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A game-changer in enhancing Endometrium Health - *Uttara Basti* as a promising alternative to PRP therapy & G-CSF instillation with superior impact on Thin Endometrium Cases

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ABSTRACT

A healthy conception results due to the influence of *Ritu, Kshetra Abu, Bija Samyoga, Garbha Sambhava Samagri* as mentioned in Ayurvedic classics, any defect in the above component can lead to *Vandyatwa*. *Kshetra* is one of the most important factors that may have its impact on conception and growing fetus as well as it is considered as the site of implantation in the *Garbhashaya* which bears the fruit of conception and can be considered endometrium. Endometrium if unhealthy or thin can impact on maintaining the balance of *Artavavaha Sroto* function. Hence, we need to explore the function of endometrium and the pathogenesis related to it. In Ayurveda among the various *Stanika* procedures, *Uttara Basti* specifically stands out as a highlighted and well-practiced therapy for addressing infertility by promoting endometrial growth and enhance embryo implantation. The specific formulation mentioned in Ayurvedic classics contains drugs which are having *Garbhasthapana* actions and they also have *Brumhaniya* properties which have its action on correcting endometrium.

Key words: Endometrium Health, Uttara Basti, Thin Endometrium, Garbhasthapana, Arthavavaha Srotas

INTRODUCTION

Endometrial health issues are recently growing concern in the gynecology practice where most of the infertile couple seek consultation. The World Health Organization estimates that 60 - 80 million couples worldwide currently suffer from infertility. Infertility varies across the regions of the world and is estimated

to affect 8% - 12% of couples worldwide.^[3] According to the International Federation of Gynecology and Obstetrics manual (2015), the causes are peritoneal factors (35%), tubal factors (30%), ovulatory factor (20%), and uterine factor (15%). Among these uterine factors, as-endometrial abnormalities play an important role in the causation of infertility. The majority of times unexplained infertility is associated with endometrium morphology.

In the realm of reproductive health, two significant terms are "endometrium" and "thin endometrium." The endometrium refers to the tissue lining the innermost part of the uterus. On the other hand, a thin endometrium is characterized by this tissue being thinner than the usual thickness. While a normal endometrium is typical, a thin endometrium can pose challenges for fertility and pregnancy. Implantation is a crucial stage where the blastocyst attaches to the endometrium during the secretory phase of the menstrual cycle. The interaction between the

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developing embryo and maternal tissue is pivotal for the successful completion of the implantation process. For successful embryo implantation, an endometrium should normally have a thickness of 8 mm or more. A thin endometrium is one that has a thickness of less than 6 mm. This Endometrium can be understood as *Kshetra* where *Arthava* has its role.

Arthava is the *Upadhatu* of *Rasa* and its function depends directly based on *Rasadhatavagni* which is the important factor maintaining metabolism at the level of *Upadhatu Arthava*. Hence the treatment aims at not only improving the endometrial health related to *Arthava* but also aims to maintain the function of *Agni*, *Rasa* and *Rasa Dhatavagni*.

Hence the treatment modality what we adopt aims to improve the quality and quantity of endometrium. *Uttara Basti* plays a vital role in improving all the aspects related to *Kshetra* and correcting the vitiated *Vata* and improving the *Sthanika Raja* in terms of endometrial tissue.

Causes of thin Endometrium

- 1. Hormonal Imbalance:** Fluctuations in hormone levels, particularly estrogen and progesterone, can affect the thickness of the endometrium. Low levels of estrogen, for example, can lead to inadequate growth of the endometrial lining.
- 2. Medical Conditions:** Certain medical conditions such as polycystic ovary syndrome (PCOS), endometriosis, or thyroid disorders can impact the thickness of the endometrium.
- 3. Age:** As women age, especially approaching menopause, hormonal changes can lead to a thinner endometrial lining.
- 4. Uterine Factors:** Structural abnormalities of the uterus, such as scarring from previous surgeries or infections, can hinder the growth of the endometrium.
- 5. Medications and Treatments:** Certain medications, such as those used for cancer treatment (chemotherapy or radiation therapy),

can affect the thickness of the endometrium. Additionally, prolonged use of hormonal contraceptives may influence endometrial thickness.

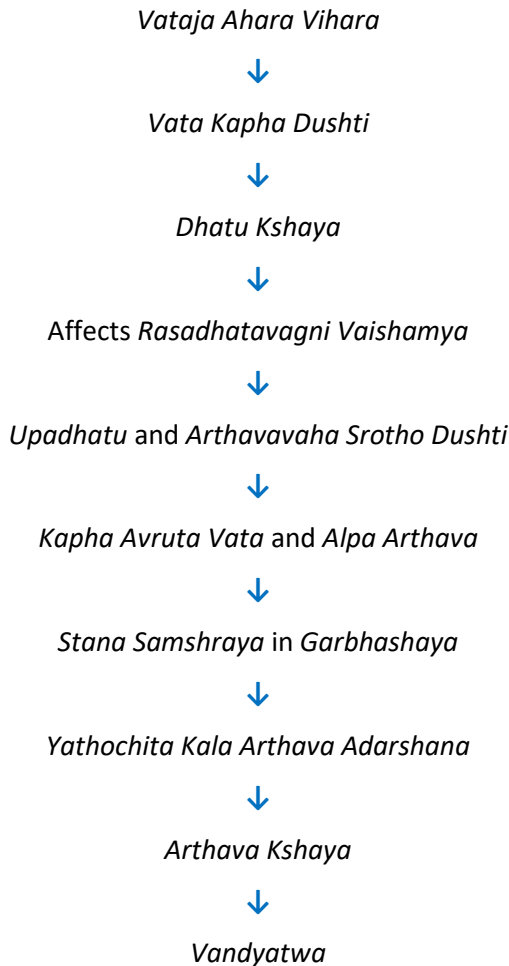
- 6. Lifestyle Factors:** Smoking, excessive alcohol consumption, poor nutrition, and extreme exercise can all impact hormone levels and consequently affect the thickness of the endometrium.
- 7. Reproductive Disorders:** Conditions like Asherman's syndrome, characterized by intrauterine adhesions, can lead to a thin endometrium due to scar tissue formation.
- 8. Chronic Illness:** Chronic conditions such as diabetes or autoimmune disorders can indirectly affect endometrial health by disrupting hormonal balance or compromising overall health⁹.
- 9. Infections:** Infections of the reproductive system, such as pelvic inflammatory disease (PID), can cause inflammation and scarring, which may affect the endometrium.
- 10. Environmental Factors:** Exposure to environmental toxins or pollutants may have an impact on reproductive health, potentially influencing endometrial thickness.

Idiopathic: cases suggest that thin endometrium may not always be linked to a specific disease process. It can be influenced by individual uterine architecture or intrinsic properties of the endometrium affecting its growth.

Miwa *et al.* (2009) demonstrated that thin endometrium is characterized by poor growth of glandular epithelium, high uterine blood flow impedance, reduced vascular endothelial growth factor (VEGF) expression, and inadequate vascular development. They proposed that elevated blood flow impedance in radial arteries acts as a trigger, impairing glandular epithelium growth, leading to decreased VEGF levels. The resulting low VEGF levels further hinder vascular development, creating a detrimental cycle that ultimately results in a thin endometrium.

Understanding these potential causes can help us diagnose and address thin endometrium, potentially improving fertility outcomes for affected individuals.

Samprapti Ghataka of thin Endometrium according to Ayurveda

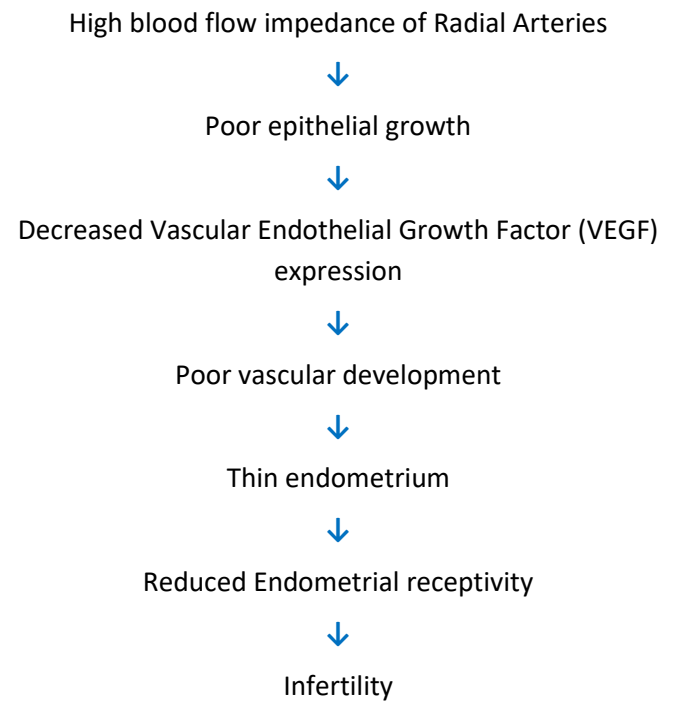


Samprapti Ghatakas

- Doshas - Vata Kapha (Vata Pradhana)
- Dushyas - Rasa, Rakta and Artava
- Agni - Jataragni, Dhatwagni
- Agni Dushti - Jatargni Mandya, Dhatavagni Mandya
- Srotas - Rasavaha, Raktavaha and Artavaha Srotas
- Srothodushti - Sanga
- Sanchara Staana - Rasavaha, Raktavaha and Artavaha Srotas
- Udbhava Staana - Aamashaya

- Vyakta Staana - Garbhashaya
- Adhishtana - Garbhashaya
- Vyadhi Marga - Abhyantara
- Sadya Asadhyatwa - Sadhya

Pathology of Thin Endometrium leading to Infertility^[6]



Understanding the Concept of Uttara Basti, G-CSF Instillation and PRP therapy

Uttara Basti

"Uttara Basti" is a combination of two words, namely 'Uttara' and 'Basti'. Analyzing the components, the prefix 'ut' in 'Uttara' conveys a sense of superiority, indicating an elevated status for Uttara Basti. The suffix 'Tara' is employed to signify a comparatively superior or improved state. Administering Uttara Basti during the Ritu Kala, akin to the menstrual proliferative phase, is considered ideal. During this period, blood vessel stumps break, and new arterioles grow, facilitating easy absorption of administered drugs. The broken glands further enhance absorption possibilities. Utilizing oil-based solutions ensures slow absorption. Uttara Basti exhibits various actions, including effects on blood vessels, haemostasis, and coagulation. It also stimulates the uterus and shows systemic actions like anti-estrogenic effects. In simpler terms, giving Uttara

Basti during *Rutu Kala* allows for effective absorption and beneficial actions in the body.

Granulocyte Colony-Stimulating Factor

G-CSF, or granulocyte colony-stimulating factor, is a glycoprotein produced by various cells such as bone marrow cells, stromal cells, mononuclear cells, fibroblasts, natural killer (NK) cells, and endometrial cells. Its primary function involves stimulating the growth and differentiation of neutrophils within the bone marrow and regulating their release into the bloodstream. The discovery and purification of G-CSF in mice date back to 1983, and its human form was subsequently cloned three years later in 1986.

G-CSF appears to modulate certain neutrophil functions as well as the distribution of neutrophils and progenitor cells within the body. G-CSF possesses unique and interesting characteristics among the family of hematopoietic growth factors.^[1]

Platelet rich plasma (PRP)

Platelet rich plasma (PRP) has gained a lot of acceptance, being a non-operative treatment for multiple medical disorders. In orthopaedics along with sports medicine it is being used routinely for pain relief via the promotion of natural healing in musculoskeletal et al diseases like arthritis, tendonitis, ligamentous strains and tears. Especially PRP injections have been used for athletic injuries, resulting in exceptional healing with rapid return to routine activities with complete pain relief.^[2]

Autologous PRP is derived from an individual’s whole blood, then centrifuged to remove red blood cells. The remaining plasma has a 5-10 times greater concentration of growth factors as compared to whole blood.

PRP Composition & Activation

PRP, or platelet-rich plasma, is composed of platelets rich in cytokines and growth factors stored within α-granules. These growth factors include Platelet-derived growth factor (PDGF), insulin-like growth factors (IGF), vascular endothelial growth factors (VEGF), platelet-derived angiogenic factor, epidermal growth factors

(EGF), connective tissue growth factor (CTGF), transforming growth factor-beta (TGF-β), fibroblast growth factors (FGF), and interleukin-8. Additionally, platelets contain substances like fibronectin, vitronectin, and sphingosine-1-phosphate that initiate the wound healing process.^[3,4]

The activation of platelets induces the release of growth factors through various stimuli or substances such as thrombin, calcium chloride, and collagen. Each activation method influences both the physical composition of PRP and the quantity of released growth factors, including the kinetics of their release. Currently, there is no established evidence regarding the ideal concentrations of activators required to achieve optimum growth factor release during the PRP activation process. Consequently, varying concentrations may yield diverse results.

Indications of Uttara Basti /G-CSF instillation and PRP therapy in Infertility

Uttara Basti	G-CSF Instillation	PRP
1. <i>Anartava</i>	1. Recurrent Implantation Failure (RIF)	Its application in reproductive medicine, specifically for treating infertility, is an area of ongoing research. There is limited scientific evidence supporting the use of PRP in the context of infertility, and its efficacy and safety for such purposes are not well-established.
2. <i>Rajo Dosha</i>		
3. <i>Yoni Dosha</i>	2. Thin Endometrium	
4. <i>Vandhyatwa</i>		
5. <i>Vataja Yoni Vyapad</i>	3. Recurrent Pregnancy Loss (RPL)	
6. <i>Kapha Vataja Yoni Vyapad</i>		
7. <i>Putraghni</i>		
8. <i>Arthava Dushti</i>		

Management of Thin Endometrium in infertility and a Review on Mode of Action of Uttara Basti and analysing the effect of G-CSF and PRP therapies.

Based on the *Aushadi Taila/Kashaya/Ghritha*, Mostly we select *Vatahara Dravyas* as *Yonivyapad* and *Vandyatwa* arises due to *Vataja Dushti*.

For Example: *Phalaghritha* is indicated in *Vandyatwa* where the woman presents with thin endometrium and low receptivity.

As *Phalaghritha* contains, Ref. *Ashtanga Hrudaya Uttarasthana 34/63-67*

<i>Manjishta</i>	<i>Rubia cordifolia</i>	<i>Guru, Ruksha, Kapha Pitta Shamaka</i>
<i>Kushta</i>	<i>Saussurea lappa</i>	<i>Laghu, Ruksha, Tikshnakapha Vata Shamaka</i>
<i>Tagara</i>	<i>Valerina wallichii</i>	<i>Laghu, Snigdha, Kapha Vata Shamaka</i>
<i>Haritaki</i>	<i>Terminalia chebula</i>	<i>Laghu, Ruksha, Tridosha Shamaka</i>
<i>Vibhitaki</i>	<i>Terminalia bellerica</i>	<i>Ruksha, Laghu Balances Kapha and Pitta</i>
<i>Amalaki</i>	<i>Phyllanthus bellirica</i>	<i>Guru, Sheeta, Tridosha Hara</i>
<i>Vacha</i>	<i>Acorus calamus</i>	<i>Laghu Tikshna, Khapha Vata Shamaka</i>
<i>Haridra</i>	Turmeric	<i>Ruksha, Laghu Kapha Vata Shamaka</i>
<i>Daruharidra</i>	<i>Berberis aristata</i>	<i>Tikta, Kahaya, Kapha Pitta Shamaka</i>
<i>Madhuka</i>	<i>Glycyrrhiza</i>	<i>Guru, Snigdha, Vata Pitta Shamaka</i>
<i>Meda</i>	<i>Polygonatum cirrhifolium</i>	<i>Guru, Vata Pitta Shamaka, Kapha Vardhaka</i>
<i>Dipyaka</i>	<i>Trachyspermum roxburghianum</i>	<i>Laghu, Ruksha, Tikshna, Kapha Vata Hara</i>
<i>Katurohini</i>	<i>Trachyspermum roxburghianum</i>	<i>Ruksha, Laghu, Kapha Pitta Shamaka</i>
<i>Payasya</i>	<i>Ipomea Mauritian</i>	
<i>Kakoli</i>	<i>Roscoea procera</i>	<i>Guru Snigdha, Kapha Kara, Vata Pitta Shamaka</i>
<i>Vajigandha</i>	<i>Withania somnifera</i>	

<i>Shatavari</i>	<i>Asparagus racemosus</i>	<i>Guru, Snigdha, Vata Pitta Shamaka</i>
<i>Hingu</i>	Asafoetida	
<i>Sharkara</i>	Sugar	
<i>Ghritha</i>	Ghee	
<i>Ksheera</i>	Milk	

Chemical Composition of *Ghritha* contains plant and animal protein which function locally and builds tissue, corrects cellular functions and target endometrial tissue which helps in developing the endometrial lining.

Other drugs and combinations which can be used in Uttara Basti are as follows

Bhrami Gritha

Kalyanaka Ghritha

Shatavari Ghritha

Dhatri Ghritha

Panchagavya Ghritha

Kasisadi Taila

Ksharataila

Ksheera Bala Taila

Balaashwagandhadi Taila

A. Mode of action of Uttara Basti in Ayurveda on thin Endometrium

The mode of action of *Uttara Basti* in thin endometrium cases involves several key principles from Ayurvedic philosophy and therapeutics:

1. Pacification of Vata Dosha: According to *Ayurveda*, imbalances in the *Vata Dosha*, one of the three fundamental dosha governing the body, can lead to *Rookshata*, *Dhatu Kshaya* thus leading to thinning of tissues, including the endometrium. *Uttara Basti* is believed to have *Vatahara* property and provides *Balya* and *Bruhmana* effects to the endometrial tissue. The *Dravyas*, *Ghritha* and *Taila* preparations used in *Uttara Basti* are specifically selected to counteract vitiation of *Vata Dosha* and promote the restoration of healthy tissue function.

2. Strengthening and Nourishing the Endometrium:

The *Ayurvedic* formulations used in *Uttara Basti* are *Balya* and *Brihmana* in nature thus nourish the endometrial tissue. These formulations typically contain *Dravyas* with properties that support tissue regeneration, enhance blood circulation to the pelvic organs, and promote hormonal balance. By providing essential nutrients and important constituents directly to the endometrium, thus helps in improve the endometrial thickness and overall health.

3. Enhancing Uterine Blood Flow: *Uttara Basti* therapy is thought to enhance blood circulation to the uterus and pelvic region. Improved blood flow delivers vital nutrients, oxygen, and bioactive compounds to the endometrium, facilitating its growth and repair. Increased blood circulation also aids in the removal of metabolic wastes and toxins, promoting a healthier uterine environment conducive to optimal endometrial thickening.

4. Balancing Hormonal Function: *Ayurveda* herbs and drugs used in *Uttara Basti* formulations possess hormonal modulating properties, helping to balance hormonal function in the body. Hormonal imbalances can contribute to thin endometrium by disrupting the normal menstrual cycle and impairing endometrial growth. *Uttara Basti* aims to restore hormonal equilibrium, supporting the natural processes of endometrial thickening and regeneration.

5. Promoting Relaxation and Stress Reduction: Stress and emotional factors can influence hormonal balance and uterine function, potentially affecting endometrial health. *Uttara Basti* therapy incorporates principles of relaxation and stress reduction through its gentle and nurturing approach. The therapeutic process of *Uttara Basti*, including the warm medicated oils and supportive environment, promotes relaxation of the pelvic muscles and nervous system, which may indirectly benefit endometrial thickness and receptivity.

B. Mode of action of G-CSF Instillation on thin Endometrium

The mode of action of G-CSF in this context involves several mechanisms

1. Endometrial Regeneration: G-CSF has been shown to promote the proliferation and regeneration of endometrial tissue. By stimulating the growth and repair of the endometrium, G-CSF can help increase its thickness and improve its receptivity to embryo implantation.

2. Angiogenesis: G-CSF has angiogenic properties, meaning it can stimulate the formation of new blood vessels (angiogenesis) within the endometrial tissue. This enhanced blood flow can improve the delivery of oxygen and nutrients to the endometrium, fostering its growth and development.

3. Immune Modulation: G-CSF exerts immunomodulatory effects within the endometrium, regulating the activity of immune cells and promoting a favourable immune environment for embryo implantation. By modulating immune responses, G-CSF may help prevent rejection of the embryo and support its successful implantation.

4. Enhanced Secretory Function: G-CSF has been reported to enhance the secretory function of the endometrium, leading to the production of factors that support embryo implantation and early pregnancy maintenance. This includes factors such as cytokines, growth factors, and adhesion molecules that facilitate embryo-endometrial interactions.

5. Reduced Apoptosis: G-CSF may exert anti-apoptotic (anti-cell death) effects on endometrial cells, helping to prevent premature cell death and maintain the integrity of the endometrial lining. By reducing apoptosis, G-CSF can contribute to the preservation and thickening of the endometrium.

C. Mode of action Of PRP Instillation On thin Endometrium

In recent years, PRP therapy has gained attention as a potential treatment for thin endometrium, with emerging evidence suggesting its efficacy in improving endometrial thickness and receptivity. The mode of action of PRP in thin endometrium cases involves several key mechanisms:

1. Growth Factor Stimulation: PRP is rich in various growth factors, including platelet-derived growth

factor (PDGF), transforming growth factor-beta (TGF- β), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF). These growth factors play crucial roles in tissue regeneration, angiogenesis, and cellular proliferation. When PRP is instilled into the endometrial cavity, these growth factors stimulate the proliferation and regeneration of endometrial cells, leading to an increase in endometrial thickness.

2. Angiogenesis Promotion: PRP contains factors such as VEGF that promote angiogenesis, the formation of new blood vessels. By enhancing blood flow to the endometrium, PRP facilitates the delivery of oxygen and nutrients to the endometrial tissue, promoting its growth and development. Improved vascularity also contributes to the establishment of a more receptive environment for embryo implantation.

3. Stem Cell Recruitment and Differentiation: PRP contains bioactive molecules that can recruit and activate stem cells within the endometrium. These stem cells have the potential to differentiate into various cell types, including endometrial cells. By recruiting endogenous stem cells and promoting their differentiation into endometrial cells, PRP helps in the regeneration and thickening of the endometrial lining.

4. Anti-inflammatory Effects: PRP exhibits anti-inflammatory properties, which can help mitigate inflammation within the endometrium. Chronic inflammation is associated with thin endometrium and impaired endometrial receptivity. By reducing inflammation, PRP creates a more favourable microenvironment for endometrial growth and embryo implantation.

5. Extracellular Matrix Remodelling: PRP contains components that contribute to extracellular matrix remodelling, such as fibrin and fibronectin. This remodelling process is essential for tissue repair and regeneration. By enhancing extracellular matrix remodelling, PRP promotes the restructuring of the endometrial tissue, leading to increased thickness and improved receptivity.

PRP facilitates the regeneration and thickening of the endometrial lining, ultimately enhancing endometrial receptivity and improving pregnancy outcomes.

DISCUSSION

This article sheds light on the significance of various Ayurvedic principles and treatments in addressing infertility, particularly focusing on thin endometrium, a condition that can hinder successful conception. Ayurveda encompasses not only physical health but also psychological and spiritual well-being, aiming for a balanced state of body and mind conducive to conception and pregnancy.

The concept of "*Vandyatwa*" is intricately linked to the harmony of *Ritu*, *Kshetra* and *Bija Samyoga*, and *Garbha Sambhava Samagri*. Any imbalance or defect in these components can lead to reproductive disorders, emphasizing the importance of addressing each aspect comprehensively.

Among these components, the discussion emphasizes the pivotal role of *Kshetra*, which corresponds to the endometrium, the inner lining of the uterus. A thin or unhealthy endometrium can disrupt the implantation process and hinder pregnancy. In such conditions *Vata Dosh* imbalance is observed particularly in the *Artavavaha Srotas*, as a key factor contributing to defects in *Kshetra*.

Strengthening and nourishing the endometrium emerge as crucial objectives in the treatment of infertility, and *Uttar Basti* stands out as a highly effective therapy. Through its *Vata*-pacifying properties and *Rasayana* qualities and the drugs used in *Uttar Basti* not only addresses *Vata* imbalance but also promotes endometrial growth and enhances embryo implantation.

Comparatively, modern treatments for thin endometrium focus on enhancing endometrial thickness and receptivity through techniques like intrauterine infusion of growth factors such as G-CSF and PRP therapy. These interventions aim to stimulate endometrial regeneration and improve thickness, thereby increasing the chances of successful implantation and pregnancy. Similarly, *Uttara Basti* is a solution to various kinds of *Vandhyatwa* and ensures successful outcome. Integrating the strengths of both systems can potentially optimize outcomes in treating

infertility and related conditions, offering hope to couples seeking to conceive.

CONCLUSION

The practice of *Uttara Basti* in Ayurveda is deeply rooted in holistic principles, striving to not only rejuvenate *Arthavavaha Srotas* but also to specifically address concerns such as thin endometrium, enhancing both its thickness and receptivity. This approach not only aligns with Ayurvedic philosophy but also offers a cost-effective alternative to treatments like G-CSF and PRP instillation. Moreover, *Uttara Basti* can be easily administered in a safe and comfortable environment, making it accessible and convenient for individuals seeking natural and holistic solutions for their health concerns.

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