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Autologous platelet-rich plasma promotes regeneration of ethanol-induced endometrial damage in a canine model

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ABSTRACT

Thin and damaged endometrium represents a significant challenge in managing pregnancies, and may contribute to postpartum uterine disorders, recurrent miscarriages, and other complications. Although various treatments have been proposed, their effectiveness remains inconsistent. Recently, scientists have turned their attention to platelet-rich plasma (PRP) for its growth factors and cytokines in human medicine. However, its potential for reconstructing endometrial issues in canine models has not yet been adequately investigated. Therefore, the present study aimed to investigate the therapeutic properties of PRP on ethanol-induced endometrial damage in dogs. Twelve healthy adult mixed-breed dogs were randomly divided into four groups: group E received 95% ethanol in uterine horns to create a model of endometrial damage; group E+NS received saline 72 hours post-injury; group E+PRP received PRP 72 hours post-injury; and group NS+PRP was initially given normal saline and PRP 72 hours later. The results showed significant improvements in endometrial thickness, epithelial repair, and uterine gland density in the E+PRP group compared with the E group ($P < 0.05$). The E+NS group did not show significant differences in comparison to the E group. The results showed a decrease in bleeding and necrosis severity in the E+PRP group. Additionally, hyperemia and hemosiderosis levels in the E+PRP, E+NS, and E groups were similar. In conclusion, the utilization of PRP was successful in the treatment of ethanol-induced endometrial injury in dogs. These findings suggest that PRP may represent a promising regenerative therapy for thin endometrium and related reproductive disorders.

Keywords

Platelet-rich plasma, thin endometrium, regenerative medicine, histology, dogs

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Abbreviations

ANOVA: analysis of variance
CTGF: connective tissue growth factor
E: ethanol
EGF: epidermal growth factor

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Introduction

The endometrium plays a vital role in the female reproductive system. Structurally, it consists of blood vessels, glands, epithelial tissue, and stroma. Previous studies have indicated that alterations in uterine tissue composition and damage can significantly disrupt the normal physiological cycle, affecting embryo implantation and overall pregnancy outcomes [1-3]. Moreover, endometrium thickness is important, as it affects implantation of embryo, delivery, and fetal birth weight [4-8]. Clinical and experimental evidences have highlighted that variations in endometrial thickness can significantly influence embryo survival rates after intrauterine insemination, with thinner endometria correlating with lower survival rates [9, 10].

The pathogenesis of thin endometrium remains incompletely understood and is likely multifactorial. Several mechanisms have been proposed, including increased cellular senility, elevated collagen deposition, and decreased expression of genes, all derived from models of thin uterine disease, as well as inflammatory atrophy and immune dysfunction observed in veterinary endometritis cases [11]. As a result, a range of therapies has been developed to counteract these pathogenic pathways. For instance, the efficacy of vaginally administered sildenafil has been examined in patients who have experienced failure in in vitro fertilization (IVF) as a result of endometrial dysplasia [12]. Additionally, other treatments such as estrogen, long-acting aspirin administered in low-doses, and intrauterine infusion of granulocyte colony-stimulating factor (G-CSF) have been employed [13, 14]. Although some of these interventions have shown promising results, the effectiveness of these therapies remains inconsistent, and an optimal treatment approach for thin endometrium has not yet been established.

Platelet-rich plasma (PRP) is known for its high concentration of platelet activators that stimulate cytokine and growth factor activity. Evidence suggests that intrauterine injection of PRP can enhance endometrial growth and implantation. PRP contains a greater number of platelets compared to general circulation, which allows it to promote proliferation and repair through a rich supply of various cytokines and growth factors, such as transforming growth factor beta (TGF-β), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), connective tissue growth factor (CTGF), insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), and interleukin-8. Although platelet transfusion is applied to an increasing extent in various medical fields including osteoarthritis, nerve injury, and plastic surgery, its use in gynecological and obstetric conditions is still limited [15, 16]. To date, no published in vivo or in vitro studies have specifically evaluating the effect of PRP growth factors on the canine endometrium. Consequently, the objective of this research was to evaluate the therapeutic impact of PRP on the treatment of thinned endometrium in a canine model.

Abbreviations-Cont'd

ELISA: enzyme-linked immunosorbent assay
FGF: fibroblast growth factor
G-CSF: granulocyte colony-stimulating factor
H&E: hematoxylin and eosin
IGF: insulin-like growth factor
IVF: in vitro fertilization
MSCs: mesenchymal stem cells
NS: normal saline
PDGF: platelet-derived growth factor
PRP: platelet-rich plasma
TGF-β: transforming growth factor beta
VEGF: vascular endothelial growth factor

Results

None of the dogs showed clinical complications associated with anesthesia, surgery, or intrauterine injection procedures. In the NS+PRP group, uterine tissue exhibited a normal structure, although mild hyperemia was observed in some sections, which was considered within normal physiological limits. The endometrial cylindrical epithelium remained intact and continuous, and the density of submucosal glands was preserved at normal levels. No pathological alterations, including hemorrhage, necrosis, or hemosiderosis were detected (Figure 1). In contrast, the E and E+NS groups showed severely reduced endometrial thickness due to extensive necrosis. Epithelial regeneration was poor and intermittent in some sections. In addition, glandular density was significantly diminished, with only minimal evidence of tissue regeneration. Submucosal cellularity was severely reduced, and significant hemosiderosis associated with extensive hemorrhage was observed in these tissues (Figure 2). Conversely, the E+PRP group showed substantial histological improvement following treatment. Endometrial thickness increased significantly accompanied by marked tissue repair. Re-epithelialization of the endometrium was highly successful, with approximately 90% epithelial healing observed. A considerable degree of uterine gland regeneration was also evident. Following tissue repair, submucosal cellularity increased, while pathological changes, including hyperemia, hemorrhage, and hemosiderosis, were markedly reduced (Figure 3).

As presented in Table 1, the E+PRP group demon-

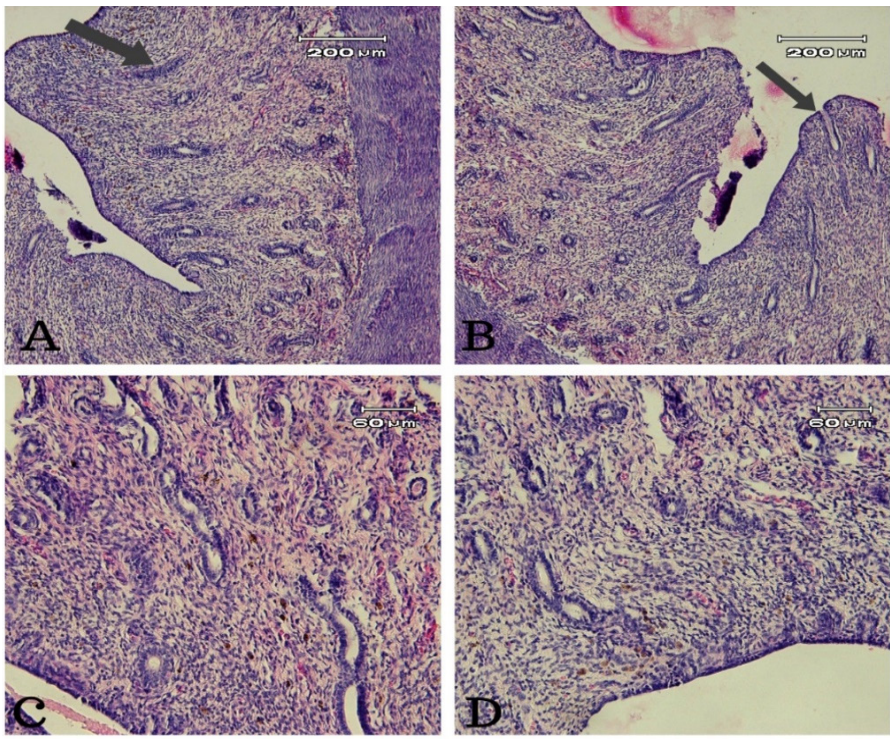

Figure 1.
Uterus of dogs, NS+PRP group.
The figure illustrates normal uterine tissue structure, featuring normal uterine glands (arrow in A) located in the endometrial submucosa, as well as integrated epithelial tissue (arrow in B) observed in all sections of the healthy group. In all pictures, the density of uterine glands and the cellularity of the submucosa were found to be consistent and normal. H&E staining.

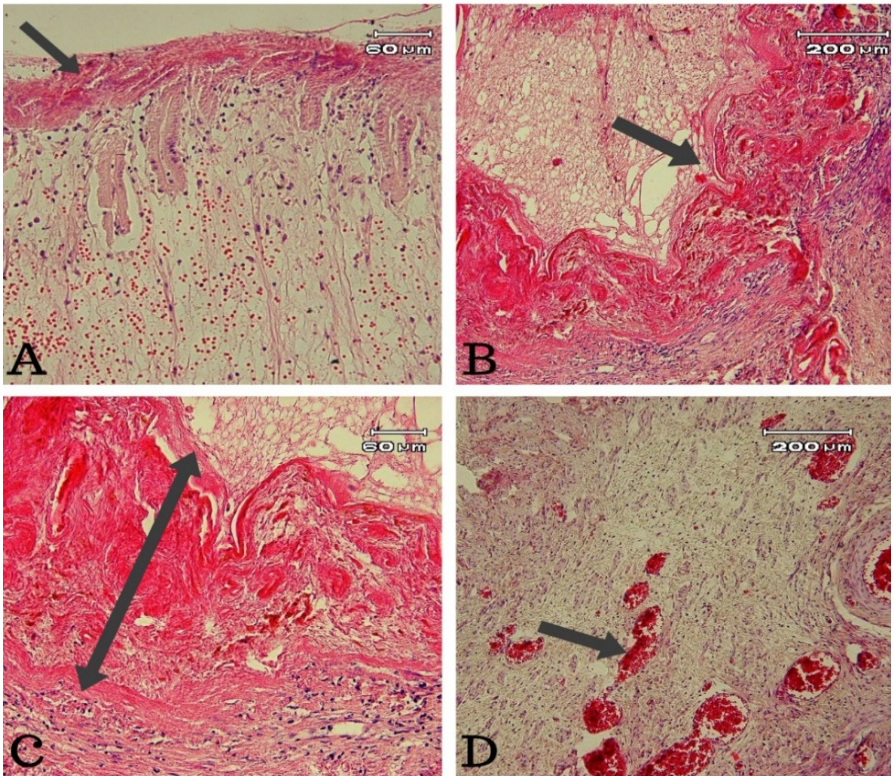

Figure 2.
Uterus of dogs, E and E+NS groups.
The figure shows extensive necrosis of the endometrial epithelium (arrows in A and B), accompanied by severe hemorrhage and hyperemia of the submucosal vessels (arrow in D). Additionally, there was a significant reduction in endometrial thickness due to necrosis and marked destruction (arrow in C) of the epithelium, submucosa, and uterine glands. H&E staining.

strated significant improvements in endometrial thickness, epithelial repair, and uterine gland density compared with the E group ($p < 0.05$). Conversely, the E+NS group showed no significant differences in these items compared with E group. The findings also indicated reduced severity of hemorrhage and necrosis in the E+PRP group compared with the E group, indicating a positive trend in improvement. In contrast, the E+NS group exhibited no changes or improvement trends relative to the E group. Furthermore, the levels of hyperemia and hemosiderosis in both the E+PRP and E+NS groups did not differ significantly from those in the E group (Table 1), though, E+PRP group showed relatively improved outcome (Figure 3).

Table 1.
Histopathologic findings in different experimental groups.

Parameter	Groups					
	E	E+NS	E+PRP	NS+PRP	Unit	P-values
Epithelial healing	10[a]	10[a]	90[b]	100[c]	%	0.025
Endometrial thickness (μm)	4.22 ± 0.91[a]	4.75 ± 1.73[a]	9.76 ± 3.41[b]	12.87 ± 4.67[c]	Mean ± SD	0.036
No. of uterus glands	3.19 ± 0.51[a]	4.22 ± 0.36[a]	21.50 ± 2.08[b]	37.62 ± 4.84[c]	Mean ± SD	< 0.0001
Hyperemia	2.0 (1.0-3.0)[a]	2.0 (1.0-2.0)[a]	1.0 (0.0-1.0)[a]	0.0 (0.0-0.0)[b]	Median (IQR)	0.025
Hemorrhage	3.0 (2.0-3.0)[a]	2.0 (2.0-3.0)[a]	1.0 (1.0-2.0)[b]	0.0 (0.0-0.0)[b]	Median (IQR)	0.036
Cellularity	2.0 (2.0-3.0)[a]	2.0 (1.0-2.0)[a]	1.0 (0.0-1.0)[b]	0.0 (0.0-1.0)[b]	Median (IQR)	0.052
Hemosiderosis	2.0 (1.0-2.0)[a]	2.0 (1.0-3.0)[a]	1.0 (0.0-1.0)a	0.0 (0.0-0.0)[b]	Median (IQR)	0.059
Necrosis	3.0 (2.0-3.0)[a]	2.0 (2.0-3.0)[a]	1.0 (1.0-2.0)[b]	0.0 (0.0-1.0)[b]	Median (IQR)	0.036

a,b,c: different letters in each row indicate statistically significant difference ($p < 0.05$)
NS: normal saline, E: ethanol, PRP: platelet rich plasma, IQR: interquartile ranges, SD: standard deviation.

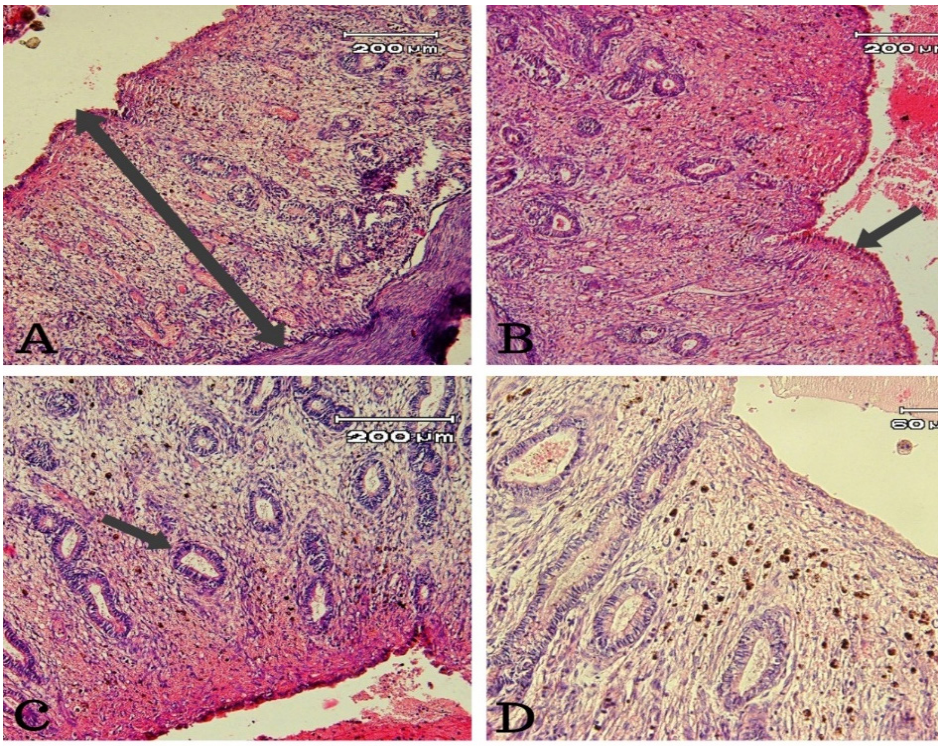

Figure 3.
Uterus of dogs, E+PRP group. This figure illustrates the improvement and repair of the submucosa (arrow in A) and increased cellularity, as well as significant healing of the endometrial epithelium (arrow in B) and regeneration of uterine glands (arrow in C). Additionally, the presence of hemosiderosis (brown cells in D) indicates prior bleeding and its subsequent healing. H&E staining.

Discussion

Endometrial thickness is a key factor in successful embryo implantation during in vitro fertilization procedures [17, 18]. Routine clinical causes of endometrial thinness include diminished production of VEGF and low levels of estrogen, leading to various proposed treatments; however, results have often been unsatisfactory [19]. Consequently, treating thin endometrium stays a significant problem in reproductive medicine.

In the present study, ethanol-induced endometrial atrophy in dogs was used as an experimental model to evaluate the beneficial impact of PRP on the thin endometrium. The results demonstrated that PRP increased the proliferation of endometrial mesenchymal and epithelial cells and facilitated blood vessel development, resulting in increased endometrial thickness and a more favorable environment for embryo implantation. Observations of uterine morphology

and histopathological examination further showed that the reparative effect of PRP extended beyond the change in endometrial thickness, as PRP treatment also improved uterus external morphology. PRP effectively improved uterine stricture and discoloration as a result of ethanol injury, returning the uterus to its normal condition. In the injured group, a decrease in the parameters including endometrial cells, glands, and blood vessels, along with epithelial cells loss, was observed. Conversely, in the group treated with PRP, these conditions improved, particularly in terms of glandular number and cell density. PRP may enhance endometrial receptivity by promoting cell proliferation, vascularization, and anti-inflammatory properties while reducing fibrosis, supported by concentrated peptides, growth factors, and cytokines, leading to improved endometrial thickness [8].

In all ethanol treated groups, hemosiderin deposits were observed within the endometrial tissue, indicating previous hemorrhage and erythrocyte degradation. Hemosiderosis is recognized as a histological marker of tissue injury and repair, reflecting phagocytosis of extravasated erythrocytes and iron accumulation within macrophages rather than ongoing necrosis [20, 21]. The presence of hemosiderin across groups, including those subsequently treated with PRP, indicates that vascular damage had occurred but was undergoing resolution, supporting the interpretation of healing rather than persistent injury.

Regenerative medicine, defined by Mason & Dunnill (2007), focuses on replacing or regenerating human tissue or organ cells to restore their normal function [22]. This innovative approach is particularly significant in treating chronic diseases that currently lack definitive cures. Key components of regenerative medicine include stem cells, growth factor-rich platelets, biological proteins, and gene therapy. The primary benefits of this treatment are its capability to regenerate tissue and the reduced risk of adverse reactions from allografts. Among the various cell types, platelet cells have garnered attention due to their rich growth factor content and ease of access [23]. Current research is exploring autologous blood products, such as PRP, to leverage the beneficial effects of growth factors in tissue repair. These growth factors release from alpha granules of the platelets, playing a fundamental role in the process of healing [24]. PRP acts as a source of chemical mediators during inflammation, releasing factors like VEGF, TGF, and EGF, which regulate migration of cells, adhesion, proliferation, and differentiation, while enhancing aggregation of the extracellular matrix [25, 26]. As was also shown in the present study; the utilization PRP has been shown to improve endometrial tissue in dogs. It is worth noting that its utilization has minimal risk of disease transmission or immune reactions due to its autologous preparation [27]. In this study, no infections or damage were observed following PRP injections.

The growth factors contained within PRP have established roles in angiogenesis, epithelial proliferation, and tissue repair. In canine PRP preparations, these mediators have been quantified at biologically active concentrations [28, 29], supporting their relevance in reproductive tissue remodeling. Mechanistically, VEGF promotes neovascularization within the endometrium, thereby improving blood supply, reducing hemorrhage and ischemic necrosis. PDGF stimulates stromal fibroblast and smooth muscle proliferation, facilitating extracellular matrix deposition and the expansion of endometrial thickness. In addition, TGF-β1 modulates epithelial stromal interactions and attenuates excessive inflammatory cellularity, contributing to a more organized tissue architecture. Collectively, these pathways provide a plausible explanation for the histological findings observed in this study, including increased endometrial thickness, improved glandular density, alongside reduced hemorrhage, cellular infiltration, and necrosis in the canine uterus under a thinned endometrium model. Although direct uterine studies in dogs are limited, the regenerative potential of PRP in canine tissues have been demonstrated in musculoskeletal and cutaneous healing contexts [30], and the same growth factor driven mechanisms can be reasonably extrapolated to endometrial repair. The present findings therefore align with the known biological activity of PRP growth factors in dogs and extend their application to reproductive physiology, highlighting PRP as a promising adjunct in managing endometrial insufficiency and related fertility disorders.

It is important to recognize that endometrial regeneration differs substantially between humans and dogs, reflecting divergent reproductive strategies. In women, the functional layer of the endometrium undergoes cyclic shedding during menstruation followed by rapid regeneration from basalis stem/progenitor cells, enabling scar free repair and receptivity for implantation [31]. In contrast, dogs are non menstruating species in which the endometrium undergoes hormonally driven remodeling characterized by prolonged proliferative and secretory phases, slow regression, and limited regenerative turnover. Canine reproductive pathology more commonly involves disorders such as cystic endometrial hyperplasia and pyometra rather than thin endometrium [20]. These species differences highlight why thin endometrium is a major clinical concern in human infertility compared to dogs. However, despite the paucity of similar studies on the canine endometrium, the results of the present study are comparable to those from human

studies. PRP administration resulted in significant rise in endometrial thickness and successful pregnancies in individuals with thinned endometrium [32, 33, 8], or during frozen embryo transfer cycles [34]. These findings align with the results of the current study.

Few studies have investigated the underlying mechanisms of PRP treatment. However, available evidence suggests that PRP may enhance endometrial receptivity by promoting cell proliferation, increasing vascularization, and exhibiting anti-inflammatory properties, while also reducing fibrosis. These effects are likely mediated by the concentrated peptides, growth factors, and cytokines present in PRP, which contribute to endometrial thickening [8]. A recent study by Montolío et al. (2025) analyzed growth factor concentrations in canine PRP preparations using canine-specific ELISA kits, and demonstrated significantly higher levels of TGF-β1 and PDGF-BB, with a strong positive correlation between platelet concentration and TGF-β1 levels. This suggests that the in house method effectively concentrates platelets and growth factors in products like PRP and platelet lysate, indicating that platelet concentration may predict specific growth factor levels [28]. Although fertility outcomes were not evaluated in the current study, the observed histomorphological improvements provide an important experimental basis for future in vivo fertility trials in dogs. Similarly, Puente et al. (2020) reported that PRP could regenerate endometrial tissue by enhancing vascularity and thickness, ultimately leading to successful pregnancies [35].

The regenerative effects observed in this study can also be compared with other biologic therapies investigated in canine regenerative medicine. Mesenchymal stem cells (MSCs) derived from adipose or endometrial tissues have demonstrated paracrine activity that promotes angiogenesis, modulates inflammation, and supports tissue repair. Canine endometrial MSCs, for example, have been characterized as multipotent and shown to exert cytoprotective effects through their secretome, suggesting potential utility in reproductive tract regeneration [36, 37]. Similarly, G CSF has been employed in canine models to mobilize progenitor cells and enhance hematopoietic recovery, with recombinant canine G CSF improving immune function and demonstrating systemic regenerative potential [38, 39]. Compared with these cell based or cytokine approaches, PRP offers a practical autologous source of growth factors such as PDGF, VEGF, and TGF-β1, which directly enhance vascular integrity, epithelial repair, and glandular regeneration. In the present study, PRP treatment reduced necrosis, improved endometrial thickness, and restored gland density, paralleling the beneficial outcomes reported with MSCs and G CSF, but with fewer technical challenges related to cell isolation, expansion, or recombinant cytokine administration. These findings support PRP as a feasible adjunctive therapy in canine uterine injury models.

Several limitations of the present study should be acknowledged. The relatively small sample size, selected in accordance with ethical principles aimed at minimizing animal use, limits the generalizability of the findings and supports classification of this work as a pilot study. Nevertheless, PRP with its reservoir of angiogenic and immunomodulatory growth factors, may offer novel adjunctive therapy for canine reproductive disorders. Although PRP has not yet been extensively investigated in conditions such as pyometra, postpartum subinvolution, or repeated breeding failure, its regenerative effects in other canine tissues [30] suggest potential benefits for restoring endometrial integrity and enhancing reproductive outcomes.

In summary, platelet-rich plasma was successfully utilized to treat ethanol-induced thin endometrium in dogs. Compared with untreated injured animals, platelet-rich plasma demonstrated the ability to improve thickness of the endometrium in dogs via rising the number of stromal glands and cells, diminution of fibrous areas, and elevating angiogenesis. In conclusion, this study offers both a theoretical and experimental foundation for the clinical application of PRP in treating thinned endometrium.

Materials and Methods

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this report, the authors used PopAi tool to rewrite some parts of the manuscript and check its grammar. After using this tool/service, the authors review and edit the content if needed and maintain full accountability and responsibility for the content of their work.

Ethical approval

All experimental procedures were performed in accordance with institutional and were approved by University/Regional Research Ethics Committee, University of Tabriz (approval ID: IR.TABRIZU.REC.1399.075).

Animals and study groups

In the present study, 12 healthy adult mixed breed dogs were included, with a mean body weight of 35 ± 4 kg and a mean age of 14 ± 2 months. The animals were maintained under controlled environmental conditions, at an average temperature of 25 °C and a 12-hour light/dark cycle. Commercial food and water were provided ad libitum throughout the study period. Only dogs in the anestrus phase of their sexual cycle were included in the study. Animals without vaginal discharge were selected for inclusion. Furthermore, those with small and smooth ovaries and quiescent uterus during laparotomy were entered to the study. To experimentally induce weak endometrium and endometrial damage, 95% ethanol was administered into the uterus, according to

previously described methods [40, 41]. The dogs were randomly assigned into four experimental groups: Group 1 (E) underwent 95% ethanol injection into uterine horns to induce endometrial damage; Group 2 (E+NS) received normal saline 72 hours after the uterine injury; Group 3 (E+PRP) received platelet-rich plasma 72 hours post-injury; and Group 4 (NS+PRP) received normal saline in both uterine horns and platelet-rich plasma 72 hours after initial injection.

Preparation of platelet-rich plasma

To prepare PRP, 20 ml blood was collected from the cephalic vein using a sodium citrate tube. The blood samples were subsequently underwent centrifugation at 1000 × g for 5 minutes, resulting in the formation of three distinct layers: platelets and white blood cells formed the upper layer, the buffy coat which is full of white blood cells was the middle layer, and the red blood cells formed the lower layer. The upper and middle layers were carefully transferred into a sterile tube to obtain leukocyte rich PRP. The separated plasma underwent a second centrifugation at 1500× g for 15 minutes using a double-spin protocol. Following centrifugation, the upper two-thirds of the platelet-poor plasma was discarded, leaving 3 ml above the pellet. The remaining pellets, which represent the platelet-rich plasma, were then homogenized and resuspended in the residual plasma to obtain about 5.3× the baseline concentration [42, 43].

Preoperative preparation and exploratory laparotomy

Exploratory laparoscopy was utilized for administration of ethanol, normal saline, and platelet-rich plasma into the uterine horns. Prior to the procedure, premedication was administered with 0.05 mg/kg of 1% acepromazine (IM, Alfasan, Worden, The Netherlands). General anesthesia was induced using 5 mg/kg of 10% ketamine (IM, Alfasan, Worden, The Netherlands) and 0.25 mg/kg of 0.5% diazepam (IV, Kimia Daru, Iran). Following endotracheal intubation, anesthesia was maintained with halothane in oxygen (Halothane BP, Nicholas Piramal India limited, India). During surgery, intravenous serum therapy was administered using 0.9% normal saline (Sodium Chloride, I.P.P.C., Tehran, Iran) together with 1 g cefazolin (Cefazolin-Exir, Exir Co., Tehran, Iran). The surgical site was prepared aseptically, and an incision was made through the linea alba to access the abdominal cavity. After identification of the uterine horns, 3 to 5 ml of either non-toxic 95% ethanol (Groups E, E+NS; and E+PRP) or normal saline (Group NS+PRP) was injected into each horn. A second Laparotomy was performed 72 hours later as previously described, and 0.5 to 1 ml of normal saline (Group E+NS) or PRP (Groups E+PRP and NS+PRP) was injected into uterine horns, except for group E in which ovariohysterectomy was carried out at this second surgery for tissue collection . The abdominal wall was then sutured in three layers. Following the intrauterine injections and surgery, the dogs were monitored for their general condition and appetite.

In the experimental groups, ovariohysterectomy was conducted to collect uterine horn samples. Premedication and general anesthesia were administered as in previous surgeries. After incising the linea alba and locating the uterine horns, the ovarian pedicles were transected using the two-forceps technique. The broad ligament and arteries were ligated and cut. A sample was then taken from the bifurcation of the uterus after the uterine body was transected using transfixation and simple ligatures. An incision was made at the bifurcation and the sample placed in 10% formalin. The abdominal wall was sutured in three layers. The sutures were removed two weeks after surgery, during which the dogs were monitored for their general condition and appetite.

Tissue sampling and histopathologic studies

In group E, tissue sampling was performed 72 hours after the injection of 95% ethanol. For the E+NS, E+PRP, and NS+PRP groups, which assessed the effects of normal saline and platelet-rich plasma in uteri with damaged endometrium, or PRP effects in normal endometrium, ovariohysterectomy was performed 14 days after the final intrauterine injections. Collected uterine tissues were transferred to the pathology laboratory for sampling, sectioning, and slide preparation. Samples were fixed in 10% buffered formalin at a volume at least ten times that of the samples. After 24 hours, the formalin was replaced, and sections were prepared from the uterine tissue for processing. The tissue preparation steps included dehydration using ascending alcohol concentrations, clarification with xylene, and removal of alcohol, followed by embedding in molten paraffin. Sections of 4 to 5 µm in thickness were prepared using a microtome, placed in an oven at 56 °C for thirty minutes, and then stained with hematoxylin and eosin. The prepared slides were evaluated by a pathologist unaware of the groups, using a conventional light microscope (Olympus-CH30, Japan) for endometrial thickness, epithelial healing, and uterine gland density. Other potential pathologic lesions, including necrosis, hyperemia, hemorrhage, cellularity, and hemosiderosis, were also examined. The mean of 3 measurements per uterine horn were calculated to account for heterogeneity. In cases where no lesions were observed, the normal state was assigned a grade of 0, mild lesions got a grade of 1, moderate lesions were given a grade of 2, and severe lesions obtained a grade of 3.

Statistical analysis

Quantitative data were analyzed using ANOVA, while the observed histopathological findings were considered semi-quantitative data, analyzed through non-parametric methods including Kruskal-Wallis for between-group comparisons, followed by post-hoc Dunn's tests for pairwise differences. SPSS statistical software (SPSS for Windows, Version 22, Inc., Chicago, Illinois, USA) was utilized to analyse the data, with a confidence level set at 95%. A P-value of less than 0.05 was accepted as statistically significant .

Authors' Contributions

R.A. and A.H.K. conceived and planned the experiments. R.A., A.H.K., S.H.J. and M.K. carried out the experiments. A.H.K., S.H.J. and M.K. contributed to sample preparation. R.A. and S.K.D. contributed to the interpretation of the results. S.K.D. took the lead in writing the manuscript. All authors provided critical feedback and helped shape the research, analysis and manuscript.

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Competing Interests

The authors declare that there is no conflict of interest.

References

1. Critchley HO, Maybin JA, Armstrong GM, Williams AR. Physiology of the endometrium and regulation of menstruation. Physiol Rev. 2020;100(3):1149-79. Doi:10.1152/physrev.00031.2019.

2. Ganieva U, Schneiderman S, Bu P, Beaman K, Dambaeva S. IL-22 regulates endometrial regeneration by enhancing tight junctions and orchestrating extracellular matrix. Front Immunol. 2022;13:955576. Doi: 10.3389/fimmu.2022.955576.

3. Goharitaban S, Abedelahi A, Hamdi K, Khazaei M, Esmaeilivand M, Niknafs B. Role of endometrial microRNAs in repeated implantation failure (mini-review). Front Cell Dev Biol. 2022;10:936173. Doi:10.3389/fcell.2022.936173.

4. Moffat R, Beutler S, Schötzau A, De Geyter M, De Geyter C. Endometrial thickness influences neonatal birth weight in pregnancies with obstetric complications achieved after fresh IVF–ICSI cycles. Arch Gynecol Obstet. 2017;296:115-22. Doi: 10.1007/s00404-017-4411-z.

5. Zhang S, Gong TT, Liu FH, Jiang YT, Sun H, Ma XX, et al. Global, regional, and national burden of endometrial cancer, 1990–2017: results from the global burden of disease study, 2017. Front Oncol. 2019;9:1440. Doi:10.3389/fonc.2019.01440.

6. Guo J, Liu S, Wang P, Ren H, Li Y. Characterization of VDR and CYP27B1 expression in the endometrium during the menstrual cycle before embryo transfer: implications for endometrial receptivity. Reprod Biol Endocrinol. 2020 ;18(1):24. Doi:10.1186/s12958-020-00579-y.

7. Liu X, Qian C, Jiang X, Zhou Y, Feng X, Ding Y, et al. Efficacy of platelet-rich plasma in the treatment of thin endometrium: a meta-analysis of randomized controlled trials. BMC Pregnancy Childbirth. 2024;24(1):567. Doi:10.1186/s12884-024-06741-3.

8. Lin Y, Qi J, Sun Y. Platelet-rich plasma as a potential new strategy in the endometrium treatment in assisted reproductive technology. Front Endocrinol. 2021;12:707584. Doi:10.3389/fendo.2021.707584.

9. Liu KE, Hartman M, Hartman A, Luo ZC, Mahutte N. The impact of a thin endometrial lining on fresh and frozen–thaw IVF outcomes: an analysis of over 40,000 embryo transfers. Hum Reprod. 2018;33(10):1883-8. Doi:10.1093/humrep/dey281.

10. Mahutte N, Hartman M, Meng L, Lanes A, Luo ZC, Liu KE. Optimal endometrial thickness in fresh and frozen-thaw in vitro fertilization cycles: an analysis of live birth rates from 96,000 autologous embryo transfers. Fertil Steril. 2022;117(4):792-800. Doi:10.1016/j.fertnstert.2021.12.025.

11. Pascottini OB, Aurich C, England G, Grahofer A. General and comparative aspects of endometritis in domestic species: A review. Reprod Domest Anim. 2023;58(Suppl 2):49-71. Doi:10.1111/rda.14390 .

12. Barad DH, Yu Y, Kushnir VA, Shohat-Tal A, Lazzaroni E, Lee HJ, et al. A randomized clinical trial of endometrial perfusion with granulocyte colony-stimulating factor in in vitro fertilization cycles: impact on endometrial thickness and clinical pregnancy rates. Fertil Steril. 2014;101(3):710-5. Doi: 10.1016/j.fertnstert.2013.12.016.

13. Li Y, Pan P, Chen X, Li L, Li Y, Yang D. Granulocyte colony-stimulating factor administration for infertile women with thin endometrium in frozen embryo transfer program. Reprod Sci. 2014;21(3):381-5. Doi:10.1177/1933719113497286

14. Gharibeh N, Aghebati-Maleki L, Madani J, Pourakbari R, Yousefi M, Ahmadian Heris J. Cell-based therapy in thin endometrium and Asherman syndrome. Stem Cell Res Ther. 2022;13(1):33. Doi:10.1186/s13287-021-02698-8.

15. Patel A, Sharma PS, Narayan P, Binu VS, Dinesh N, Pai PJ. Prevalence and predictors of infertility-specific stress in women diagnosed with primary infertility: A clinic-based study. J Hum Reprod Sci. 2016;9(1):28-34. Doi: 10.4103/0974-1208.178630.

16. Yu JH, Tong CJ, Huang QD, Ye YL, Chen G, Li H, et al. Long-term outcomes of pelvic exenterations for gynecological malignancies: a single-center retrospective cohort study. BMC Cancer. 2024;24(1):88. Doi:10.1186/s12885-024-11836-3.

17. Aghdam SH, Ghasemzadeh A, Farzadi L, Hamdi K, Navali N, Hakimi P, et al. Growth hormone: A potential treatment of patients with refractory thin endometrium: A clinical trial study. Int J Fertile Steril. 2022;16(4):251-5. Doi:10.22074/ijfs.2022.541389.1210.

18. Zheng Y, Chen B, Dai J, Xu B, Ai J, Jin L, et al. Thin endometrium is associated with higher risks of preterm birth and low birth weight after frozen single blastocyst transfer. Front Endocrinol. 2022;13:1040140. Doi:10.3389/fendo.2022.1040140.

19. Xie W, Zhou P, Qu M, Dai Z, Zhang X, Zhang C, et al. Ginsenoside Re attenuates high glucose-induced RF/6A injury via regulating PI3K/AKT inhibited HIF-1α/VEGF signaling pathway. Front Pharmacol. 2020;11:695. Doi:10.3389/fphar.2020.00695.

20. Schlafer DH. Diseases of the canine uterus. Reprod Domest Anim. 2012;47:318-322. Doi:10.1111/rda.12064.

21. Cesta MF. Normal structure, function, and histology of the spleen. Toxicol Pathol. 2006;34(5):455-465. Doi:10.1080/01926230600867743.

22. Mason C, Dunnill P. A brief definition of regenerative medicine. Regen Med. 2008;3(1):1-5. Doi:10.2217/17460751.3.1.1.

23. Anitua E, Sánchez M, Orive G, Andía I. The potential im-

pact of the preparation rich in growth factors (PRGF) in different medical fields. Biomaterials. 2007;28(31):4551-60. Doi:10.1016/j.biomaterials.2007.06.037.

24. Cole BJ, Seroyer ST, Filardo G, Bajaj S, Fortier LA. Platelet-rich plasma: where are we now and where are we going?. Sports Health. 2010;2(3):203-10. Doi:10.1177/1941738110366385.

25. Silva RF, Carmona JU, Rezende CM. Comparison of the effect of calcium gluconate and batroxobin on the release of transforming growth factor beta 1 in canine platelet concentrates. BMC Vet Res. 2012;8:121. Doi:10.1186/1746-6148-8-12.

26. Simoni M, Taylor HS. Therapeutic strategies involving uterine stem cells in reproductive medicine. Curr Opin Gynecol Obstet. 2018;30(3):209-16. Doi:10.1097/GCO.0000000000000457.

27. Freire V, Andollo N, Etxebarria J, Durán JA, Morales MC. In vitro effects of three blood derivatives on human corneal epithelial cells. Invest Ophthalmol Vis Sci. 2012;53(9):5571-78. Doi:10.1167/iovs.11-7340.

28. Montolío M, Herrera D, Roque AI, Franch J. Growth factor concentration in canine platelet-rich plasma and platelet lysate is correlated with platelet number. Comp Clin Pathol. 2025;34:645–653. Doi:10.1007/s00580-025-03674-x.

29. Lunardon T, Sumner SM, Mollabashi M, Darzenta N, Davis E, Naskou MC. Growth factor and cytokine characterization of canine platelet lysate with variable leukocyte concentration, plasma content, and heat-sensitive proteins. Front Vet Sci. 2024 ;11:1408080. Doi:10.3389/fvets.2024.1408080.

30. Sharun K, Jambagi K, Dhama K, Kumar R, Pawde AM. Therapeutic Potential of Platelet-Rich Plasma in Canine Medicine. Arch Razi Inst. 2021;76(4):721–730. Doi:10.22092/ari.2021.355953.1749.

31. Cousins FL, Filby CE, Gargett CE. Endometrial stem/progenitor cells–their role in endometrial repair and regeneration. Front Reprod Health. 2022;3:811537. Doi:10.3389/frph.2021.811537.

32. Chang Y, Li J, Chen Y, Wei L, Yang X, Shi Y, et al. Autologous platelet-rich plasma promotes endometrial growth and improves pregnancy outcome during in vitro fertilization. Int J Clin Exp Med. 2015;8(1):1286-90.

33. Nazari L, Salehpour S, Hoseini S, Zadehmodarres S, Azargashb E. Effects of autologous platelet-rich plasma on endometrial expansion in patients undergoing frozen-thawed embryo transfer: A double-blind RCT. Int J Reprod Med. 2019;17(6):443-8. Doi:10.18502/ijrm.v17i6.4816.

34. Kim H, Shin JE, Koo HS, Kwon H, Choi DH, Kim JH. Effect of autologous platelet-rich plasma treatment on refractory thin endometrium during the frozen embryo transfer cycle: a pilot study. Front Endocrinol. 2019;10:61. Doi:10.3389/fendo.2019.00061.

35. Puente Gonzalo E, Alonso Pacheco L, Vega Jiménez A, Vitale SG, Raffone A, Laganà AS. Intrauterine infusion of platelet-rich plasma for severe Asherman syndrome: a cutting-edge approach. Updates Surg. 2021;73(6):2355-62. Doi: 10.1007/s13304-020-00828-0.

36. Phyo H, Aburza A, Mellanby K, Esteves CL. Characterization of canine adipose-and endometrium-derived mesenchymal stem/stromal cells and response to lipopolysaccharide. Front Vet Sci. 2023;10:1180760. Doi:10.3389/fvets.2023.1180760.

37. Vikartovska Z, Maloveska M, Nosalova N, Hornakova L, Huniadi M, Hudakova N, Hornak S, Kalinaj B, Kubatka P, Cizkova D. Canine endometrial mesenchymal stem cells: characterization and functional assessment for cartilage repair. Int J Mol Sci. 2025;26(16):8091. Doi:10.3390/ijms26168091.

38. Ogilvie GK, Obradovich JE, Cooper MF, Walters LM, Salman MD, Boone TC. Use of recombinant canine granulocyte colony-stimulating factor to decrease myelosuppression associated with the administration of mitoxantrone in the dog. J Vet Intern Med. 1992;6(1):44-47. Doi:10.1111/j.1939-1676.1992.tb00985.x.

39. Colijn C, Foley C, Mackey MC. G-CSF treatment of canine cyclical neutropenia: a comprehensive mathematical model. Exp Hematol. 2007;35(6):898-907. Doi:10.1016/j.exphem.2007.02.015.

40. Jing Z, Qiong Z, Yonggang W, Yanping L. Rat bone marrow mesenchymal stem cells improve regeneration of thin endometrium in rat. Fertil Steril. 2014;101(2):587-94. Doi: 10.1016/j.fertnstert.2013.10.053.

41. Zhao J, Gao H, Li Y. Development of an animal model for thin endometrium using 95% ethanol. J Fertil In Vitro. 2012;2(4):109. Doi: 10.4172/2165-7491.1000109.

42. Shin HS, Woo HM, Kang BJ. Optimisation of a double-centrifugation method for preparation of canine platelet-rich plasma. BMC Vet Res. 2017;13(1):198. Doi:10.1186/s12917-017-1123-3.

43. Perazzi A, Busetto R, Martinello T, Drigo M, Pasotto D, Cian F, Patruno M, Iacopetti I. Description of a double centrifugation tube method for concentrating canine platelets. BMC Vet Res. 2013;9(1):146. Doi:10.1186/1746-6148-9-146.

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