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ORIGINAL ARTICLE

Role of Human Chorionic Gonadotropin in Suppression of Preterm Labor

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ABSTRACT

Objective: To determine the mean prolongation of pregnancy via human Chorionic gonadotropin (H.C.G) in patients presenting with preterm labor.

Materials and methods: This descriptive case study was conducted in obstetrics and gynecology department, Women and children teaching hospital Dera Ismail khan from October 21, 2019, to April 20, 2020.

Result: A total of 123 pregnant women with preterm labor were included in the study. Average age was 25.44 years+4.70sd with range 16-35 years. Prolongation of pregnancy by human chorionic gonadotropin (HCG) of more than 30 days. Fifty-eight (47.2%) of preterm women were observed with prolongation of pregnancy of less than 30 days.

Practical implication: Suppression of Preterm Labor in the females using H.C.G.

Conclusion: The trial concluded that HCG is the better option in the prolongation of pregnancy in women with preterm delivery.

Keywords: Preterm delivery, Prolongation of pregnancy, NICU.

INTRODUCTION

American college of obstetrics and gynecology (ACOG) in 1995 has defined preterm labor as labour which take place after 20 weeks and before 37 weeks of pregnancy. Preterm labors constitutes about 10% of total labourours but since 70% of infants mortality is due to this. This problem is considered as one of the international indices in assessment of health condition worldwide [(1)] Preterm delivery is a major medical, economic, social and important problem worldwide and specifically in developing countries where neonatal services are grossly impaired. [(2-4)] Despite the many medical and social advances, the incidence of preterm delivery and its attended high perinatal morbidity and mortality has remained almost constant. It is therefore important to find cost effective ways of addressing prematurity issues in poor settings and thereby conservation scarce resources' currently being spent on the expensive care of preterm babies.[5] Human chorionic gonadotropin (H.C.G) is heterodimer glycoprotein produced primarily in the placenta and has multiple endocrine, paracrine and immunoregulatory actions [(6)]. The importance of H.C.G. in maintaining of early pregnancy has been widely accepted, reports have highlighted a potential role of H.C.G in maintaining uterine quiescence in the third trimester. H.C.G. exerts a potent concentration dependent inhibitory effect on human myometrium contractions [(7)]. The H.C.G. receptors in human myometrium are down regulated following the onset of labour, in both term and preterm deliveries [(6, 7)]. Intrauterine HCG infusion was associated with endometrial synchrony and reprograming of stromal development following ovarian stimulation. [(8)] Embryo implantation defects contribute to 70% of all pregnancy losses and are responsible for the low efficacy of embryo transfer during in vitro fertilization (IVF) protocols, necessitating transfer of multiple embryos.[(9)] Impaired endometrial receptivity remains one of the most significant barriers to the establishment of pregnancy, and its causes are often multifactorial in nature. Failed endometrial receptivity results from disease processes, including endometriosis. Successful pregnancy involves controlled down regulations of the maternal immune system with increased tolerance of foetal cells expressing paternal HLA antigen. This is mediated principally by human chorionic gonadotropin which has a documented ability to alter the action of T cells, dentritic cells and natural killer cells as well as increasing vascularization.[(10)] Studies on animal models have reaffirmed that hCG treatment mimics the benefits of pregnancy.[11] H.G.C in vitro acts by a type of mechanism connected to gas that can activate the plasma membrane of adenylate cyclase, thereby reducing specific gap junctions of myomemtrial cells and eventually decreasing surface tension of intracellular calcium, thus keeping myometer in zero phase of labour and causing uterine relaxation . The power of H.C.G in suppression of preterm labour might be due to direct restrain of myometer responses y production of eidcosaniods. H.C.G induces the production of eicosaniods that are like prostacyclines, that immediately cause loosening of myometer muscles. Recent data suggests that H.C.G might have a role as an endogenous tocolytic agent in normal pregnancy. A significant decrease in serum H.C.G level was found 2-3 weeks about the spontaneous onset of labour that might contribute to increasing the contractility in the uterine muscle and gradually initiating the onset of labor. One of the studies showed the 31.4±17.06 days average prolongation of pregnancy.[12] Preterm birth is common problem which require a prompt treatment and has a recurrence tendency. This study will provide us with regional statistics of efficacy of HCG in the prolongation of preterm birth. By conducting this study, one can know how much preterm deliveries could be prevented with HCG and build a hope for those others who lose their babies just because they are born preterm due to pre-term. Moreover, my study will add to the increasing body of evidence which suggests that preterm deliveries could be prevented by HCG therapy. My study will be beneficial for both gynecologists and alert mothers.

MATERIALS AND METHODS

This descriptive case study was conducted in Zanana Teaching Hospital Dera Ismail Khan from October, 2019 To April, 2020. Sample size was 123**,** using 31.4±17.06 days average prolongation of HCG, 95% confidence level and with absolute error of 0.05 (Yu et al 2023). Sampling technique used was convenient non-probability sampling. All patients were admitted in labor room and hemoglobin concentration, urinalysis and microscopical examination, blood group and RH typing, blood sugar was done for all of them. Ultrasound was performed to exclude confounders. Gestational age was determined by last menstrual period and first trimester ultrasound dating. Informed written consent was obtain from all the patients. Also demographic information was noted. In order to speed up fetal lung maturation two dose of Inj. Betamethasone 12mg, 24 hours apart were given to all patients in order to prevent any streptococcal infection. H.C.G was given in a dose of 5000 units' intramuscular injection followed by a drip of 10,000 units in 500ml of dextrose 5% at the rate of 20 drops per minute. Half hourly assessment of uterine contractions, maternal vital signs, fetal heart rate monitoring was done. Patients were kept under observation 24 hours after cessation of uterine contractions and arrest of labour, follow up were performed in antenatal clinics. At each visit blood pressure, pulse rate and fetal heart rate were recorded. Signs and symptoms of preterm labour were reviewed. At the time of delivery, neonatal weight and weeks of gestation were determined to calculate duration of prolongation of pregnancy was recorded. All the collected information was entered into SPSS version 10. Frequency and percentages were used for qualitative variables like parity and previous history of preterm history. Mean+ SD was calculated for continuous variables like age, gestational age and prolongation of pregnancy. Prolongation of pregnancy was stratified among age, gestational age, parity and previous history of preterm delivery using chi square test. P-value <0.05

were considered as significant. All the results were presented as tables and graphs.

RESULTS

A total of 123 pregnant women with preterm labor were included in the study. Majority of the patients were educated, married and house wife. Average age of the patients was 25.44 years+4.70SD with range 16-35 years. Patient's age was divided in four categories, out of which most common age group for preterm labour was 26-30 years. There were 23(18.7%) patients were of the age less than 25 years. Thirty three (26.8%) patients were in the age range of 21-25 years, 56(45.5%) were of age range 26-30 years and 11(8.9%) presented at age more than 30 years of age. (Table 1)

The gestational age of the women at presentation shows that majority 69(56.10%) of the patients were having less than 25 weeks of gestation while 54(43.9%) presenting more than 25 weeks of gestation. (Fig No 1)

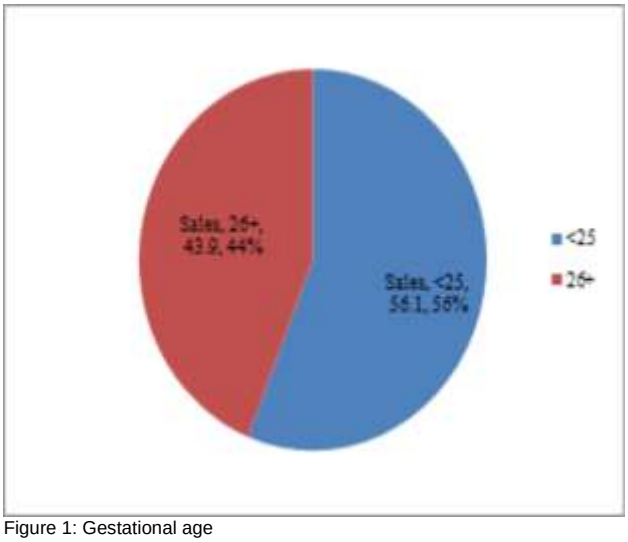

Figure 1: Gestational age

The majority of patients shows prolongation of pregnancy by Human Chorionic Gonadotropin (HCG) of more than 30days. Fifty eight (47.2%) of preterm women were observed with prolongation of pregnancy of less than 30 days. (Table 2)

Table 1: Age wise distribution of the patients

	Frequency	Percent	Mean +sd
<= 20.00	23	18.7	25.44years+4.70
21.00 - 25.00	33	26.8	25.44years+4.70
26.00 - 30.00	56	45.5	25.44years+4.70
31.00+	11	8.9	25.44years+4.70
Total	123	100	25.44years+4.70

Table 2: Prolongation of pregnancy of human chorionic gonadotropin

	Frequency	Percent	Mean +Sd
<= 30.00	58	47.2	29.85days+5.33
31.00+	65	52.8	29.85days+5.33
Total	123	100	29.85days+5.33

Age wise distribution shows that prolongation of pregnancy by HCG in younger age was little bit high as that of elder age group but it was statistically insignificant with p-value 0.747. The 12(52.2%) patients having age less than or equal to 20 years of age have prolongation of pregnancy of less than 30 days while 11(47.8%) patients having age less than or equal to 20 years of age have prolongation of pregnancy of more than 30 days, age 26-30 years contain 28(50%) patients have prolongation of pregnancy of less than 30 days and remaining patients have more than 30 days. (Table 3)

Table 3: Age wise distribution of prolongation of pregnancy

Age	Prolongation of Pregnancy <30 Days	Prolongation of Pregnancy >30 Days	Total	P-Value
<= 20.00	12 52.2%	11 47.8%	23 100.0%	0.747 %
21.00 - 25.00	14 42.4%	19 57.6%	33 100.0%	
26.00 - 30.00	28 50.0%	28 50.0%	56 100%	
31.00+	4 36.4%	7 63.6%	11 100%	
Total	58 47.2%	65 52.8%	123 100%	

Stratification of prolongation of pregnancy over gestational age, parity and history of preterm labour shows that prolongation of pregnancy by HCG was insignificant in our study. (Table 4)

DISCUSSION

Preterm birth remains one of the main causes of perinatal mortality and long-term morbidity. More than 70% of the total perinatal mortality can be attributed to preterm birth.[13] The rate of preterm birth is increasing across low- and middle-income countries, affecting 8.6% of births in high-income countries and between 7.4% to 13.3% in low- and middle- income countries.[14] Preterm birth is a leading cause of perinatal morbidity including respiratory distress syndrome (RDS), chronic lung disease, intraventricularhaem-orrhage, sepsis, cerebral palsy and other forms of neuro-developmental impairment.[15] Numerous studies described the role of several tocolytic drugs in eliminating the incidence of preterm labor, but only few studies compared drugs of the same group. Several agents have been used for the inhibition of uterine contractility, but it remains unclear what the first-line tocolytic agent should be.[16] Previously reported studies in the hCG-treated non-human primate in Women17,18 are now validated in women. Endometrial stromal a-SMA induction occurs during the early stages of pregnancy, in response to hCG, and at the initiation of decidualization.[17,19,20] Its expression is critical for preventing stromal apoptosis.[21,22] and regulates differentiation during decidualization, including the secretion of the decidual marker protein, insulin-like growth factor binding protein-1.[20,22] Carlos et al, observed that H.C.G. may play a significant role in maintaining pregnancy well after first trimester.[23] Mechanism of action of H.C.G. in treatment of threatened abortion maybe reduction of resistance against arterial blood flow.[24,25] Slattery et al, demonstrated that H.C.G. exerts a significant concentration dependent relaxant effect on human myometrial tissues in the third trimester of pregnancy.[26] Kurtzman et al reported the role of H.C.G. in maintenance of early pregnancy and its role in the maintenance of the later stage of pregnancy, by directly and indirectly promoting uterine quiescence. As an endogenous tocolytic, H.C.G. maybe an ideal candidate for the therapy of preterm labour.[27] Ali et al, observed that the mean prolongation of pregnancy was 28.8 days in HCG traeted group and 15 days in placebo group and there was statistically significant difference between the two groups (p value<0.001) regarding the delivery before 37 weeks and the proportion of infants weighing less than 2.5 kg. They stated that HCG exhibits potent tocolysis, with no fetal side effects.[28] Ibtissam Youssif AL Saffar et al conducted a study, using H.C.G., on 57 women with preterm labour in Bhagdad, Iraq from April 2006 till November 2006 and concluded that H.C.G. exhibits potent tocolysis, thereby prolonging pregnancy durations in women with preterm labor, without causing any adverse maternal/neonatal side effects.[29] Sakhavar N et al, in their clinical trial study concluded that H.C.G. & Magnesium sulphate have similar tocolytic efficacy but since H.C.G. has no maternal & fetal side effects, it is a good alternative drug in suppression of preterm labour.[30] Lorzadeh N et al., in their study found that delivery was delayed for 48hrs in 90.3% of women receiving H.C.G. The mean birth weight in their study was 2334gm, which is almost similar to that found in our

study. Also no adverse maternal/neonatal side effects were observed by them.[31] A preliminary study which involved administration of hCG or placebo to women in preterm labour reported signi®cant improvement in terms of prolongation of pregnancy and smaller numbers of infants with birthweights less than 2500g in the treatment group.[32]

CONCLUSION

In conclusion, the results of this study demonstrate that HCG is effective in prolonging pregnancy. H.C.G. exhibits potent tocolysis with no maternal/neonatal side effects. However further studies with greater number of subjects and ones where either cervical length measurement using transvaginal sonography or fetal fibronectin are incorporated into the definition of preterm labor need to be done to arrive at a final conclusion.

REFERENCES

1 Cunningham FG, Gant NF , leveo KI,glisterap LC. Williams abstetrics. 22nd,Ed ,new york mcgraw-hill 2005; P. 856-8.

2 Bradshaw SC, Brotman RM. Making inroads into improving treatment of 1bacterial vaginosis – striving for long-term cure. BMC Infect Diseas 2015; 15: 292.

3 Esber A, Vicetti Miguel RD, Cherpes TL. Risk of Bacterial Vaginosis Among Women With Herpes Simplex Virus Type 2 Infection: A Systematic Review and Meta-analysis. J Infect Dis 2015; 212: 8.

4 Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015; 64: 1.

5 Gravett MG, Rubens CE. Global Alliance to Prevent Prematurity, and Stillbirth Technical Team. A framework for strategic investments in research to reduce the global burden of preterm birth. Am J Obstet Gynecol 2012; 207(5): 368–73.

6 Ticconi C, Piccione E, Belmonte A, Reo CV. HCG- A new kid on the block in prematurity prevention. J maternal-Fetal neonatal med obstet Gynecol 2006; 19: 11.

7 Slattery MM, Brennam C, O" leary MJ, Morrison JJ. Human chorionic gonadotropin inhibition of pregnant human myometrial contractility. Br j Obstet Gynecol 2001; 108: 704-8.

8 Strug MR, Su R, Young JE, Dodds WG, Shavell VI, Díaz-Gimeno P. Intrauterine human chorionic gonadotropin infusion in oocyte donors promotes endometrial synchrony and induction of early decidual markers for stromal survival: a randomized clinical trial. Hum Reprod 2016 Jul; 31(7): 1552-61.

9 Strug MR, Renwei SU, Young JE, Dodds WG, Shavell VI, Díaz-Gimeno P, et al. Intrauterine human chorionic gonadotropin infusion in oocyte donors promotes endometrial synchrony and induction of early decidual markers for stromal survival: a randomized clinical trial. Hum Reprod 2016 Jul; 31(7): 1552–1561.

10 Bansal AS. Human Chorionic Gonadotropin–Can Nature's Own anti-rejection agent Help in reducing chronic rejection in Solid Organ transplantation. Reproductive Immunol Open Acc 2016; 1: 1.

11 Rao CV. Potential Therapy for Rheumatoid Arthritis and Sjögren Syndrome with Human Chorionic Gonadotropin. Reprod Sci 2016 May; 23(5): 566-71.

12 Goswami P, Agrawal V. Human Chorionic Gonadotropin (H.C.G.) in Suppression of Preterm Labour. J Evolution Med Dental Sci 2015; 4(49): 8475-82.

13 Slattery MM, Morrison JJ. Preterm delivery. Lancet. 2002360(9344):1489-97. 14. WHO. World Health Statistics. www.who.int/gho/publications/world_health , 2012.

15 Saigal S,Doyle LW. An overview of mortality and sequale of preterm birth from infancy to adulthood. Lancet 2008; 371: 261-9.

16 American College of Obstetricians and Gynecologists Committee on Practice Bulletins: ACOG practice bulletin no. 43: Clinical management guidelines for obstetrician gynecologists. May 2003. Management of preterm labour. Obstet Gynecol 2003; 101: 1039-47.

17 FazleabasAT, DonnellyKM, Srinivasan S, Fortman JD, Miller JB. Modulation of the baboon (Papio anubis) uterine endometrium by chorionic gonadotrophin during the period of uterine receptivity. Proc Natl Acad Sci USA 1999; 96: 2543–8.

18 Afshar Y, Jeong JW, Roqueiro D, DeMayo F, Lydon J, Radtke F, Radnor R, Miele L, Fazleabas A. Notch1 mediates uterine stromal differentiation and is critical for complete decidualization in the mouse. FASEB J 2012a; 26: 282–94.

19 Christensen S, Verhage HG, Nowak G, de Lanerolle P, Fleming S, Bell SC, Fazleabas AT, Hild-Petito S. Smooth muscle myosin II and alpha smooth muscle actin expression in the baboon (Papio anubis) uterus is associated with glandular secretory activity and stromal cell transformation. Biol Reprod 1995; 53: 598–608.

20 Kim JJ, Jaffe RC, Fazleabas AT. Insulin-like growth factor binding protein-1 expression in baboon endometrial stromal cells: regulation by filamentous actin and requirement for de novo protein synthesis. Endocrinol 1999; 140: 997–1004.

21 Lovely LP, Fazleabas AT, Fritz MA, McAdams DG, Lessey BA. Prevention of endometrial apoptosis: randomized prospective comparison of human chorionic gonadotropin versus progesterone treatment in the luteal phase. J Clin Endocrinol Metab 2005; 90: 2351–6.

22 Jasinska A, Strakova Z, Szmidt M, Fazleabas AT. Human chorionic gonadotropin and decidualization in vitro inhibits cytochalasin- D-induced apoptosis in cultured endometrial stromal fibroblasts. Endocrinol 2006; 147: 4112–21.

23 Ticconi C, Piccione E, Belmonte A, Reo CV. HCG- A new kid on the block in prematurity prevention. Journal of Maternal-Fetal and Neonatal Medicine, Obstet Gynecol 2006; 19th: 11 November.

24 Reshef F, Lei ZM, Rao Chv, Pridham DD. The presence of gonadotropin receptors in non–Pregnant human uterus, human placenta, fetal membranes and deciduas. J Clin Endocrinol Metab 1999; 70: 421– 9.

25 Toth P, Gimes G, Paulin F, Rao Ch V. HCG treatment in early gestation: its impact on uterine blood flow and pregnancy outcome [abstract]. Fertil Steril 1998; 70: s46.

26 Slattery MM, Brennan C, O´Leary, MJ, Morrison JJ. Human chorionic gonadotropin inhibition of pregnant human myometrial contractility. Br J Obstet Gynecol 2001; 108: 704-8.

27 Kurtzman JT, Spinnato JA, Goldsmith LJ, Zimmerman MJ, Klem M, Lei ZM, Rao CV. Human chorionic gonadotropin exhibits potent inhibition of preterm delivery in a small animal model. Am J Obstet Gynecol 1999; 181: 853-7.

28 Ali FM, Fateen B, Ezzet A, Badawy H, Ramadan A, El-tobge A. Treatment of preterm labour with human chorionic gonadotropin: a new modality. Obstet Gynecol 2000; 95: 104.

29 AL – Saffar IY, Salih HI. Human chorionic gonadotropin in treatment of preterm labour. The Iraqi Postgraduate Med J 2010; 9(3): 526-32

30 Sakhavar N, Mirteimoori M, Teimoori B. Magnesium Sulfate versus HCG (Human Chorionic Gonadotropin) in Suppression of Preterm Labour. Shiraz E-Medical J 2008; 9(3): 156-60

31 Lorzadeh N, Kazemirad S, Lorzadrh M, Dehnori A. A comparison of human chorionic gonadotropin with Magnesium Sulphate in inhibition of preterm labour. J Med Sci 2007; 7(4): 640-4.

32 Ali AF, Fateen B, Ezzet A, Badway H, Ramadan A, El-Tobge A. Treatment of preterm labour with human chorionic gonadotropin: a new modality. Obstet Gynecol 2000; 95: S61.