Original Article

Threatened Miscarriage

Pak Armed Forces Med J 2012; 62 (1): 42 - 5

EFFICACY OF DYDROGESTERONE IN THE MANAGEMENT OF THREATENED MISCARRIAGE IN THE FIRST TRIMESTER

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ABSTRACT

Objective: To study the efficacy of dydrogesterone in pregnant women with threatened miscarriage in the first trimester.

Study design: Randomized control trial.

Place and duration of study: Department of Obstetrics and Gynaecology, Military Hospital Rawalpindi from Jan 2008 to Dec 2008.

Patients and Methods: One hundred and fifty two pregnant women presenting to the Gynae and Obs department (MH Rwp) before 12th gestational week were selected on the basis of slight pain or vaginal bleeding, no cervical dilatation and a viable pregnancy on ultrasound. They were divided randomly into two groups each containing 76 patients with the help of simple random number table, after obtaining their consent and explaining all the risks and benefits to them. Bias was controlled by double blinding. Patients in group A received oral dydrogesterone (10mg twice daily) and patients in group B received placebo. Treatment was continued till the 12th gestational week and patients were followed up 4 weekly after the completion of treatment till the 20th gestational week. Improvement was judged by continuation of pregnancy and remittance of symptoms.

Results: Patients in group A had a greater improvement in the symptoms of pain and vaginal bleeding but the difference between the two groups was not statistically significant. However the number of patients who had a normal growth and whose pregnancies continued was significantly higher in group A.

Conclusion: It was concluded that the continuing pregnancy success rate was significantly higher in women treated with dydrogesterone compared with women who received placebo treatment.

Keywords: Miscarriage, Threatened, Ultrasonography

INTRODUCTION

Threatened miscarriage is bleeding of intrauterine origin occurring before 20th completed week, with or without uterine contractions, without dilatation of the cervix and without expulsion of the products of conception[1]. There is bleeding but the fetus is still alive[2]. Threatened miscarriage complicates 15% of pregnancies, and 20% of these will progress to a miscarriage[3].

The incidence of fetal loss in threatened miscarriage after detection of embryonic/fetal heart activity is 3.4%[4].

Progesterone is essential for the successful implantation and maintenance of pregnancy, therefore disorders related to inadequate progesterone secretion by the corpus luteum are likely to affect the outcome of pregnancy[5].

It has been suggested that hormonal support with Dydrogesterone can increase the chances of a successful pregnancy in women with threatened miscarriage[6].

The aim of this study was to determine first hand whether hormonal supplementation with Dydrogesterone in threatened miscarriage during the first trimester of pregnancy will actually improve the pregnancy outcome in our patients. As this drug is being widely used in clinical practice while its therapeutic value is still under debate, so our study will help in providing future references regarding the usefulness of this drug and will open new horizons for further research in this direction.

PATIENTS AND METHODS

This randomized controlled trial was carried out at the department of obstetrics and gynaecology, Military Hospital Rawalpindi from Jan 2008 to Dec 2008.

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Received:25 Aug 2010; Accepted 22 Sep 2011

A total of 152 pregnant women presenting to the Gynae and Obs department before 12th gestational week were selected on the basis of slight pain or vaginal bleeding, no cervical dilatation and a viable pregnancy on ultrasound. Patients were excluded if they had recurrent miscarriages, cervical incompetence, uterine anomalies, incomplete, missed or septic miscarriage and all patients in whom Dydrogesterone was contraindicated. They were divided randomly into two groups each containing 76 patients with the help of simple random number table, after taking their consent & explaining all the risks and benefits to them. Ethics committee approval was sought. Bias was controlled by double blinding. Patients in group A received oral dydrogesterone (10 mg twice daily) and patients in group B received placebo. Treatment was continued till the 12th gestational week and patients were followed up 4 weekly after the completion of treatment till the 20th week of gestation. Drug was considered to be efficacious when there was:

Normal growth of fetus on ultrasound, for which 3 parameters were used

- Increase in size of gestational sac.
- Increase in CRL.
- Presence of fetal cardiac activity.

At each followup ultrasound scan, size of the gestational sac and crown rump length (CRL) were measured and presence or absence of fetal cardiac activity was noted and they were compared to the previous ultrasound. Increase in the size of the sac and CRL and presence of the fetal cardiac activity were used to assess the growth of the fetus.

On initial assessment the patient's severity of pain was scored on the VAS from 1 to 10 and then during the duration of treatment and the follow-up period improvement or worsening of pain score was assessed on the visual analogue scale. The number of episodes of bleeding/spotting per day were counted and then increase or decrease in the number of these episodes was noted for each patient on a predesigned proforma.

Twentieth week was taken as the cut off point because threatened miscarriage is defined as bleeding of intrauterine origin occurring before 20th completed week.

Conservative management included bed rest and a placebo.

Data was analyzed using SPSS version 15. Descriptive statistics were used to describe the data. Chi-square test was applied to compare study variables between both the groups. *P*-value <0.05 was considered significant.

RESULTS

Out of 152 women, 76 received oral Dydrogesterone (group A) and 76 women received conservative management (group B). Average age in group A was 25.23±5.76 years while in group B it was 27.42±6.58 years (p>0.05). The number of patients who had a normal growth on ultrasound for which increase in the size of gestational sac and CRL and presence of fetal cardiac activity were assessed (p=0.041) and whose pregnancies continued (p=0.030) was significantly higher in group A (Table 1). Patients in group A had a greater improvement in the symptoms of pain and vaginal bleeding but the difference

Table-1: Comparison of normal growth and continuation of pregnancy between both the groups.

Variables	Group A (n=76)	Group B (n=76)	*P* value
Normal growth on ultrasound(assessed on the basis of increase in size of gest sac and CRL, and presence of fetal cardiac activity)	56 (74%)	43 (57%)	0.041
Continuation of pregnancy(till the 20th week of gestation)	54 (71%)	40 (53%)	0.030

Table-2: Comparison of improvement in pain and vaginal bleeding between both the groups.

Variables	Group A (n=76)	Group B (n=76)	*P* value
Improvement in pain (on V.A.S)	41 (54%)	36 (47%)	0.517
Improvement in vaginal bleeding(bleeding stopped or the number of bleeding episodes per day reduced)	47 (62%)	38 (50%)	0.191

between the two groups was not statistically significant (Table 2).

DISCUSSION

Kalinka and Szekeres-Bartho conducted a study to evaluate the effect of dydrogesterone on pregnancy outcome of patients with threatened miscarriage. Twenty-seven patients were treated for 10 days with dydrogesterone (30-40 mg/day). Sixteen healthy pregnant controls received no treatment. Serum progesterone and estradiol concentrations as well as urine PIBF concentrations were measured by enzyme-linked immunosorbent assay (ELISA). Serum progesterone concentrations in control patients increased as pregnancy progressed but not in patients with threatened miscarriage. Following dydrogesterone treatment, initially low PIBF concentrations of patients with threatened miscarriage significantly increased to reach the PIBF level found in healthy controls. These data suggest that by inducing PIBF production, dydrogesterone might improve pregnancy success rates in patients with threatened miscarriage[7].

Omar et al. conducted a study to determine whether therapy with dydrogesterone in threatened miscarriage during the first trimester of pregnancy will improve pregnancy outcome. Pregnant women presenting to the obstetric and gynaecology clinic admitting center with vaginal bleeding before 13 weeks gestation were evaluated for entry into the study. Women were excluded if they had a history of recurrent miscarriage. The continuing pregnancy success rate was significantly higher in women treated with dydrogesterone (95.9%) compared with women who received conservative treatment (86.3%). It was concluded that corpus luteal support with dydrogesterone reduces the incidence of pregnancy loss in threatened miscarriage during the first trimester in women without a history of recurrent miscarriage[8]. Similar outcome has been seen in our study.

A study by Pandian to determine whether dydrogesterone was more effective than conservative management alone in preventing miscarriage in women with vaginal bleeding up to week 16 of pregnancy in 191 women concluded that compared with conservative management, dydrogesterone had beneficial effects on maintaining pregnancy in women with threatened miscarriage[9]. This is the same as outcome seen in our study.

Another study was conducted by El Zibdeh, Yousef in the department of Obstetrics and Gynaecology, Islamic Hospital, Amman, Jordan. The aim of this study was to determine whether dydrogesterone helps to preserve pregnancy in women with threatened miscarriage. A total of 146 women who presented with mild or moderate vaginal bleeding during the first trimester of pregnancy were randomised to receive oral dydrogesterone (10mg twice daily) (n=86) or no treatment (n=60). Dydrogesterone was continued until 1 week after the bleeding had stopped. The incidence of miscarriage was significantly lower in the dydrogesterone group than in the untreated group (17.5% vs. 25%). It was concluded that Dydrogesterone has beneficial effects in women with threatened miscarriage[10]. Similar outcome has been seen in our study.

Fifty women with previous diagnosis of inadequate luteal phase and threatened abortion underwent a prospective, randomized, double-blind study conducted by et al. The primary objective was to establish the effects of vaginal progesterone in reducing both pain and uterine contractions. The secondary objective of the study was to evaluate the outcome of the pregnancies. The use of progesterone was effective both on pain relief and on the frequency of the uterine contractions. In conclusion, patients with threatened miscarriage benefit from vaginal progesterone by a reduction of uterine contractions and pain. The use of vaginal progesterone also improved the outcome of pregnancies complicated by threatened miscarriage and previous diagnosis of inadequate luteal phase[11].

CONCLUSION

The continuing pregnancy success rate was significantly higher in women treated with dydrogesterone compared with women who

received placebo treatment. By providing corpus luteal support, dydrogesterone reduces the frequency of pregnancy loss in threatened miscarriage during the first trimester.

REFERENCES

1. Garmel SH. Early Pregnancy Risks. In: Decherney AH, Nathan L (edi). Current Obstetric & gynecologic diagnosis & treatment. New York: Mc GrawHill 2003; 272-85.
2. Impey L. Obstetrics& gynecology.2nd ed. Oxford: Blackwell publishing 2004.
3. Rosevear SK. Handbook of gynecology management. Oxford: Blackwell Science 2002.
4. Tannirandorn Y, Sangsawang S, Manotaya S, Uerpairojkit B, Samritpradit P, Charoenvidhya D. Fetal loss in threatened abortion after embryonic/fetal heart activity. Int J Gynecol Obstet 2003; 81: 263-6.
5. Arredondo F, Noble LS. Endocrinology of recurrent pregnancy loss. Semin Reprod Med 2006; 24:33-9.
6. El-Zibdeh MY. Dydrogesterone in the reduction of recurrent spontaneous abortions. J Steroid Biochem Mol Biol 2005; 97:431-4.
7. Kalinka J, Szekeres-Bartho J. The impact of dydrogesterone supplementation on hormonal profile and progesterone induced blocking factor in women with threatened abortion. Am J Reprod Immunol 2005; 53: 166-71.
8. Omar MH, Mashita MK, Lim PS, Jamil MA. Dydrogesterone in threatened abortion: pregnancy outcome. J Steroid Biochem Mol Biol 2005; 97:421-5.
9. Pandian RU. Dydrogesterone in threatened miscarriage: a Malaysian experience 2009; 65 suppl 1:S47-50.
10. El-Zibdeh MY, Yousef LT. Dydrogesterone support in threatened miscarriage 2009; 65 suppl 1:S43-6.
11. Plagiano A, Bulletti C, Pace MC, DE Ziegler D, Cicinelli E, Izzo A. Effects of vaginal progesterone on pain and uterine contractility in patients with threatened abortion before twelve weeks of pregnancy. Ann N Y Acad Sci 2004; 1034:200-10.