

Endometrial and Junctional Zone Volume Measurements in unexplained Infertility: The effect of Sildenafil Citrate (Viagra™)

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Synopsis

Sildenafil citrate (Viagra™) was used in a double blind cross-over trial to determine its effect on endometrial and junctional zone volumes in both unexplained infertility and a control group of apparently fertile women. Tissue development was assessed using T₂-weighted magnetic resonance imaging of the pelvis, at three different time points in the menstrual cycle (early follicular phase, ovulation, mid-luteal phase). There was no difference in volumes between the placebo and Viagra™ cycles. At ovulation endometrial and junctional zone volumes were smaller in the infertility compared to the control group although the difference was not statistically significant (P>0.1 for both tissues).

Introduction

An adequate pelvic blood supply is essential for normal reproductive and physiological performance. It has been postulated, but not proved, that a disturbance of this blood supply may be responsible for some cases of unexplained infertility in women¹. Implantation and clinical pregnancy rates depend on both the endometrial receptivity and the quality of the embryos. However non-invasive measurements of endometrial thickness by ultrasound have not been predictive of conception². MRI has previously been used to measure endometrial and junctional zone thickness³ with good correlation to ultrasound data. The 3D nature of MRI lends itself to the non-invasive measurements of endometrial and junctional zone volume, which may prove to be better predictors of implantation and pregnancy rates than thickness, as this measure is not dependent on the shape of the endometrium.

The use of sildenafil citrate (Viagra™) in the female pelvis is still in the experimental stages however a recent ultrasound study⁴, of the use of sildenafil citrate in women with infertility problems, showed that the drug helped to improve the uterine artery blood flow and endometrial thickness.

Methods

Approval for this study was obtained from the Local Hospital ethics committee. This work was a sub-study of a wider project involving measurements of tissue development and blood flow using 3D ultrasound and MRI. The study was split into two groups of women. The control group was made up of 23 volunteers (average age 30 years old) with regular menstrual cycles, who had no known infertility problems. The second group was made up of 23 women (average age 35 years old) with unexplained infertility. All these women were not using hormonal contraception or an intrauterine device. Both groups of patients were randomized to either sildenafil citrate or an identical placebo in a double-blind fashion and the allocation was crossed-over in the second menstrual cycle. For those in the treatment cycle, 50 mg of sildenafil citrate was given orally 3 times a day from the 5th day of the menstrual cycle until ovulation. Ovulation was determined by 3D ultrasound and confirmed by serology.

Magnetic resonance imaging was carried out up to three times during each menstrual cycle. Scans were carried out during the early follicular phase of the cycle (10 to 5 days before ovulation), around ovulation (-3 to +3 days from ovulation) and mid-luteal phase (4 to 9 days after ovulation). Each volunteer had at least 6 days between consecutive scans. Ovulation dates were confirmed after the end of the menstrual cycle and some data was reclassified to a different phase, whilst data lying outside the group range was removed from analysis. A 0.5 T scanner with a Marconi (S.M.I.S.) Console was used for the imaging. To determine the endometrial and junctional zone development high-resolution Fast Spin-Echo images were acquired in the sagittal plane. A 256x256 image matrix was used, with an in-plane resolution of 1.172 mm and slice thickness 7 mm, inter-slice spacing 0.5 mm, with 12 slices acquired during the scan. Endometrial and junctional zone volumes were measured using Analyze® (Mayo Foundation). Each volume was measured 5 times to obtain an average value.

Results

Table 1 shows the mean volume results from the control group. Data was only included if there was measurements from both the placebo and Viagra™ cycles at each individual time point. Table 2 shows the mean volume results from the infertility patients. Wilcoxon Signed Ranks Test applied to the data showed no statistical difference between the placebo and Viagra™ cycles at any time point (all P-values > 0.1).

Discussion/Conclusions

All groups showed an increase in endometrial and junctional zone volumes between the early follicular phase and ovulation scans. This is in good agreement with a previous study of thickness³. No difference was found between the placebo and Viagra™ cycles for either group of women, although the infertility junctional zone volume increased slightly on the Viagra™ cycle around ovulation. In general the volumes of uterine tissue were smaller in the infertility group than the control although this difference was not statistically significant (P>0.1 for both tissues at all time points).

Acknowledgements

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References

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Control Group	Endometrium			Junctional Zone		
	N	Placebo	Drug	N	Placebo	Drug
Early Follicular	16	2.2 (0.3)	2.2 (0.4)	12	15.3 (2.8)	15.6 (2.3)
Ovulation	16	3.9 (0.6)	3.6 (0.7)	15	19.5 (3.7)	19.8 (3.7)
Mid-Luteal	14	3.0 (0.5)	3.0 (0.7)	11	19.5 (3.4)	19.0 (3.3)

Table 1. Mean volumes (in ml) of uterine tissue for control group (std. error in brackets).

Infertility Group	Endometrium			Junctional Zone		
	N	Placebo	Drug	N	Placebo	Drug
Early Follicular	9	1.4 (0.3)	1.5 (0.4)	8	11.9 (2.8)	12.2 (2.9)
Ovulation	20	2.8 (0.3)	2.9 (0.2)	20	16.3 (1.4)	18.0 (1.6)
Mid-Luteal	13	2.7 (0.3)	2.8 (0.4)	13	18.7 (2.5)	18.8 (2.4)

Table 2. Mean volumes (in ml) of uterine tissue for infertility group (std. error in brackets).