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ORIGINAL ARTICLE

Comparison of Various Progesterone Drugs in Reducing Miscarriages

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ABTRACT

Background: Threatened abortion is a common complication of pregnancy. In order to prevent miscarriage progesterone in various forms is administered in patients. This is done to allow pregnancy to proceed further beyond twenty week of gestation.
Aim: To compare gravibinan (injected) with utrogestan/cyclogest (intra vaginal administration) in reduction of miscarriages.
Study design: Case control study
Place and duration of study: Department of Obstetrics & Gynecologiy, Mohtrama Benzair Bhutto Shaheed Medical College Mirpur and Department of Pediatric, Shaikh Zayed Hospital Lahore from 1st April 2020 to 30th September 2020.
Methodology: Pregnant women, who had vaginal bleeding until 20 weeks of their pregnancy, were assessed for inclusion. Participants were divided into three groups. Group A was given gravibinan, Group B was given utrogestan and Group C was given cyclogest.
Results: Women infested with gravibinan had 20% those who still had miscarriage while the number of miscarriages significantly decreased to 14.2% in utrogestan group and 13.63% in cyclogest group (p<0.005).
Conclusion: Cyclogest proved a better drug of choice for reducing miscarriages.
Keywords: Miscarriages, progesterone, pregnancy

INTRODUCTION

Estrogen and progesterone are the chief sex hormones in females that help and sustain early stages of pregnancy. These hormones are not only responsible for secretory changes in the lining of the endometrium and successful implantation of embryo but also improve vascularization, maintain gestational sac and support the developing baby.[1] Results of many studies suggest that reduction in the secretion of progesterone can be the causative factor for recurrent miscarrgies.[2-4]

Progestogen belongs to the group of drugs, called progestin. Progestins are synthetic form of naturally occurring hormone progesterone. These drugs are specifically designed to interact with progesterone receptors just like natural progesterone. These synthetic form of progesterone helps in the treatment of advance uterine cancer, abnormal bleeding due to hormonal imbalance, prevents abnormal thickening of uterus lining and facilitate the continuation of early pregnancy[5-7]

Pakistan is a highly populated developing country with an average low GDP. The annual birth rate is 27.4 births/1,000 population (2020 est.) during a year with annual miscarriage rate as 10-12%.[8] Lack of knowledge, malnourished and poor nutrition of mothers, low socioeconomic status, maternal age, prior stillbirths, hormonal imbalance, poor health care[9] and other such related complications lead to a high miscarriage ratio in this country. There is no significant data for the estimation of miscarriage rate in Pakistan. The prevalence of spontaneous recurrent miscarriages in India is 32%[10] which creates an immense distress among parents and adversely effects mother health.

Various progesterone based drugs have been assigned for prevention of miscarriages in different researches. Gravibinan (a drug) is given in the form of injectable to treat threatened miscarriages.[11] In comparison to gravibinan, the utrogestan can be administered both orally and also in the form of capsule through vagina or birth canal. It has shown maximum effectiveness with minimal side effects.[12] Cyclogest (vaginal suppository) can also be used to prevent miscarriages. Result of the study showed that rate of the abortion was reduced clinically with progesterone suppository.[13]

The present study was designed to compare the role of various progesterone drugs for reduction of recurrent miscarriages in females.

MATERIALS AND METHODS

It was a case control study including married women above the age of 18 years. The study included those pregnant women who were visiting gynecological outdoor departments of Mirpur Azad Kashmir and Shaikh Zayed Hospital Lahore. These pregnant women had vaginal bleeding until 20 weeks of their pregnancy. Each participants of the study underwent a general and pelvic examination including pelvic ultrasound as well as complete blood tests. Those women having any other systemic disease and loss of conception tissue were

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excluded from the study. These women either had no history or had a single or multiple miscarriages. Clinical history and demographic details were documented via structured questionnaire. The gravida and parity of each patient was noted. A total of 100 women with various miscarriage history were divided into two groups (groups A and Group B). Group A were administered gravibinan injections while utrogestan was given to Group B women. The outcome results were recorded.

Data analysis was conducted by using SPSS software version 21. Chi square was used to analyse qualitative while T-test was used for analyzing quantitative variables. The p-values <0.05 were considered as significant.

RESULTS

Fifty seven percent were those women who had already undergone miscarriage prior to recent conception. Within these women 44% had conceived for three months period. Ten percent female were given clomiphene citrate for attaining conception while 13% were on gonadotropin treatment. Rest of the women had a spontaneous pregnancy (Fig 1).

There were 34 such women who were having a parity level between 0-2 and had a history of miscarriages in their 1st trimester. While 15 women having a gravid level 0-2 had also misconceived before in their trimester. Nine women with the same parity level lost their previous conception in their 2nd trimester. It can evidently be noticed that as the parity increased the number of miscarriages reduced (Table 1).

A total of 69 participants were given gravibinan for prevention of miscarriages in them. Out of these 55 pregnant women continued their pregnancy while 14 had a miscarriage. Similarly out of 35 women who were administered progesterone therapy only 5 could not continue their pregnancy. Utrogestan in combination with cyclogest was given to 22 pregnant women. Only three of them had a miscarriage Table 2.

Thepercentage of miscarriages was noticed as highest in gravibinan administrated group in comparison to other two drugs as shown by Fig 2.

Fig. 1: Percentage illustration of previous miscarriage (A), previous conception (B), clomiphene citrate (C), gonadotrophin (D), spontaneous (E), later miscarriage (F) and continued pregnancy (G) in pregnant women

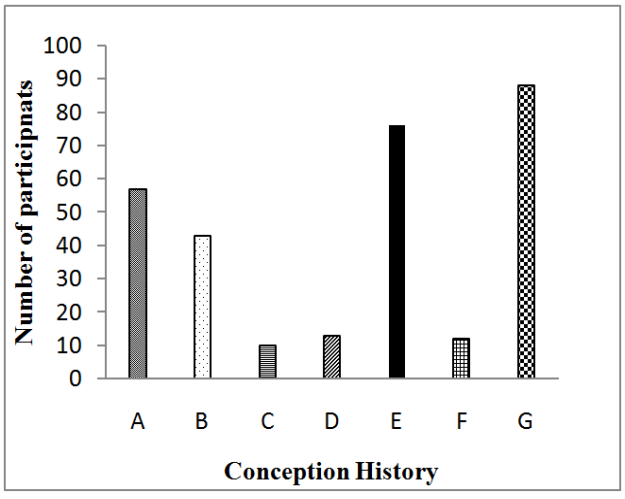


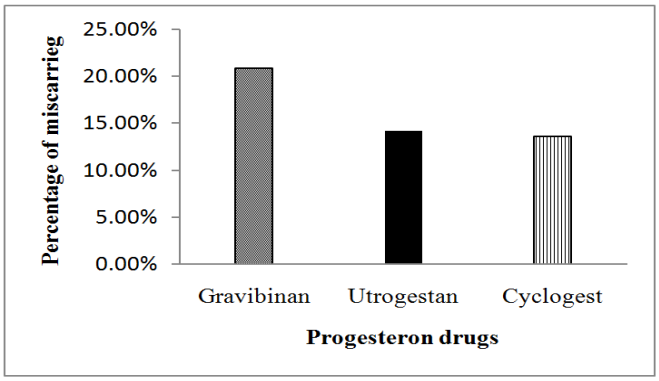
Table 1: Comparison of gravid and parity with miscarriage rate

Gravida & Parity	Previous Miscarriage (No. of pregnant women)			
	1st Trimester		2nd Trimester	
	G	P	G	P
G 0-2 &P 0-2	15	34	3	9
G 3-5 & P 3-4	24	10	5	1
G >6 & P >5	7	2	3	1
Total	46		11	

Table 2: Comparison of progesterone drugs for prevention of miscarriages

Variable	Administered	Continued Pregnancy	Miscarriage
Gravibinan	43	34	9
Utrogestan	35	30	5
Cyclogest	22	19	3
Total	100	83	17

Fig. 2: Comparison of miscarriages percentage among progesterone drugs



DISCUSSION

Immune reaction is influences by pro-inflammatory cytokines which are associated with miscarriages and level of blocking factor (PIBF) induced by progesterone This causes transferring of cytokines from one type to another resulting in increased production of type 2cytokines.[14] Recent literature proposes that progesterone can decrease miscarriages in women[15].

Miscarriage rate in developing countries like Pakistan escalated many folds within past few years. Poor contraceptive methods, diet and deprived female health care system are some of the key factors of high rate of miscarriages in this country.[9] Infertility treatment includes use of clomiphene citrate which is generally used to stimulates hormones that release mature egg. It is used in common clinical settings.[16] Like clomiphene citrate, gonadotrophin can also be used in ovulation induction.[17] In the present study, 10% to13% of enrolled women were given clomiphene citrate and gonadotrophin hormone to maintain and support their pregnancy.

Various progesterone based drugs are used to sustain early stages of pregnancy. Gravibinan, utrogestan and cyclogestare some of the common progesterone used to assist and maintain pregnancy in women[11-13] In the current study cyclogest seemed to be most reliable progetserone source for protection of miscarriage followed by utrogestin. Various studies suggested that the abortion rate was significantly and clinically reduced in women who

were having cyclogest suppositories as progesterone course[13,18].

The number of live births delivered by women has well been reported to reduce chances of miscarriage. This effect is caused by various factors. One of them is the reason that women with higher parity levels have decreased pregnancy related stress in them. A study in this context analysed data collected from first trimester which showed that those women with previous miscarriage history has increased pregnancy related anxiety[19]. An increase in parity significantly effect in decreasing pregnancy related anxiety[20] as also observed in current study.

CONCLUSION

Cyclogest proved a better drug in reduction of miscarriages followed by utrogestan.

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