studies utilizing stem cell therapy to treat endometrial disorders such as endometrial atrophy and Asherman's syndrome.[10,11] The outcomes of these diverse studies vary; some are fruitful and promising, while others are inconclusive.[12] Therefore, this review aimed to find evidence regarding the role of stem cells in obstetrics and gynecology.

MATERIALS AND METHODS

This review used the help of several databases, the PubMed, Wiley Online Library, and ScienceDirect (Table 1). Articles search were carried out in the mid-March to early April 2023. Inclusion criteria consisted of all articles in English, both research and review, related to the topic of the review (stem cell and obstetrics and gynecology), and open access. The exclusion criteria were unrelated research and results, incomplete data, and articles in languages other than English. The articles included in this research wre those from the last 10 years.

The basic characteristics of the research are displayed in a tabular form (Table 2). Review and extraction of the contents of the article are presented in the form of a narrative and presented in the discussion section.

The articles included in this review had been guaranteed for quality. Each article had been confirmed and reviewed in the journal with the help of Scimago Journal Rankings. Each article was then assessed for validity with the help of the NIH Quality Assessment Tool. In searching for articles and assessing them, the authors avoided bias that could be caused by authors, affiliations, sponsors, regions, and journals, thus the focus was on the articles' quality.

RESULTS AND DISCUSSION

From the search conducted, a total of 1,016 articles were included in this review. After that, deduplication was carried out, and 64 duplicate articles were obtained. After further screening, 21 articles were found that matched the research inclusion criteria. After reading the full text to see if the contents of the articles obtained were appropriate and included in the review, there were 15 articles that matched the topic of the review, so 6 articles were excluded.

The reasons for article exclusion were: it was not in accordance with the purpose of this review (n=5), and one was an editorial article. The article search flowchart for this review is shown in Figure 1. Of the 15 studies obtained, there were eleven review articles, two research articles, one prospective article study, and one experimental article.

Table 1. Search queries of this literature review

Databases	Search queries	Hits
PubMed	("Stem Cell") AND ("Obstetric") and ("Stem Cell") AND ("Gynecology")	154
Wiley Online Library	(Stem cell AND Obstetrics) and (Stem cell AND Gynecology)	852
ScienceDirect	Stem cell, Obstetrics, Gynecology	10

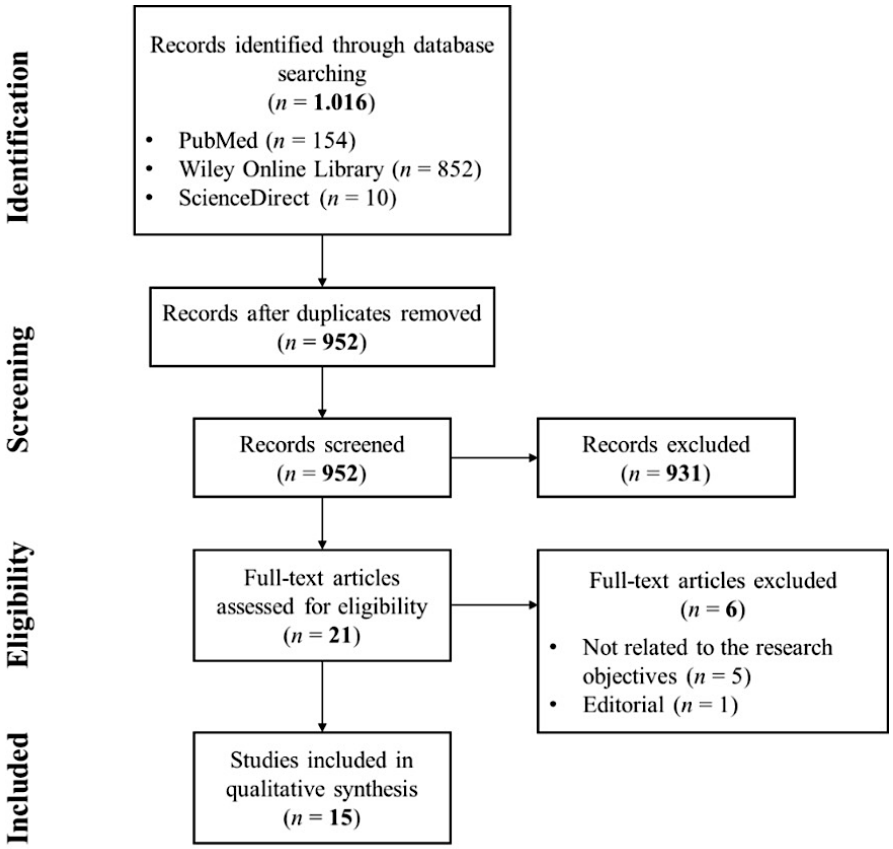

Figure 1. Flow diagram of article selection

Table 2. Study characteristics and findings

First Author (Years)	Titles	Types	Findings
Lane FL (2012)[13]	"Stem cells in gynecology"	Review article	• Mesenchymal and muscle-derived stem cells used in urinary and anal incontinence treatment to engraft after transplantation. It also has bulking effect, elicit trophic effect on the host, and can modulate inflammation, which improve histological, functional, and clinical outcomes. • Existing data support the potency of stem cell transplantation for pelvic floor disorder treatment, fistula repair, graft material improvement, as well as vaginal tissue engineering.
Hanna CB (2014)[14]	"Ovarian germline stem cells: An unlimited source of oocytes?"	Review article	• There is evidence that germline stem cells (GSCs) can self-renew and survive in oocyte development.

Mutlu L (2015)[15]	"The Endometrium as a Source of Mesenchymal Stem Cells for Regenerative Medicine"	Review article	• The endometrium can be a source of non-embryonic stem cells with remarkable differentiation capacity. • Endometrium-derived stem cells are capable of differentiating into neuronal phenotypes (dopamine producing cells, oligodendrocyte-like cells, cholinergic neuron-like cells), megakaryocyte-like cells, cardiomyocyte-like cells, urothelial cells, insulin producing cells, and other mesenchymal cell types.
Dziadosz M (2016)[16]	"Human amniotic fluid: A source of stem cells for possible therapeutic use"	Review article	• Amniotic fluid stem cells easy retrieval, high proliferation rate, differentiation potential into all embryonic germ cell layers and stability of both genetics and phenotype.
Edessy M (2016)[8]	"Autologous Stem Cells Therapy, The First Baby of Idiopathic Premature Ovarian Failure"	Prospective study	• Stem cell therapy and transplantation in premature ovarian failure (POF) is a good procedure in hope of a healthy pregnancy and baby, and showed good clinical, histopathology, and immunohistochemical outcome.
James JL (2016)[17]	"Stem Cells and Pregnancy Disorders: From Pathological Mechanism to Therapeutic Horizons"	Review article	• Stem cells are being used for early pregnancy disorder (infertility problem, Asherman's syndrome). • Stem cell treatment appears most promising in placental pathologies such as placental infarction, chronic villitis, and FGR.
Hamid AA (2017)[18]	"Highly potent stem cells from full-term amniotic fluid: A realistic perspective"	Review article	• Amniotic fluid derived stem cells have high differentiation potential, rapid expansion, and low immunogenic properties, and have multiple possible application including neural, cardiac, lung epithelial, kidney, bone, and cartilage regeneration.
Mohamed SA (2017)[19]	"Human Mesenchymal Stem Cells Partially Reverse Infertility in Chemotherapy-Induced Ovarian Failure"	Research article	• Intraovarian administered bone marrow mesenchymal stem cells (BMSCs) are able to restore ovarian hormone production and reactivate folliculogenesis in chemotherapy-induced ovarian failure mouse model.
Azizi R (2018)[10]	"Stem cell therapy in Asherman's syndrome and thin endometrium: Stem cell-based therapy"	Review article	• Transplantation of different stem cells with a diverse source in the endometrial zone can reduce fibrotic area. It also resulted in increased number of glands, angiogenesis stimulation, endometrium thickness enhancement, better formed tissue construction, as well as increased pregnancy rate.
He Y (2018)[9]	"The therapeutic potential of bone marrow mesenchymal stem cells in premature ovarian failure"	Review article	• Bone marrow stem cells are a good candidate for transplantation in premature ovarian failure (POF) because bone marrow stem cells can migrate to the injured ovary and secrete crucial cytokines that function an as anti-inflammation, antifibrosis, antiapoptotic, and immunoregulation, which improves ovarian function. • However, current therapeutic ratio in clinical trials can ensure ovarian reserve recovery in patients with POF.
Santamaria XM (2018)[20]	"Uterine stem cells: from basic research to advanced cell therapies"	Review article	• Endometrial stem cells used in therapy of Asherman's syndrome as well as endometrial atrophy. • There is potential use of myometrium stem cells, but it has drawback, such as developmental errors such as chromosomal abnormalities and genetic and epigenetic defect, could promote the developmental of tumor initiating cells (TICs) and thus contribute to myometrial tumors such as leiomyoma, leiomyosarcoma.
Hu J (2019)[11]	"Effects of menstrual blood-derived stem cells on endometrial injury repair"	Experimental (in vitro)	• Model mice treated with menstrual blood stem cells exhibited increased endometrial thickness and increased the pregnancy rates. • By stimulating the expression of vimentin, VEGF, and keratin, stem cells derived from menstrual blood may facilitate the repair of endometrial lesions in rodents.
Sarma UC (2019)[21]	"Oocyte from stem cells"	Review Article	• The use of oogonial stem cells (OSCs) and embryonic stem cells (ESCs) for the production of new oocytes to repopulate follicle-depleted ovaries is a prospective of stem cells application for fertility preservation.
El Sabeh M (2020)[22]	"Uterine stem cells and benign gynecological disorders: Role in pathobiology and therapeutic implications"	Review article	• Stem cells enhanced the proliferation and renewal of normal or injured endometrium, but they also have the ability to cause ectopic endometrial growth (endometriosis), uterine leiomyoma, and adenomyosis.
Zhang Y (2021)[23]	"Mesenchymal stem cell transplantation for vaginal repair in an ovariectomized rhesus macaque model"	Research article	• The content of collagen I, elastin, and microvascular density in the lamina propria of the vagina increased significantly in the MSC group compared with the saline group. And the fraction of smooth muscle in the muscularis of vagina increased significantly in the MSC group. • In addition, MSC transplantation improved the biomechanical properties of the vagina by enhancing the elastic modulus.

Reproductive tissues are currently acknowledged as source of progenitor cell or SCs. Stem cells originated from reproductive tissues have been widely studied for their possible use in other areas, for example, hematological disease treatment as well as bone tissue engineering.[24] In short, stem cells possess the capacity to undergo self-renewal or multiple cell divisions but still remains undifferentiated. Multipotency is defines as the ability to differentiate into any types of mature cell. Morula-derived totipotent SCs are able to differentiate into both embryonic and also extraembryonic cell types. It can also generate a viable and complete organism. Pluripotent SCs are derived from totipotent cells. Pluripotent SCs can differentiate into any type of germ layers' tissues, including embryonic tissues, i.e. umbilical cord, amniotic fluid cells, amnion, and placenta). Being derived from the interior cell mass of a blastocyst, embryonic stem cells are pluripotent. Multipotent SCs, e.g. mesenchymal and hematopoietic SCs, differentiate into multiple tissues originating from a single embryonic layer. Unipotent cells, such as muscle satellite cells, produce only their own cell type but have a greater capacity for self-renewal compared to fully mature cells. Theoretically, the more rudimentary or "potent" the SC, the greater its propensity for unrestrained cell division and oncogenic potential. However, there are some issues about the oncogenic potential of pluripotent SCs like embryonic and induced pluripotent SCs, that is the non-pluripotent cell sources are not inherently oncogenic.[24]

Embryonic SCs offer a potential treatments for re-generative diseases, despite the controversy surrounding their sources, which has slowed progress in this area. Nonetheless, multipotent SCs are currently being isolated from a variety of fetal tissues, which currently are easily obtained from the specimens of diagnostic tests during pregnancy termination and delivery. In the field of regenerative medicine, in order to heal or restore damaged or diseased urogenital tract organs (i.e. urinary sphincter, pelvic floor, vagina, uterus, and ovary), SCs are present in both the preclinical as well as clinical phases of research. In obstetrics researches, SC transplantation has been concentrated primarily on fetal therapy.[24]

Over the past decade, embryonic, fetal, and extrafetal tissues, as well as adult gonads, have been used to isolate stem cells. The inner cell mass of the blastocyst is the origin of extra–fetal tissues such as placenta and amniotic membranes. They contain a heterogeneous population of progenitor cells, presumably due to their shared origin. This consists of hematopoietic, trophoblastic, mesenchymal, and possibly even more primitive SCs. Despite the fact that the composition of amniotic fluid varies with embryonic health and gestational age, mesenchymal SC can be consistently isolated at any gestational age. Amniotic fluid and placental mesenchymal SC have been demonstrated to differentiate into the majority of mesodermal cell types, but also can differentiate into ectodermal and endodermal cell types.[25] Other cell types, such as a population of CD–117 positive cells, have been isolated from amniotic fluid. They express pluripotential markers and perform self–renewal up to more than 50 population doublings, with the same telomere length. Their use as allogeneic and autologous cell sources is currently being studied in the field of regenerative medicine. To do so, supportive facility dedicated to their characterization, immunogenicity, as well as storage, is necessary.[26]

From numerous fetal tissues, embryonic SCs have been isolated. Early gestational HSC from liver and bone marrow are well-characterized,[27] whereas placental HSC have only been studied relatively recently.[28] Primitive human fetal mesenchymal SC (hfMSC) collected from all parts of the developing fetus with higher proliferative ability express more telomerase with longer telomeres than their adult counterparts.[29-31] In addition, hfMSC can differentiate rapidly into muscle and neuronal lineages. Moreover, compared to later perinatal and adult sources of MSC, they have also been demonstrated to have more robust differentiation down the osteogenic lineage, and thus indicating their potential for bone tissue engineering in postnatal applications.[32] Primitive hfMSCs are rapidly transduced through the integration of vectors. They do not express HLA–II nor CD80 and CD86 costimulatory molecules, suggesting their applicability for gene therapy as well as their allogeneic use ex vivo.[33,34]

Blood remaining within the umbilical cord as well as placenta following delivery was routinely disposed until recently. Now that it is known that this blood contains both hematopoietic stem cells and pluripotent mesenchymal cells, clinical application as well as the investigation of umbilical cord blood in hematopoietic transplantation as well as regenerative medicine have significantly increased.[35]

Historically, it has been recognized that umbilical cord blood contains hematopoietic SCs with the capacity to produce clonogenic progeny. Knuddtzon first confirmed the presence of hematopoietic clonogenic cells in in vitro cord blood in 1974.[36] Broxmeyer and associates confirmed the presence of hematopoietic stem cells in cord blood in a report published in 1989.[37] Additional research confirmed their clonogenic potential, capacity for self-renewal, and expansion in vitro.[38,39] The umbilical cord remains was deemed to have no scientific value. In 2004, it was determined that these

cells were MSCs as they expressed CD105, CD73, CD51, CD44, and CD29, lacked CD45 and CD34 expression. Other than that, they are also able to transform into adipogenic and osteogenic cells. As for now, umbilical cord MSCs can be originated from the entire or parts of umbilical cord, including perivascular, intervascular, and subamniotic zones of subendothelial layer, as well as Wharton's jelly.[40]

Human embryo becomes affixed to the developing placenta via a stalk in the third week of gestation. During 5th week, primitive umbilical cord takes the form of an umbilical ring. At 10th week, after gastrointestinal maturation in the neonate, the umbilicus appears as a fistula connecting to the umbilical cord.[41]

Wharton's jelly is an elastic and gelatinous matrix composed of mucopolysaccharides, primarily chondroitin sulphate and hyaluronic acid that protects the umbilical cord epithelium. Wharton's fluid, along with amnion, shield three blood vessels that are important for fetal and embryonic development. A single large umbilical vessel provides placental blood, which is abundant in nutrients and oxygen, to develop fetus. In the final trimester, it also provides the mother's vital antibodies. A pair smaller umbilical vessel return blood containing carbon dioxide, pollutants, and other contaminants from the fetus.[41]

Blood in the umbilical vessels, vessel walls, and Wharton's fluid can provide stem cells from the umbilical cord. Cord blood is usually collected at delivery using a sterile collection container containing an anticoagulant (typically citrate or heparin) and one or more collecting needles. It can be collected intrauterine or extrauterine, in both spontaneous deliveries and caesarean sections, without causing suffering to the mother or child.[41] Typically, the units are transported to a laboratory for cell separation in order to isolate the buffy coat and/or stem cell-rich cell preparations. There are numerous ways to extract cells from cord blood, including centrifugal elutriation, starch-based methods, rouleaux formation, as well as density-gradient methods.[42-44]

The HSC population within UCB has a greater capacity to proliferate and differentiate than HSC obtained from bone marrow as well as peripheral blood. Moreover, it is simpler to collect UCB because it poses fewer risks to the maternal donor, has a lower risk of infection, is readily available, and the Human Leukocyte Antigen (HLA) typing criteria are less stringent, resulting in less graft-versus-host disease.[45-47]

Mesenchymal stem cells (MSCs) are in fact multipotent adult stromal cells with the capacity to differentiate into various cell lineages. The Umbilical Cord MSCs (UCMSCs) are one of the most desirable sources of MSCs for clinical applications. UCMSCs have a superior capacity for differentiation, migration, and self-renewal compared to other types of MSCs and can be collected invasively. There is mounting evidence that UCMSCs aid in the restoration of damaged endometrium. In a rodent model, for instance, UCMSC transplantation recovers endometrial thickness and reduces excessive fibrosis. These UCMSCs strengthen the endometrial response towards hormones as well as endometrial proliferation and angiogenesis. Moreover, endometrial stromal cells (ESCs) serve as an important cellular component within the endometrium essential for the endometrium's normal physiological functions. These ESCs are involved in implantation as well as the maintenance of pregnancy.[48]

From several journals obtained through database searches, we obtained several findings related to stem cells in the field of obstetrics and gynecology. The first was the potential for direct use of stem cells in obstetric and gynecological diseases. The second was the use of stem cells sourced from the fields of obstetrics and gynecology.

Several articles showed the benefit of stem cells to repair the endometrium. Gargett's article discussed adult stem cells and bone marrow-derived stem cells in human endometrium. The adult stem cells are clogenic cells, tissue-reconstructing cells, side population cells, and menstrual blood stem or progenitor cells. Bone marrow-derived SCs include hemopoietic, mesenchymal, and endothelial progenitor cells that circulate in small numbers in injured tissues. These evidences suggest the presence of human endometrial stem cells that can be activated for cases of dysfunctional thin endometrium or atrophic endometrium. In addition, stem cells can be transplanted to treat Asherman's syndrome.[13,19] The same finding was found in the article by Azizi, which stated that several studies were performed for the regeneration of human endometrium, and it was found that stem cells (from various sources, adult stem cells, such as menstrual blood stem cells and bone marrow) can increase the number of menstrual volume and endometrial thickness in Asherman's syndrome.[10] Research by Hu (2019) showed that SCs can increase endometrial thickness and increase the likelihood of pregnancy, using menstrual blood-derived SCs under in vitro conditions.[11] A study by Santamaria also stated the same, that endometrial SCs can be used in Asherman's syndrome and endometrial atrophy.[20] Another article was written by Zhang et al. that evaluated how mesenchymal stem cell (MSC) therapy can repair weak vaginal tissue in an ovariectomized rhesus macaque

model. This study found that vaginal MSC transplantation could repair the weak vaginal tissue by promoting extracellular matrix ingrowth, neovascularization, and smooth muscle formation and improve the biomechanical properties of the vagina, providing a new prospective treatment for POP.[23]

Although the rigorous mechanism is not entirely understood; mesenchymal stem cells (MSCs) can be used in allogeneic transplantations without immuno-suppressive therapy. MSCs secrete a plethora of immune-modulating cytokines, such as Interleukin-10 and Transforming Growth Factor β (TGF-β), that create an immune-suppressed zone around the area of MSCs implantation. Whereas, the administration of MSCs has been shown to improve the clinical symptoms of graft-versus-host disease in clinical trials. It has demonstrated that spectrum of reproductive dysfunction can be treated by allogeneic BMSCs.[19] Apart from endometrium and thickening repairing, stem cells have also been tried to treat Premature Ovarian Failure (POF). Edessy et al. (2016) conducted a trial with patients suffering from premature ovarian failure. Bone marrow stem cells were injected into the ovaries via laparoscopy, then the patients were followed up every month for hormonal, clinical, and pregnancy checks. It was found that stem cell transplantation can improve the hormone profile of patients with premature ovarian failure, and restore menstruation and even patients can get pregnant and give birth at term. Histopathological and immunohisto-chemical examinations can also show an increase in the results, from atrophic endometrium to secretory endometrium and good glandular function.[8]

An article by He (2018) also discusses a similar issue on the bone marrow stem cells (BMSCs) transplant for the treatment of POF. These BMSCs are adult SC with low immunogenicity, mostly located in the bone marrow. The advantages of BMSCs are that they are easy to isolate and propagate in vitro. These cells can also migrate to the site of tissue injury, due to their paracrine and immunomodulating properties, and differentiate into specific cell types by induction of various factors that mimic the environment surrounding the damaged tissue. In addition, BMSCs have antiapoptotic, anti-fibrotic effects, angiogenesis, anti-inflammatory, and immunoregulation. Thus, these BMSCs have become good candidates for transplantation into POF patients, despite their current drawbacks.[9] The same results are found in Mohamed's article that intraovarian-administered BMSCs are able to restore ovarian hormone production and reactivate folliculogenesis in chemotherapy-induced ovarian failure mouse model.[19] Human BMSCs could work as a potential treatment modality that either rescues follicles undergoing early atresia or quiescent primordial follicles from the adverse effects of CTX in the ovarian microenvironment. Millions of women take fertility treatments each year due to age-related or non-age-related loss of oocytes. In young women who are sterile especially by CTX, those treatments offer only uncertain improvements in their fertility. If oocytes remain viable, it is potential to reestablish fertility using a stem cell administration for the revival of folliculogenesis. This evaluation of the regenerative use of BMSCs gives a chance to women affected by POF and direct us to enquire if fertility restoration using BMSCs is a viable therapeutic option.[19]

In addition, there are articles that show the possibility of restoring one's fertility by using stem cells. A study by Hanna et al. (2014) explained that the potential of germline stem cells in the process of oocyte development may be able to open this up.[14] The article by Sarma (2019) shows the potential of stem cells to preserve fertility by using oogonial stem cells, embryonic stem cells, and induced pluripotent stem cells.[21] There are also potential use of stem cells to treat placental pregnancy disorders such as placental infarction, chronic villitis, and FGR.[19]

In the field of gynecology, there are several potential benefits from the use of stem cells, such as in cases of stress urinary incontinence and anal incontinence. So far, the choice of therapy for both cases are still limited, such as through surgery. Both of these are caused by the same basic pathogenesis, the loss of muscle integrity and function, so that building muscle from a cellular level is an ideal management concept. In addition, the application of stem cells in the field of gynecology is not limited to this, such as in repairing vaginal tissue, repairing fistulas, and increasing grafting materials.[14]

Other studies stated that stem cells from obstetrics and gynecology field, such as endometrial stem cells, myometrial stem cells, and amniotic stem cells could be used as therapy modality. The advantages of endo-metrium stem cells are that they have remarkable differentiation ability, i.e. neuronal (dopamine produc-ing cells, cholinergic neuron-like cells, oligodendrocyte-like cells), insulin producing cells, cardiomyocyte-like cells, megakaryocyte-like, urothelial cells, and other mesenchymal cell types.[17] Amniotic fluid stem cells also have special consideration because it is easy to retrieve, having high proliferation rate, ability to differentiate into many type of cells, stability in both phenotype and genotype, and low immunogenic profile.[18,20]

Despite of all those abilities, there are some drawbacks, especially with uterine source of stem cells. When in developmental process, and the stem cells have errors,

such as chromosomal abnormalities, epigenetic and genetic defect, which could potentially turn the stem cells into Tumor Initiating Cells (TICs), thus can contribute to ectopic growth of endometrium (endometriosis), leiomyoma, leiomyosarcomas, and adenomyosis.[21,23]

CONCLUSION

This review showed that there are many advantages of stem cells in obstetrics and gynecology, both in infertility and in repairing tissue damage. However, it is necessary to conduct further and in-depth research to ensure the safety profile of stem cells in human in the field of obstetrics and gynecology.

DISCLOSURES

Acknowledgment

We thank for all lecturers, colleagues, and Doctoral Programme Faculty of Medicine Universitas Sriwijaya, Palembang, South Sumatera, Indonesia for the contributions and suggestions in this literature review.

Conflict of interest

All authors declare no conflict of interest.

Funding

This study did not receive any specific grants from public, commercial, or non-profit funding agencies.

Author contribution

Each of the authors made contributions to all processes in this research, including preparation, data collection and analysis, drafting, as well as approval for publication of this manuscript.

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