ORIGINAL ARTICLE

Comparison of Progesterone Alone and Progesterone and Human Chorionic Gonadotrophin in Combination in the Management of Threatened Abortion

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ABSTRACT

Objective: To compare the efficacy of progesterone alone and progesterone plus human chorionic gonadotrophin in the management of threatened abortion.
Study design: Quasi experimental
Duration & settings of study: The study was conducted in the department of Obstetrics & Gynaecology Unit-I, at Bahawal Victoria Hospital, Bahawalpur from 01-11-2007 to 31-10-2008.
Material & method: Total 60 patients admitted with threatened miscarriage at gestational age 5-14 weeks having viable pregnancy were studied .The diagnosis was made on history, examination and viability was confirmed on ultrasonography. Patients were divided into two groups A and B. Group-A was given Progesterone & Group-B was given Progesterone plus hCG .It was observed whether the vaginal bleeding stopped, abdominal discomfort/pain settled and pregnancy continued to second trimester or not.
Results: Vaginal bleeding settled in Group-A in 16 (53.33%) and in Group-B 25 (83.33%) patients and in the rest of the patients i.e. 14 (46.67%) in Group-A and 5 (16.67%) in Group-B the bleeding persisted. Abdominal pain/discomfort settled in Group-A 15 (50%) of the patients and in Group-B 25 (83.33%). The most important variable was persistence of pregnancy upto 2nd trimester. In this study, Group-A, showed persistence of pregnancy upto 2nd trimester in 17(56.67%) and in Group-B 25(83.33%).
Conclusion: Management of threatened abortion with progesterone plus hCG has better outcome as compare to progesterone alone.
Keywords: abortion, Progesterone, Human Chorionic Gonadotrophin

INTRODUCTION

Threatened abortion is a common occurrence that complicates at least a quarter (25%) of clinically diagnosed pregnancies[1].

Miscarriage is associated with chromosomal abnormality of the conceptus in over 50% of cases[2]. Other risk factors for miscarriage include maternal age over 34 years[3], maternal infection such as genital herpes simplex, human immunodeficiency virus-1 and vaginal colonization with group B streptococci. Maternal endocrine abnormalities such as uncontrolled diabetes mellitus and insufficient production of progesterone by the corpus luteum[2] polycystic ovary syndrome, maternal autoimmune factors such as phospholipids antibodies, and a previous history of two or more miscarriages are other suggested factors associated with miscarriage. Miscarriage is associated with considerable physical and psychological morbidity.

Owing to the documented physiological role of progesterone in maintaining pregnancy, it has been used to treat women with threatened miscarriage for over 30 years. The historical rationale was that a progesterone deficiency would lead to miscarriage. [2] The therapeutic value of progesterone in preventing or treating threatened miscarriage has not well established yet[4]. But there are few studies which showed that corpus luteum support with dydrogesterone (progesterone) reduce the incidence of pregnancy loss in threatened abortion[5].

The importance of progesterone on the maintenance of pregnancy was demonstrated by the successful use of progesterone antagonists, such as mifepristone (RU 486) in the elective induction of abortion[6]. But there is no sufficient evidence to support the routine use of progestogens alone for the treatment of threatened miscarriage.

As some studies revealed that functional extragonadal gonadotrophin receptors are located in several sites of the human body[7] human chorionic gonadotrophin is produced principally by syncytiotrophoblast. It is luteotrophic hormone hCG appears as early as the 8th day of gestation. The highest levels are found between the 6th and 13th weeks of pregnancy. The human chorionic gonadotrophin/luteinizing hormone (hCG/LH) receptor messenger RNA and protein were found in the endothelial and vascular smooth muscle layers of the human uterine arteries. In vivo administration of

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hCG decreased the blood flow resistance in the human uterus and in vitro increased vasodilating eicosanoids in the vascular wall. The hCG might also participate in angiogenesis, enhancing long-term clinical results[8].

The results of some studies raise the possibility that hCG's effect might be explained by two mechanisms; the hormone can act directly on vascular smooth muscle through its own receptor or increase the level of the steroid hormone estradiol and/or progesterone, thus indirectly lowering vascular resistance in the uterine circulation and improving implantation[9].

Although these studies[2,9] describe their (Progesteorne**,** hCG) possible benefits but did not guide us that which one is more beneficial either prescribing only progesterone or giving in combination with hCG. As threatened miscarriage is a common health problem and miscarriage can cause serious morbidity among childbearing women. Any treatment which might prove to be effective is worth investigation

MATERIAL & METHODS

It was a quasi experimental study conducted in the department of Obstetrics & Gynecology at Bahawal Victoria Hospital Bahawalpur. The duration of study was one year from November 2007 to October 2008 All patient (non hypertensive & non diabetic) admitted with threatened miscarriage at gestational age 5-14 weeks having viable pregnancy were included. The diagnosis was made on history, examination and viability was confirmed on ultrasonography.

A proforma was used to collect data from patients admitted in Gynecology after taking verbal consent patients were fully informed about the side effects of drugs. Patients were divided into two groups A and B keeping in mind their age, parity and gestational age so as to make two comparable groups. Group-A was given Progesterone (tab. Duphaston-10mg twice daily) till 14 weeks.

Group-B was given Progesterone (tab. duphaston-10mg twice daily) plus hCG (inj. Gonacor 5000iu twice weekly) till 14 weeks. It was observed whether the vaginal bleeding stopped, abdominal discomfort/pain settled and pregnancy continued to second trimester or not.

The collected data was entered in SPSS version 10 for analysis. Frequencies were determined for the cessation of vaginal bleeding, settlement of abdominal pain and the number of patients reaching the second trimester in each group. Mean and S.D was calculated for age, gestational age, parity and weight/height. Tables were formed percentages were calculated to know the statistical significance between two groups. Chi square and T test was applied to compare the outcome.

RESULTS

A total of 60 patients with threatened miscarriage fulfilling inclusion/exclusion criteria were studied to determine the efficacy of progesterone alone and the progesterone plus human chorionic gonadotrophin in the management of threatened abortion. In this study, majority of the patients belong to age group between 31-35 years. Regarding comparison of gestational age, majority of the patients were found between 5-8 weeks of gestation. In Group-A, it was found in 19(63.33%) and in Group-B, 20(66.67%) and the mean gestational age in both groups was 8.07+2.55 and 7.45+1.99 respectively (Table 1) P value was 0.581.

Among main variables of this study one was vaginal bleeding and comparison of this variables is shown in Table 2, where in Group-A 16(53.33%) and in Group-B 25(83.33%) patients the bleeding settled and in the rest of the patients i.e. 14(46.7%) in Group-A and 5(16.7%) in Group-B the bleeding persisted. This shows the significance difference in both groups as the P value was 0.012.

Another outcome variable was abdominal discomfort/pain, it was also analyzed and chi-square test was applied which showed that in Group-A 15(50%) of the patients the pain settled and in Group-B 25(83.33%) and P value was 0.006 which is statistically significant (Table 3).

Among other study variables, the most important variable was persistence of pregnancy upto 2nd trimester. In this study, Group-A, showed persistence of pregnancy upto 2nd trimester in 17(56.7%) and in Group-B 25(83.33%). P value was 0.024 which is statistically significant (Table 4).

Table 1: A Comparison in gestational age (before treatment) in both groups

Duration of Gestation (in weeks)	**Group A**		**Group B**		Total
	=n	**%age**	**=n**	**%age**	
5-8	19	63.33	20	66.67	39(65%)
9-11	08	26.67	09	30	17(28.3%)
12-14	03	10	01	3.33	04(6.7%)
Total	30	100	30	100	60(100%)
Mean/S.D	8.07+ 2.55		7.45+ 1.99		

P Value: 0.581

Table 2: A comparison of per vaginal bleeding in both groups (after treatment)

Bleeding status	**Group A**		**Group B**		**Total**
	=n	**%age**	**=n**	**%age**	
Settled	16	53.3	25	83.3	41(68.3%)
Persisted	14	46.7	05	16.7	19(31.7%)

x^2 = 6.239 P Value 0.012

Table 3: A comparison of abdominal discomfort/ pain in both groups (after treatment)

Abdominal discomfort/pain	Group A		Group B		Total
	=n	%age	=n	%age	
Settled	15	50	25	83.3	40(66.7%)
Persisted	15	50	05	16.7	20(33.3%)
Total	30	100	30	100	60(100%)

X^2 = 7.500 P Value=0.006

Table 4: A comparison of pregnancy outcome in both groups (after treatment)

Pregnancy outcome	Group A		Group B		Total
	=n	%age	=n	%age	
Persisted	17	56.7	25	83.3	42(70%)
Aborted	13	43.33	05	16.67	18(30%)
Total	30	100	30	100	60(100%)

X^2= 5.079 P Value = 0.024

DISCUSSION

Miscarriage is pregnancy loss before 24 weeks' gestation based on the first day of the last menstrual period. Threatened miscarriage is manifested by vaginal bleeding, with or without abdominal pain, while the cervix is closed and the fetus is viable and inside the uterine cavity.

Progesterones are a group of hormones, which bind to the progesterone receptors; they include both the natural female sex hormone and the synthetic forms. Progesterone is secreted during early pregnancy from the ovary by corpus luteum. The functional corpus luteum is essential for the implantation and maintenance of early pregnancy through the production of progesterone.

On the other hand, for a long time, it was believed that gonadotrophin receptors were localized and had an effect only on gonadal tissues. Researchers in different laboratories, especially Professor Rao's group, found and characterized in detail luteinizing hormone/human chorionic gonadotrophin (LH/hCG) receptors in several nongonadal tissues including placenta and fetal membranes[10] myometrium[11] fallopian tube.

Numerous studies were directed towards characterizing in detail the vascular LH/hCG receptors and their functional relevance[12]. These studies showed that the human uterine artery contains LH/hCG receptor protein and messenger RNA (mRNA). Regarding function, it was hypothesized that hCG can influence local eicosanoid metabolism in the vascular wall, thus regulating the smooth muscle tone. The basis for this hypothesis was the earlier finding that hCG regulates local eicosanoid production in the ovaries[13].

Regarding use of progesterone alone for the treatment of threatened miscarriages, a study conducted byHayfaa A Wahabi and colleagues[2] it was concluded that there is no evidence to support the routine use of progesterones alone for the treatment of threatened miscarriage. Information regarding the potential harm to the mother or child, or both, with the use of progesterone in the treatment of threatened miscarriage is lacking.

But another study conducted by Peter Toth[9] describes that the combination of progesterone with magnesium or hCG yielded better results. The best response, even in the case of the most severe clinical signs, was achieved with the combination of magnesium, progesterone, and hCG. The first-trimester abortion rate was then as low as 16.6%. Regarding the data, the combination of magnesium with only hCG yielded almost the same success rate (18.1% abortion rate). Thus, magnesium and hCG therapy was almost as effective as its further combination with progesterone. Calculating the change in abortion rate as a percentile after hCG addition to therapy, there was a 46.8% decrease compared with magnesium treatment only. Contrary to this, progesterone addition (25% abortion rate) decreased the abortion rate by only 18.4% compared with magnesium treatment only.

In light of the study mentioned above, progesterone alone is not effective for the management of threatened miscarriage. But some evidences regarding progesterone with the combination of hCG are influencing to use this combination. My study is also in the view that the use of progesterone with hCG has better outcome as compare to progesterone alone. In the study, the patients were divided in two groups, Group-A was allotted for the patients treated with progesterone alone and Group-B to the patients treated with progesterone along with hCG administration. Gestational age was also similar in both the studies with 8.07 and 7.45 weeks mean in both groups respectively. These results are also in agreement with the study mentioned above, where the mean gestational age is 7 weeks, which is very close to our findings.

The main outcome of this study is based on three variables i.e. per vaginal bleeding; abdominal pain and persistence of pregnancy upto 2nd trimester. Data regarding patients' age, reproductive history, body mass index and gestational age in both groups, no major difference was observed. The main outcome of this study was settlement of per-vaginal bleeding, abdominal pain and persistence of pregnancy from first trimester to second trimester. Settlement of per vaginal bleeding in patients administered with progesterone alone was 53.33% while the patients treated with progesterone along with hCG showed 83.33% success rate.

Abdominal pain in Group-A was settled in 50% of the patients while 83.33% of the patients in Group-B get rid of it. Persistence of pregnancy upto 2nd trimester (>14 weeks) was the most important and considerable outcome which was 56.67% with progesterone alone while in the patients treated with progesterone +hCG was 83.33%. These main outcomes are comparable to a study conducted by Peter Toth[7,5] where progesterone in combination with hCG shown more success as compare to progesterone alone.

CONCLUSION

Management of threatened abortion with progesterone plus hCG has better outcome as compare to progesterone alone

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