# Should Human Chorionic Gonadotropin Supplementation be Used as a Routine Prophylaxis in High Risk Pregnancies?

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**Summary**

A randomised study of human chorionic gonadotropin (hCG) supplementation in 100 patients of high risk pregnancy was carried out in a large tertiary hospital of North India. Human chorionic gonadotropin injections were given in a dose of 2000 I.U. biweekly from the diagnosis of pregnancy till 16th week. The results showed that 16% patients in hCG group and 28% patients in control group had spontaneous abortions ($p>0.05$). However, after excluding patients with congenital malformation of uterus, patients in hCG group had significantly higher number of successful pregnancy outcome than control group (90.2% vs 72.9%, $p=0.039$). The present study supports the hypothesis that hCG supplementation may have a role in high risk pregnancies.

## Introduction

For centuries, spontaneous abortion, because of its social impact, has been the focus of interest to the obstetricians. Early pregnancy loss is a big psychological trauma to the patient especially if it occurs repeatedly. In almost half of the cases no apparent cause is found and traditionally hormonal factors have been blamed for abortion in these cases (Lauritsen 1972, Harrison 1985). As the hormones for maintenance of pregnancy are produced by corpus luteum in early pregnancy, dysfunction of corpus luteum may be the cause in loss of these pregnancies (Blumenfeld and Ruach 1992). Luteal phase defects have also been blamed for recurrent abortions in patients in whom pregnancy is generated by ovulation inducing drugs (Blumenfeld and Ruach 1992). Deficient luteal support may also be responsible for abortions in patients with congenital malformation of uterus like bicornuate or septate uterus (Rajan 1992). In all such situations human chorionic gonadotrophin (hCG) supplementation may play a role in providing luteal support because it acts as an effective luteotrophic agent with the ability to increase steroidogenesis (Rajan 1992). It has also been shown to prolong corpus luteum function. The present study was designed to test the hypothesis if hCG in dosages of 2000 IU biweekly causes decreased pregnancy wastage rates in patients with high risk pregnancy.

## Material and Methods

One hundred consecutive patients from Antenatal Clinic of S.G.T.B. Hospital, Amritsar or admitted in the Department of Obstetrics and Gynaecology, Medical College, Amritsar were enrolled for study. Each pregnant patient in whom the pregnancy

was previous (either generated by ovulation induction or the patient had suffered from previous recurrent abortions or patients with congenital malformation of uterus) was randomly allocated to two groups. Group I (hCG group) comprised of 50 patients who were given treatment with hCG injections supplemented with progesterone and tocolytics. Group II (Control group) comprised of 50 patients who were given progesterone and tocolytics only. A detailed medical and obstetric history was taken from each patient and complete general physical examination was done. All patients underwent following investigations: hemogram, bleeding time, clotting time, ABO and Rh group, urine examination, VDRL and fasting blood sugar. Ultrasound examination was done for confirming pregnancy and malformation of uterus. Other causes of spontaneous abortions such as cervical incompetence, TORCH infections, syphilis and medical causes like uncontrolled diabetes, chronic renal insufficiency etc. were ruled out by appropriate tests prior to enrolment. Ultrasound was also used to confirm menstrual date that the pregnancy was under eight weeks gestation. Informed consent was taken from all patients before commencing therapy. hCG injections were used in the dosages of 2000 I.U biweekly from diagnosis of pregnancy till 16th week. In all other aspects the pregnancies were managed normally. Fortnightly evaluation of foetal growth and well being was done by ultrasonography. Patients were asked regarding any history of bleeding per vaginum (PV) or pain in abdomen or any other side effects. A response was considered if a live baby beyond 36 week was delivered either through vaginal route or by caesarean section. The patients who aborted were considered as non responders. In these patients, curettage was done and specimens were sent for histopathology for confirmation of pregnancy. The statistical analysis was done using Chi-square for categorial variables and student's 't' test for quantitative variables.

## Results

The mean age of patients in both groups was similar (26±3.2 vs 25.9 ± 3.2 years, p >0.05). The Obstetric status of the patients in both groups was also similar (Table I). The mean period of gestation at the start of therapy was also similar in both groups. Eight patients in hCG group and 14 patients in control group had spontaneous abortions (Table II). Forty two patients in hCG group delivered live babies (40 full term, 2 preterm) while 36 patients in control group delivered live babies (31 full term, 5 pre term, p>0.05).

**Table I Clinical characteristics of patients**

| | HCG (n=50) | Control (n=50) | p |
|---|---|---|---|
| Mean age (years) | 26±3.2 | 25.9±3.2 | NS |
| Primigravida | 7(14%) | 8(16%) | NS |
| Abortion 3+ | 26(52%) | 29(58%) | NS |
| Uterus malformation | 9(18%) | 2(4%) | 0.026 |

Comparison of outcome of pregnancy after excluding patients with congenital malformation of uterus (n=41 in hCG group and n=48 in control group) showed that only 4 patients in hCG group and 13 in control group had spontaneous abortions while 37 in hCG group and 35 in control group had live births (1 pre term in hCG group, 4 pre term in control group; odds ratio 3.44, p=0.039). The type of labour and mode of delivery in both groups were similar. The difference in outcome became more significant if pre term live births were excluded (p=0.026). There were 8 patients in both groups who conceived with ovulation inducing drugs. Two patients in hCG group and 4 patients in control group had abortion while 6 patients in hCG group had full term live births compared to 4 in control group (p>0.05). There were 9 patients in hCG group who had congenital malformation of uterus out of which 4 had spontaneous abortion, one had preterm delivery and 4 had full term live delivery. There were only 2 patient with congenital malformation of uterus in control group out of which one had spontaneous abortion while other had pre term delivery. The rate of complications like bleeding PV, preterm labour and premature rupture of

**Table II : Pregnancy outcome in different groups**

| Groups | I | | | II | | | III | | | IV | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | hCG | Control | p | hCG | Control | P | hCG | Control | p | hCG | Control | p |
| Spontaneous abortion | 8 | 14 | NS | 4 | 13 | NS | 4 | 1 | NS | 3 | 1 | * |
| Pre term live births | 2 | 5 | | 1 | 4 | | 1 | 1 | | | | |
| Full term | 40 | 31 | NS | 36 | 31 | 0.039* | 4 | | | 4 | 3 | NS |
| n | 50 | 50 | | 41 | 48 | | 9 | 2 | | 8 | 8 | |

I Overall Group II Patient group excluding congenital malformation of uterus III–Patient group with congenital malformation of uterus

IV patient group with ovulation induction drugs

* Odds ratio 3.44 confidence interval (0.93-15.96)

**Table III Comparison of different parameters among both groups**

| | HCG | Control | p |
|---|---|---|---|
| **Mode of delivery** | | | |
| Normal delivery | 18 | 19 | NS |
| Caesarean | 24 | 17 | NS |
| **Infant parameters at birth** | | | |
| Birth weight (Kg) (Mean +SD) | 2.92 (0.4) | 2.65 (0.5) | 0.004 |
| APGAR (Mean + SD) | 9.4 (1.2) | 9.3 (1.7) | NS |
| **Complications** | | | |
| Bleeding PV | 9 | 10 | NS |
| Pre term labour | 1 | 2 | NS |

SD standard deviation

membranes were similar in both groups (hCG group – 21.4%, 2.3%, none vs 25%, 5.4%, 5.4% in control group respectively).

## Discussion

The present study showed that patients in hCG group had less number of abortions as compared to the control group although the difference was not statistically significant. However, after excluding patients with congenital malformation of uterus, hCG group had significantly higher number of successful pregnancy outcome compared to control group (p=0.039). The difference between two group became more significant if preterm live births were excluded (p=0.026). There are many studies in literature evaluating the role of hCG in recurrent abortions (Harrison 1985), Blumenfeld and Ruach 1992, Svigos 1982, Desai et al. 1995) but its role has never been evaluated in patients with congenital malformation of uterus. The present study did show that there were less number of abortions in patients with congenital malformation of uterus but may be because of small number of patients, the difference did not reach statistical significance. Luteal phase defects seem to be responsible for recurrent abortions (Horta et al 1977). HCG helps in maintaining the corpus luteum at the crucial time by providing hormonal support to the growing foetus (Harrison 1985). In the present study, the successful pregnancy outcome was 84% in hCG group and 72% in control group. After excluding patients with congenital malformation of uterus, this figure rose to 90.2% for hCG group and 72.9% for control group. There was statistically no difference in the rate of complications in both groups, however, the new born babies had higher birth weight in hCG group than control group (p<0.05, Table III). APGAR score of new born babies in both groups was similar.

Although hCG as a molecule was discovered many decades ago, the exact mechanism of action is not known (Harrison 1985). It is assumed that endogenous hCG is of low bioactivity and therefore, incapable of adequately stimulating the corpus luteum to secrete normal amounts of sex steroids and growth factors. The commercially administered hCG is manufactured from human pooled pregnant urine and contains substances with immunomodulatory influence. It also leads to regulation of blood flow in the uterine vascular system in early gestation, stimulates angiogenesis, decreases local vascular resistance and improves implantation (Harrison 1993).

In conclusion, the present study supports the view that hCG may be considered as a routine supplementation in women with recurrent abortions where other causes have been ruled out and in patients conceived with ovulation induction. It may have some role in patients with congenital malformation of uterus, however, this needs confirmation from further studies. Use of hCG should be restricted in selective cases after evaluation only while random use by general pratitioner and auxiliary workers should be discouraged.

## References


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