Original Article

The Effect of Magnesium Sulfate Infusion in Women Undergoing Intracytoplasmic Sperm Injection with Respect to Endometrial Thickness and Endometrial Blood Flow

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Abstract

Background: Magnesium sulfate administration to women undergoing intracytoplasmic sperm injection (ICSI) can significantly increase endometrial receptivity and sub-endometrial vascularity. **Objectives:** To investigate the effect of magnesium sulfate in subfertile women undergoing ICSI cycles to shed more light on its impact on vascular parameters of endometrium as well as its thickness. **Materials and Methods:** This randomized controlled clinical trial enrolled 100 subfertile women with an age range of 20 to 39 years. Those women were all subjected to gonadotropin hormone-releasing hormone antagonist protocol and stimulation by recombinant follicle-stimulating hormone (rFSH) at Al-Nahrain Fertility Center, Baghdad, Iraq. On the day of endometrial thickness (ET), the enrolled women were randomly allocated into either an interventional group (n = 50) or a reference group (n = 50). The intervention was 4 g infusion of magnesium sulfate over 20 min (magnesium sulfate ampoule 50% 2.5 g in 5 mL, Pioneer, Sulaymaniyah, Iraq), whereas the reference group received glucose water 5% 200 mL (glucose 5% [W/V] 500 mL, B. Braun, Germany). **Results:** Comparison of mean ET, mean resistive index (RI), mean pulsatility index (PI), and pregnancy rate between the magnesium group and the control group revealed that the mean ET was significantly higher, the mean pulsatility and resistive indices were significantly lower in an interventional group compared to the study group (P < 0.05). In addition, there was a significant improvement in the pregnancy rate (P = 0.047). **Conclusion:** The use of magnesium sulfate infusion is associated with improved pregnancy outcomes, ET, and endometrial blood flow in women undergoing ICSI.

Keywords: Infertility, intracytoplasmic sperm injection (ICSI), magnesium sulfate

Introduction

Infertility is a common health problem globally and in our country. It affects about 8–10% of couples worldwide.[1] The definition of infertility appears to lack clear consensus among healthcare workers dealing with this problem; however, the inability of a female partner to get pregnant following one year of unprotected regular intercourse is accepted as a general definition of infertility.[2] It can be primary when no previous pregnancy has occurred, or secondary when a previous successful pregnancy has been reported by the afflicted couple.[3]

The list of causes behind infertility is somewhat long; however, causes can be grouped into four major categories: male factors, female factors, combined male and female factors, and unexplained infertility.[4] Female infertility can be caused by a variety of conditions affecting the ovary, the fallopian tubes, the uterus, or other anatomical or physiological aspects of natural reproduction in humans.[5] Infertility and repeated early pregnancy loss may occur because of abnormalities affecting the endometrial thickness (ET) and its normal vascularity.[6] Thin endometrium of less than 7 mm has been associated with poor pregnancy outcomes in subfertile women undergoing assisted reproduction, and poor endometrial and ovarian vascularity were also predictors of poor pregnancy outcomes in such a cohort of women.[7]

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In a recent Iraqi study, Fahad *et al*. evaluated the role of magnesium sulfate in fertility and, in particular, studied its effect on endometrial blood flow and implantation.[8] Fahad *et al*. concluded that magnesium sulfate administration to women undergoing intracytoplasmic sperm injection (ICSI) can significantly increase endometrial receptivity and sub-endometrial vascularity; in addition, the implantation rate was also improved.[8] Magnesium sulfate has been tried in diseases other than infertility and has been proven to be effective in altering placental and sub-endometrial vascular resistance in cases of pre-eclampsia and the risk of preterm labor.[9,10]

In this study, the student aimed to investigate the effect of magnesium sulfate in subfertile women undergoing ICSI cycles to shed more light on its impact on the vascular parameters of the endometrium as well as its thickness.

Materials and Methods

Study design and patients

This randomized controlled clinical trial enrolled 100 subfertile women with an age range of 20 to 39 years old, from 2020 to 2022. Those women were all subjected to gonadotropin hormone-releasing hormone antagonist protocol and stimulation by recombinant follicle-stimulating hormone (rFSH) at Al-Nahrain Fertility Center, Baghdad, Iraq.

On the day of ET, enrolled women were randomly allocated into either an interventional group ($n = 50$) or a reference group ($n = 50$). The intervention was 4 g infusion of magnesium sulfate over 20 min (magnesium sulfate ampoule 50% 2.5 g in 5 mL, Pioneer, Sulaymaniyah, Iraq), whereas the reference group received glucose water 5% 200 mL (glucose 5% [W/V] 500 mL, B. Braun, Germany). Transvaginal color and power Doppler ultrasonography (The SonoAce-X6 Ultrasound Set's 6 MHz vaginal probe was used to perform the transvaginal scan, Medison, Seoul, South Korea) were used to measure ET and blood flow indices (pulsatility index [PI] and resistive index [RI]). Two or three high-quality embryos were transplanted after the cultivated embryos' quality was evaluated. The luteal phase was supported with vaginal progesterone (400 mg twice daily). A serum *β*-HCG test was carried out 14 days after the embryo transplantation.

Statistical analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 23.0 (SPSS, IBM Company, Chicago, IL 60606, USA). Variables were expressed as mean, standard deviation, range, number, and percentage. The chi-square test and independent samples student *t* test were used to calculate the *P* value, which was considered significant at a cutoff of 0.05.

Ethical approval

All individuals involved in this study were informed, and consent was obtained verbally from parents before the collection of samples. The study was approved by the Committee on Publication Ethics at the College of Medicine, Al-Qadisiyah University, under reference number 0799 on February 12, 2020.

Results

The mean age of the magnesium group was statistically comparable to that of the control group, 30.14 ± 3.68 years vs. 29.58 ± 4.25 years, respectively ($P = 0.483$). There was also no significant difference in mean body mass index

Table 1: Demographic characteristics and fertility history of subfertile women enrolled in this study

Characteristic	Magnesium group $n = 50$	Control group $n = 50$	*P*
Age (years)			
Mean ± SD	30.14 ± 3.68	29.58 ± 4.25	0.483 I
Range	20–39	20–39	NS
BMI (kg/m^2)			
Mean ± SD	24.29 ± 3.16	24.50 ± 2.53	0.715 I
Range	20–31.6	18.3–29	NS
Cause			
Male factor, *n* (%)	16 (32.0%)	18 (36.0%)	0.184
Female factor, *n* (%)	26 (52.0%)	22 (44.0%)	C
Combined factors, *n* (%)	7 (14.0%)	4 (8.0%)	NS
Unexplained, *n* (%)	1 (2.0%)	6 (12.0%)	
Type			
Primary, *n* (%)	38 (76.0%)	32 (64.0%)	0.190
Secondary, *n* (%)	12 (24.0%)	18 (36.0%)	C
			NS
Duration (years)			
Mean ± SD	7.52 ± 4.01	7.02 ± 3.01	0.482 I
Range	2–14	3–13	NS

C: chi-square test, *n*: number of cases, I: independent samples *t* test, SD: standard deviation, NS: not significant

(BMI) between the study group and the control group, $24.29 \pm 3.16\,kg/m^2$ vs. $24.50 \pm 2.53\,kg/m^2$, respectively ($P = 0.715$). With respect to the causes of infertility, enrolled women had a variety of causes that were grouped into male factors, female factors, combined male and female factors, and unexplained infertility; comparison between the study and control groups with respect to the causes of infertility revealed no significant difference ($P = 0.184$). There were also no significant variations in the type and duration of infertility between the two groups ($P > 0.05$). [Table 1] Comparison of mean serum hormonal levels between the magnesium group and the control group is shown in Table 2, and there were no significant variations ($P > 0.05$). A comparison of mean ET, mean RI, mean PI, and pregnancy rate between the magnesium group and the control group is shown in Table 3. The mean ET was significantly higher, while the mean pulsatility and resistive indices were significantly lower in the interventional group compared to the study group ($P < 0.05$).

Table 2: Comparison of mean serum hormonal levels between the magnesium group and control group

Characteristic	Magnesium group $n = 50$	Control group $n = 50$	P
FSH (mIU/mL)			
Mean ± SD	6.67 ± 1.98	7.00 ± 1.57	0.352 I
Range	2.18–12.29	3.1–10	NS
LH (mIU/mL)			
Mean ± SD	6.31 ± 2.51	5.42 ± 2.52	0.080 I
Range	1.67–17.27	1.8–10	NS
Prolactin (ng/mL)			
Mean ± SD	14.91 ± 4.30	13.60 ± 5.13	0.169 I
Range	6.13–22.9	2.2–25	NS
TSH (mIU/mL)			
Mean ± SD	1.89 ± 0.71	2.07 ± 0.82	0.234 I
Range	0.7–4.2	0.3–3.2	NS
E_2 (pg/mL)			
Mean ± SD	33.28 ± 12.68	31.76 ± 8.46	0.480 I
Range	13.7–73	20.6–50	NS
Testosterone (nmol/L)			
Mean ± SD	0.72 ± 0.27	1.02 ± 1.89	0.273 I
Range	0.04–1.6	0.03–10	NS
AMH (ng/dL)			
Mean ± SD	2.71 ± 1.07	2.75 ± 0.87	0.860 I
Range	0.5–5.5	1.4–4.7	NS

FSH: follicle-stimulating hormone, LH: luteinizing hormone, TSH: thyroid stimulating hormone, E_2: estradiol, AMH: anti-Mullerian hormone, NS: not significant, I: independent samples *t* test, SD: standard deviation

Table 3: Comparison of mean endometrial thickness, mean resistive index (RI), mean pulsatility index (PI), and pregnancy rate between the magnesium group and control group

Characteristic	Magnesium group $n = 50$	Control group $n = 50$	P
Endometrial thickness (mm)			
Mean ± SD	8.63 ± 1.02	8.17 ± 0.98	0.023 I*
Range	7–10.7	6.6–10.5	
Resistive index (RI)			
Mean ± SD	0.57 ± 0.09	0.62 ± 0.14	0.040 I*
Range	0.43–0.85	0.41–0.9	
Pulsatility index (PI)			
Mean ± SD	0.82 ± 0.17	0.94 ± 0.35	0.030 I*
Range	0.5–1.13	0.48–1.7	
Pregnancy			
Negative	31 (62.0%)	40 (80.0%)	0.047 C*
Positive	19 (38.0%)	10 (20.0%)	

SD: standard deviation, *n*: number of cases, I: independent samples *t* test, C: chi-square test

*Significant at $P \leq 0.05$

Discussion

The use of a variety of methods and techniques has been evaluated to increase the yield of assisted reproductive technologies; however, until now, there is a significant fraction of failure of *in vitro* fertilization (IVF) and ICSI procedures. For that reason, researchers are ongoingly evaluating a variety of therapeutic interventions to improve fertility outcomes. One of these approaches is to improve blood flow to the endometrium and increase its thickness. Among these therapeutic interventions, a number of pharmacological agents have been used, and none of them have been proven to be superior to the others. In this interventional study, we aimed to explore the role of magnesium sulfate infusion in this regard.

We have shown that magnesium sulfate was associated with a higher pregnancy rate. This finding was in line with a previous Iraqi study conducted by Fahad *et al*.[8] In addition, our results were compatible with theirs with respect to the improvement in sub-endometrial blood flow by significantly reducing the magnitude of PI and RI.

Several ultrasound factors, such as uterine ET and blood flow, have been investigated to assess uterine receptivity. The blood content has been emphasized in a few studies as a significant indicator of uterine acceptance. Additionally, some research has recognized uterine blood and endometrial flow as factors that influence the improvement of pregnancy likelihood during IVF cycles.[11,12]

Traditionally, an ET exceeding 7 mm and the presence of a triple-layered endometrial pattern were historically deemed indicative of endometrial receptivity.[13] Nevertheless, several research endeavors have demonstrated suboptimal rates of implantation despite favorable ET values and the existence of a triple-layered endometrial pattern. Additionally, investigations have proposed inadequate uterine perfusion as a novel etiology of unexplained infertility.[14,15] Furthermore, the circulation rate of blood within the endometrium throughout the typical menstrual cycle has been associated with heightened activity and manifestation of numerous angiogenic factors.[16]

Several studies in Iraq have been conducted regarding the evaluation of Ovarian Response Indexes as predictors to the outcome of intracytoplasmic sperm injection in addition to study the role of Serum Vascular Endothelial Growth Factor in Pregnant Women with Different Types of Assisted Reproductive Techniques.[17-19]

Conclusion

The use of magnesium sulfate infusion is associated with improved pregnancy outcomes, ET, and endometrial blood flow in women undergoing ICSI.

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Conflicts of interest

There are no conflicts of interest.

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