

Research Article

Effect of Administration of Sildenafil Citrate in Management of Cases With Recurrent Unexplained Miscarriage at First Trimester in El-Minia Maternity Hospital

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Abstract

Introduction: Recurrent miscarriage (RM). Which is defined as three or more consecutive miscarriages before the 20th week of gestation affects 0.5-1% of couples. **Aim of the work:** Endometrial growth seems to be dependent on uterine artery blood flow. The importance of endometrial development on pregnancy outcome has been reported. **Patients & method:** Setting :the present study was carried out in Minia maternity and children university hospital. During the period form 1st of June 2016 until 31st May 2017. **Results:** Presence of uncontrolled D.M. or hepatic or cardiac or thyroid impairment or already diagnosed as APS. **Discussion:** Recurrent miscarriage is the loss of two or more consecutive pregnancies before the 20th week of gestation. **Recommendation:** From the results of our study we may conclude the following points: Oral sildenafil in low dose may increase uterine artery blood flow. Which is reflected by P.I.R.I. The use of low dose oral sildenafil in luteal phase may improve pregnancy outcome. Using sildenafil citrate in low dose increases incidence of pregnancy occurrence oral sildenafil in low dose reduces incidence of occurrence of unexplained miscarriage lastly. We may recommend low dose oral sildenafil for the cases of unexplained recurrent miscarriage .

Keywords: RM: recurrent miscarriage, HSG: hystrosalpigogram, APS: anti-phospholipid syndrome.

Introduction

Recurrent miscarriage (rm), which is defined as three or more consecutive miscarriages before the 20th week of gestation affects 0.5-1% of couples (Nybo Andersen et al., 2002).

Primary rm refers to women with no prior successful pregnancy, whereas secondary RM referes to women with no prior successful pregnancy, whereas secondary RM refers to losses following a live birth (Szekeres – Bartho and Balasch, 2008).

Both fetal and maternal factors are involved in the pathophysiology of RM. Fetal underlying mechanisms include genetic or developmental abnormalities, while uterine pathology, endocrine dysfunction, anti-phospholipid syndrome and thrombophilic disorders have been identified as maternal factors. In ~50% of the cases neither of the above can be identified.

Cases in whom no apparent cause of abortion could not be found are considered as cases of

idiopathic recurrent miscarriage. These cases are estimated to be 50% of all abortion cases.

In cases of unexplained recurrent miscarriage many modalities of treatment had been suggested e.g. aspirin (Rai et al., 2000), prednisolone (Quenby et al., 2003), progesterone (Oates-Whitehead et al., 2003), metformin (Glueck et al., 2002), heparin (Dinisio et al., 2005) and sildenafil acetate (Jerzak et al., 2008).

Endometrial growth seems to be dependent on uterine artery blood flow. The importance of endometrial development on pregnancy outcome has been reported (Kelly et al ., 2001).

Patients & method

Setting:

The present study was carried out in minia maternity and children university hospital, during the period form 1st of June 2016 until 31st May 2017.

Funding:

This project was funded from Minia university as a part of a research support for the candidate and carried out under shared supervision of professor Kamal El-Din Abdullhameed, professor Mamdouh Tawfik and lecturer Haitham Bahaa, Obstetrics & Gynecology department, Minia Faculty of Medicine.

Ethical issues:

Ethical permission was sought from a local research ethics committee (REC) of the department. The potential benefits and inconveniences of all aspects of the study were clearly stated in the ethical application forms to the corresponding committee to access the fills and dealing anonymously with the retrieved data .

Participants:

Randomized sample consists of 120 patients suffering of recurrent miscarriage at 1st

trimester without definite cause who attend to infertility outpatient clinic in Minia

Inclusion criteria:

- Age: 20-35 years old
- Patient has history of 3 or more 1st trimester abortion
- Regular cycles with good ovulation
- Normal hormonal profile (FSH, LH, Prolactin)
- Normal hystoscopic examination or at least normal hystosalpigogram (HSG)
- Patient is free of any chronic disorders or Anti-phospholipid syndrome (APS)

Exclusion criteria:

- Age : less than 20 or more than 35 years old
- presence of any uterine malformation e.g. fibroids, polyps, bicornuate or septate uterus.
- Presence of polycystic ovaries (PCO) or endometriosis.
- Abnormal karyotyping
- Presence of uncontrolled D.M. or renal or hepatic or cardiac or thyroid impairment or already diagnosed as APS

Table (1) : Demographic and some clinical data of the all studied cases.

Variable		Description (120 cases)
Age (year) mean ± SD (range)		28.2±3.3(20-35)
Weight (kg) mean ± SD (range)		74.1 ±5.6 (58-93)
No. of previous abortion, mean ± SD (range)		3.9 ±1.1 (3-7)
residence	rural	68(56.7%)
	urban	52(43.3%)
Socioeconomic level	low	54(45.0%)
	moderate	44(36.6%)
	high	22(18.4%)
History of ANC	poor	21(17.5%)
	fair	58(48.3%)
	good	41(34.2%)
Degree of consanguinity	1 st	30(25.0%)
	2 nd	51(42.5%)
	3 rd	39(32.5%)

Categorical data are presented in the form of frequency and percent. Quantitative data are presented in the form of mean ± SD (range).

Discussion

Recurrent miscarriage is the loss of two or more consecutive pregnancies before the 20th week of gestation (El-Far et al., 2014). It is either primary (women without previous live born infant) or secondary (woman with at least one prior live born infant) (Ford and Schurst, 2009).

It has been reported that 1% to 2% of women experience recurrent miscarriage (Ohams et al., 2015). Multiple etiologies for recurrent miscarriage have been reported including autoimmune (20%), endocrine (17% - 20%), anatomic (10% - 15%), genetic (2% - 5%) factors and infection (0.5% - 5%), (El-Far et al., 2014).

Also, the rate of miscarriage increases with a maternal age of less than 18 years or more than 35 years and also increase with increasing number of previous miscarriages and parity (Branch et al., 2010).

There are many drugs which were suggested for cases of unexplained recurrent miscarriage of these aspirin (Rai et al., 2000), prednisolone (Quenby et al., 2003), sildenafil acetate (Jerzak et al., 2008), progesterone (Oates – Whitehead et al., 2003), metformin (Glueck et al., 2002) and also, heparin (Dinisio et al., 2005).

Sildenafil (compound UK \square 92, 480) was synthesized by Pfizer scientists, it was initially studied for use in hypertension and angina pectoris, following this, Pfizer decided to market it for erectile dysfunction, rather than for angina. The drug was patented in 1996 (Benni and Patil, 2016) it is now used to treat multiple human diseases such as: pulmonary hypertension, Raynaud's syndrome besides of erect dysfunction (Luna et al., 2015) and also in now used for other medical indications such as cardiovascular conditions and diabetes mellitus, depression, pre-eclampsia, IUGR infertility patients with Ashermank's syndrome, inflammation, chronic heart failure and renal insufficiency and even to cancer treatment (Zhu and Strada 2007).

Conclusions & recommendation

From the results of our study we may conclude the following points:

Oral sildenafil in low dose may increase uterine artery blood flow, which is reflected by PI,RI.

The use of low dose oral sildenafil in luteal phase may improve pregnancy outcome.

Using sildenafil citrate in low dose increases incidence of pregnancy occurrence.

Oral sildenafil in low dose reduces incidence of occurrence of unexplained miscarriage.

Lastly, we may recommend low dose oral sildenafil for the cases of unexplained recurrent miscarriage.

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