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Effect of Hyperbaric Oxygen Therapy on Enhancing Fertility (Literature Review)

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ABSTRACT

Ovulatory disorders, damage to the fallopian tubes, uterine issues, and conditions such as endometriosis have been identified as primary causes of female infertility. This article aims to explore the potential of hyperbaric oxygen therapy in enhancing fertility. Hyperbaric Oxygen Therapy (HBOT) is a medical procedure that involves inhaling pure oxygen (100%) within a chamber or room under pressure higher than normal atmospheric pressure, specifically over 1 absolute atmosphere (ATA), to accelerate and enhance the body's healing and recovery abilities. Under elevated atmospheric pressure, gaseous oxygen can dissolve more readily into the blood plasma. Research results suggest that HBOT holds potential in improving fertility due to endometrial receptivity issues and may also boost male fertility. Future studies need to be conducted on the impact, safety, and mechanisms of HBOT in relation to enhancing female fertility

INTRODUCTION

In an era marked by sophisticated technological advancements, we witness a monumental revolution in reproductive technology that has breathed new life into the hopes of couples previously burdened by despair due to infertility. A prestigious study, published by the American Society for Reproductive Medicine, suggests that significant strides in this science have made a notable impact on the success rates of infertility therapies, thus illuminating horizons of hope previously unexplored.

However, in the odyssey to overcome the challenges of infertility, it's vital not to overlook the complexities and obstacles that continue to plague this journey. A predominant challenge faced by both practitioners and patients is the detection and identification of key risk factors contributing to infertility. This process often demands a comprehensive diagnostic approach and the implementation of varied therapeutic strategies, each presenting its own spectrum of success.

Key factors at the forefront of the battle against infertility include, but aren't limited to, the quality of cultivated embryos, the endometrium's responsiveness to the presence of an embryo, recurring failures in the implantation process, and dilemmas associated with sperm integrity and ovarian reserve viability. In-depth research into these elements is not only critical in deciphering the biological puzzle behind infertility but is also fundamental in designing interventions that are most effective and tailored to individual needs.

In a broader global perspective, the World Health Organisation (WHO) views infertility not merely as a medical issue, but as a monumental challenge in the context of global health. Referring to the definition of infertility as the inability to conceive after one year of unprotected efforts, empirical data from the WHO reveals that approximately 15% of couples worldwide are ensnared in this intricate health dilemma. Intriguingly, the paradox arises when we find that the majority of couples grappling with infertility reside in developing nations. Detailed statistical analysis uncovers a myriad of infertility causative factors: up

to 30% are attributed to male-associated factors, 40% arise from a combination of male and female factors, and the remaining 20-70% result from specific health issues experienced by women. These significant findings not only highlight the crucial role of women in the dynamics of infertility but also underscore the urgency to provide comprehensive and holistic medical interventions to effectively address this global health challenge.

In reproductive science, a deep focus on female infertility has revealed primary causes of conditions that hinder conception. Ovulation disorders, damage to the fallopian tubes, uterine issues, and conditions like endometriosis have been pinpointed as the main culprits. Solutions to these challenges have been meticulously considered in medical literature.

For instance, ovulation disorders, a frequent cause of female infertility, can be addressed through sex hormone therapy, proven to be effective. Similarly, obstructions in the fallopian tubes can be treated with surgical procedures that allow the egg's passage from the ovaries to the uterus. However, it's essential to note that each of these treatment methods isn't devoid of risks and side effects. Hence, a profound medical approach and individualization in determining the treatment strategy are imperative.

One of the most significant breakthroughs in medical science to tackle infertility is In Vitro Fertilization (IVF), offering renewed hope for numerous couples. Since the birth of the first IVF baby in 1978, this technology has continually evolved alongside deeper research. However, while IVF success rates have surged, the reality remains that not every IVF attempt will prove successful.

Data from the European Society of Human Reproduction and Embryology (ESHRE) indicates that the success rate of IVF has improved over time. However, it's crucial to remember that patient expectations don't always align with reality, and the failure of IVF can be a challenging experience. As such, a holistic approach that considers both the physical and emotional aspects of patients, as well as clear education about realistic expectations in the process, remains crucial in reproductive medicine. With a better understanding and appropriate support,

couples facing infertility can make better decisions about the treatments they choose.

Amidst the rising prevalence of infertility, a global challenge, many couples struggling with reproductive issues are seeking solutions outside of conventional medical practices we're familiar with. One approach gaining attention is complementary and alternative medicine (CAM).

CAM encompasses a set of treatment methods originating from various health traditions worldwide and fundamentally differs from the conventional medical approaches that have become standard. Many of these therapies have stood the test of time and are deeply rooted in their originating cultures, but only recently began gaining scientific recognition. For instance, traditional Chinese medicine, used for thousands of years to address various health issues, emphasizes the balance of energy in the body and its influence on fertility.

Additionally, CAM includes Ayurvedic treatments from India, focusing on harmony between body, mind, and spirit. There's also a focus on food as medicine, with certain foods believed to positively impact fertility and reproductive health.

All of these reflect an intriguing shift in addressing infertility, with more couples exploring CAM options as either a supplement or alternative to conventional medical approaches. However, it's essential to note that while some CAM therapies have demonstrated benefits in scientific research, not all are strongly evidence-based. Therefore, therapy choices should be made wisely, considering various factors, and always in consultation with a competent healthcare professional.

Aromatherapy, using natural essential oils, has emerged as an increasingly popular approach to improving physical and emotional well-being. There's a belief that certain essential oils can support the reproductive system and boost fertility. Concurrently, vitamin therapy and dietary focus underscore the importance of nutrient intake in supporting reproductive health.

In efforts to cope with the emotional strain often accompanying infertility, psychotherapy is frequently employed to help couples manage their

stress and emotions. Meanwhile, spa therapies like massage and acupuncture aim to enhance blood circulation to reproductive organs, potentially benefiting fertility.

Interestingly, one promising alternative therapy in the infertility context is oxygen therapy. Findings from various studies suggest that increased oxygen supply to reproductive tissues can positively impact conception chances.

The endometrium's quality, the mucous membrane lining of the uterus, plays a crucial role in conception and embryo implantation. Leading reproductive expert, Dr. Nasser Al-Asmar, emphasizes that often the endometrium's quality is a primary infertility cause in women, especially regarding its capacity to accept embryos. In reproductive physiology, the endometrium serves as the "fertile ground" where embryos attach and grow. However, various factors can influence this endometrium's quality and response, including factors like uterine health, proper hormonal balance, and adequate vascularization and oxygenation. Thus, a deep understanding of the endometrium's role in fertility is vital in addressing infertility.

Using a holistic approach in assessing infertility causes enables experts to provide patients with more accurate intervention recommendations. Cutting-edge technologies like transvaginal Doppler sonography have become a primary diagnostic tool in assessing endometrium quality. Through this method, gynecologists can visually see and gather information on blood flow in the endometrium, offering critical insights into its health and readiness for implantation.

Furthermore, one indicator often considered in assessing endometrial quality is its thickness. Although empirical evidence suggests pregnancies can occur with an endometrium thickness of just 4 mm, it's generally accepted that a thicker endometrium offers better implantation success chances. A study by Cervello et al. (2017) indicated that a thinner endometrium typically correlates with decreased rates of successful implantation, pregnancy, and births. Therefore, maintaining endometrial quality is an essential aspect of

enhancing the chances of success for women trying to conceive.

Hyperbaric Oxygen Therapy (HBOT) is a medical approach where patients inhale 100% pure oxygen at atmospheric pressures higher than usual within a high-pressure chamber. This concept is based on the principle that by increasing oxygen pressure inside the body, cells and tissues receive an enhanced and optimal oxygen supply, thereby aiding healing and regeneration processes.

Interestingly, while HBOT was not initially designed specifically for fertility issues, its application has shown impressive results in enhancing fertility, especially in men. Empirical studies reveal that after undergoing two months of HBOT, there was a significant improvement in sperm motility and spermatogenesis, the sperm formation process. This suggests HBOT's potential in improving sperm quality, contributing to increased fertilization chances.

Fertility in both men and women can be influenced by various factors, including genetic, hormonal, environmental, and lifestyle. However, field experiences indicate that HBOT can contribute positively to addressing infertility issues. By enhancing oxygen supply to reproductive tissues, tissue repair and regeneration processes can be optimized, increasing the chances of successful pregnancy for couples trying to have children.

To strengthen this argument, it's crucial for researchers to conduct more in-depth and comprehensive studies on HBOT's benefits in the fertility context, providing stronger empirical evidence and uncovering other potential benefits of this therapy.

METHODS

Preparation before undergoing HBOT is a vital step in ensuring the success and safety of this procedure. Based on theoretical concepts and medical guidelines, the preparations to be considered are as follows:

- 1) Patients are advised to quit smoking for two weeks before starting HBOT. This recommendation is because tobacco can cause vasoconstriction, potentially reducing the oxygen flow to body tissues.
- 2) Certain medications, such as vitamin C, morphine, and alcohol, should be ceased at least eight hours before undergoing HBOT. This is to avoid any drug interactions with the oxygen therapy that could affect the results.
- 3) Physical preparation for the patient includes wearing clothing made of 100% cotton. Furthermore, patients must remove jewellery, hearing aids, and avoid the use of petroleum-based lotions, cosmetics, and items containing plastic and electronic devices. This is to avoid the risk of fires in the high-pressure hyperbaric oxygen chamber.
- 4) Patients must remove contact lenses before entering the HBOT chamber. This is to prevent bubble formation between the lens and the cornea, which could disrupt vision.
- 5) Patients are also not allowed to bring items like newspapers, magazines, or books into the HBOT chamber. This is to prevent possible spark generation due to high oxygen pressure.
- 6) Before undergoing HBOT, patients should be evaluated by a doctor knowledgeable in hyperbarics. This evaluation involves a health check of the patient and determining if there are any contraindications that might make HBOT unsafe for the patient.
- 7) During the HBOT session, patients will be under a specific oxygen pressure for 90 minutes, with a 5-minute break every 30 minutes. This is done to avoid oxygen poisoning in the patient.
- 8) HBOT involves a multidisciplinary collaboration, with various medical fields involved in patient care. The aim is to ensure a comprehensive approach to treatment.

- 9) Every HBOT session should conclude with an evaluation of therapy progress and monitoring for possible hyperbaric complications in the patient. Additionally, patients are also taught to breathe normally and avoid eating large meals or foods that can produce gas before the treatment, to prevent barotrauma to the digestive system.

RESULTS AND DISCUSSION

Based on the study conducted by Chen, J., Huang, F., Fu, J. et al. (2023), their aim was to investigate the effects of hyperbaric oxygen therapy (HBOT) on endometrial growth and pregnancy outcomes in patients with thin endometria that were difficult to treat during frozen embryo transfer (FET) cycles. A thin endometrium is often considered suboptimal for embryo implantation, and until now, there has been no effective therapy to address this issue.

In this study, the researchers attempted to address the challenge of treating thin endometria using HBOT as an adjunct therapy. They gathered data from patients who had previously experienced at least one cancelled embryo transfer cycle due to a thin endometrium, despite having undergone standard and adjunctive treatments. Patients were divided into two groups: an HBOT group, who received daily HBOT for at least 10 days during the proliferative phase, and a control group who underwent cycles without HBOT.

The study results included measurements of endometrial thickness, intrauterine pregnancy rates, embryo implantation rates, miscarriage rates, and more. Using appropriate comparative analysis, the researchers evaluated whether HBOT positively affected endometrial growth and pregnancy outcomes in patients with challenging thin endometria. The findings provide additional insights into the potential of hyperbaric therapy to enhance fertility, supporting or complementing findings from articles discussing the relationship of hyperbaric therapy to fertility.

A study by Feng, J., Wang, J., Zhang, Y., Zhang, Y., Jia, L., Zhang, D., Zhang, J., Han, Y., &

Luo, S. (2021) highlighted the increasing incidence of infertility in women due to social pressures, late marriages, and delayed childbirth. Conventional solutions for addressing infertility include hormone therapy, in vitro fertilization (IVF), and embryo transfer, but there are limitations regarding unsatisfactory obstetric outcomes and potential severe side effects.

This research emphasizes the role of hyperbaric oxygen therapy (HBOT) as an approach to treating female infertility. This therapy falls under Complementary and Alternative Medicine (CAM), which is gradually becoming an alternative to conventional therapies. Existing findings suggest that CAM, including HBOT, can harmonize and regulate women's bodily conditions holistically for enhanced therapeutic effects.

However, it's essential to note that there's debate concerning the effectiveness of CAM, including HBOT, in treating infertility. Some randomized clinical trials (RCTs) assert that CAM doesn't have a clear impact on infertility, and the underlying mechanisms aren't yet agreed upon. Thus, even though HBOT is mentioned in this article as part of CAM, further research is needed to deeply understand its impacts, safety, and mechanisms in relation to improving female fertility.

A study by Mitrović, A., Nikolić, B., Dragojević, S., Brkić, P., Ljubić, A., & Jovanović, T. (2006) observed a group of infertile women undergoing hyperbaric oxygen (HBO) therapy and evaluated their endometrial development using transvaginal color doppler. The results demonstrated that HBO therapy positively impacted the endometrium, particularly regarding thickness and quality. In the cycles that received HBO therapy, endometrial thickness at ovulation reached 11.0 ± 2.6 mm, and the desired endometrial quality was significantly better than cycles without HBO therapy.

Furthermore, the study noted changes in uterine blood vessel resistance and subendometrial capillary tissue during HBO therapy. Uterine blood vessel resistance was slightly higher than expected,

but the subendometrial capillary showed intense capillary structures with low resistance. This suggests that HBO therapy can enhance endometrial vascularization and oxygenation, essential factors for optimal endometrial receptivity.

The study provided evidence that HBO therapy could be an excellent option for enhancing fertility in women with infertility issues potentially caused by endometrial receptivity problems. With increased endometrial vascularization and oxygenation, HBO therapy can improve endometrial receptivity and, therefore, the chances of embryo implantation and successful pregnancy. Consequently, this study supports the argument that HBO therapy has potential fertility benefits for women struggling to conceive.

In the study by Özgök Kangal, K., & Özgök, Y. (2021), a retrospective analysis of the medical records of male infertility patients undergoing HBOT sessions from January 1, 2015, to December 31, 2019, was carried out. The study indicated a total of 15 male patients were included.

These patients were grouped into three categories: group 1 with sperm DNA fragmentation issues, group 2 with globozoospermia conditions, and group 3 with azoospermia. In 10 out of the 15 patients, procedures such as round spermatid injection (ROSI), intrauterine insemination (IUI), or intracytoplasmic sperm injection (ICSI) were conducted. A total of 31 embryos were successfully obtained, and out of this number, 19 (61%) were successfully transferred. The globozoospermia group had the highest number of embryos, at 15, followed by the azoospermia patients obtaining 10 embryos, and the sperm DNA fragmentation patients obtaining 6 embryos ($p=0.515$).

Results indicated that three (30%) healthy pregnancies were achieved in total. Additionally, an increase in sperm count in patients ($n=9$) post-HBOT was observed, moving from 8.4 ± 11.1 million/mL before HBOT to 15.7 ± 15.0 million/mL post-HBOT (excluding patients with azoospermia). Furthermore, the TESE (testicular sperm epididymis excision) outcomes analyzed in azoospermia patients showed positive changes in 4 patients (80%). Conversely, a

50% improvement was observed in group 1 based on sperm DNA fragmentation post-HBOT ($p=0.500$).

Overall, this research shows that the globozoospermia group obtained the highest number of embryos, and there was an increase in sperm count in patients post-HBOT. However, more research is needed to better understand the relationship between HBOT and male infertility. The findings suggest a positive potential of HBOT.

CONCLUSION

HBOT has the potential to improve fertility caused by endometrial receptivity issues and may also potentially enhance male fertility. Further studies are needed regarding the impact, safety, and mechanism of HBOT in relation to enhancing female fertility. Additionally, Complementary and Alternative Medicine (CAM) in the form of HBOT is an option in improving fertility.

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