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Study the Suppression of Preterm Labor Using Human Chorionic Gonadotropin Hormone Compared with Magnesium Sulphate

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Abstract

Preterm labor is known as delivery prior to 37 completed weeks of gestation. Because 10% of total labors are preterm and 70% of neonatal mortality is caused by this problem, preterm labor is a significant problem in obstetrics, pediatrics & midwifery. This study aims at comparing the efficacy as well as adverse effects profile of (human chorionic gonadotropin hormone and magnesium sulphate) in suppression of preterm labor.

This study was designed as a prospective comparative randomized clinical trial done from 4th April to 1st September 2020. The study population included pregnant women with preterm labor, who were admitted to Salah Al Din General Hospital, in Tikrit city. Sixty two cases who consented (Informed written consent was obtained from all the patients) were randomly allocated to 2 different intervention groups, named A and B. Group A and B consisted of 30 and 32 pregnant women, respectively. All cases were admitted in labour room and baseline investigations were done. Group A: For patients of group A: received an intravenously loading dose of 4 g (1 g/min) Magnesium sulphate. A continual infusion of 2 g per 1 hr was then administrated. The infusion was continued until 12 h of uterine quiescence is done. Group B: (32 women), intramuscular injection Human Chorionic Gonadotropin was administered as an initial dose of 5000 IU. Half hourly assessment of uterine contractions, maternal vital signs, fetal heart rate monitoring was done. All of the patients were under monitoring in the hospital until 24 h of the end of drug infusion. Also, both of the groups received Betamethasone, 12 mg every 24 hr for 2 doses. Patients were under control until the end of pregnancy.

It was foun that Delay of Labour for ≥21 day was higher among Human Chorionic Gonadotropin group (68.8%) than among MgSO4 group (60%), and delivery within <2 days was higher among HCG group (9.4%) than among MgSO4 group (6.7%). The mean duration in hours from time of start of treatment with Magnesium sulphate to the contraction suppression was (2.9±0.08) lower than of the HCG treatment group (3.11±0.13). The commonest side effect of MgSO4 was thirst (50%), hyperthermia (46.67), and head ache (30%), dizziness (30%), while there is no side effect among HCG group except single case complained of head ache (3.13%),

It was concluded that magnesium sulphate is better than Human Chorionic Gonadotropin in stopping preterm labour with faster onset of action than Human Chorionic Gonadotropin but had side effects for mothers more than Human Chorionic Gonadotropin.

Keywords:; **Preterm Labor; hCG Magnesium Sulphate; Suppression**

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دراسة قمع الولادة المبكرة باستخدام هرمون موجهة الغدد التناسلية المشيمية البشرية مقارنة بكبريتات المغنيسيوم

ورقاء واثق, مصرية رشاد حسين

الخلاصة

يُعرف المخاض المبكر بالولادة قبل 37 أسبوعًا من الحمل. نظرًا لأن 10٪ من إجمالي المخاض خدج و 70٪ من وفيات الأطفال حديثي الولادة ناتجة عن هذه المشكلة ، فإن المخاض قبل الأوان يمثل مشكلة كبيرة في التوليد وطب الأطفال والقبالة.. تهدف هذه الدراسة إلى مقارنة الفعالية وكذلك التأثيرات الضائرة (هرمون موجهة الغدد التناسلية المشيمائية البشرية وكبريتات المغنيسيوم) في قمع المخاض قبل الأوان.

تم تصميم هذه الدراسة كتجربة سريرية عشوائية مقارنة مستقبلية أجريت في الفترة من 4 أبريل إلى 1 سبتمبر 2020. شمل مجتمع الدراسة النساء الحوامل اللواتي يعانين من الولادة المبكرة ، والذين تم إدخالهم إلى مستشفى صلاح الدين العام في مدينة تكريت. ثمانون حالة وافقوا (تم الحصول على موافقة خطية مستنيرة من جميع المرضى) تم تخصيصهم بشكل عشوائي لمجموعتين مختلفتين من التدخل ، المسماة A و B. المجموعة A و B تتألف من 30 و 32 امرأة حامل ، على التوالي. تم قبول جميع الحالات في غرفة المخاض وتم إجراء التحقيقات الأساسية. المجموعة أ: المجموعة أ: تلقى مرضى المجموعة ب جرعة تحميل في الوريد من 4 جم (1 جم / دقيقة) من كبريتات المغنيسيوم. تم بعد ذلك إعطاء التسريب المستمر لـ 2 جم h-1. استمر التسريب حتى اكتمال 12 ساعة من سكون الرحم. بالنسبة للمرضى من المجموعة ب (32 امرأة) ، تم إعطاء هرمون الغدد التناسلية المشيمية البشرية عن طريق الوريد بجرعة أولية من 5000 وحدة دولية في الحقن العضلي. تم إجراء تقييم نصف ساعة لتقلصات الرحم والعلامات الحيوية للأم ومراقبة معدل ضربات قلب الجنين. كان جميع المرضى تحت المراقبة في المستشفى حتى 24 ساعة من نهاية حقن الدواء. أيضًا ، تلقت كلتا المجموعتين عرض بيتاميثازون 12 ملغ جرعتان .

تم التوصل الى ان تأخر المخاض لمدة 21 يومًا كان أعلى بين مجموعة هرمون الغدد التناسلية المشيمية البشرية (68.8٪) منه بين مجموعة كبريتات المفغنيسيوم (60٪) ، وكانت الولادة خلال أقل من يومين أعلى بين مجموعة هرمون الغدد التناسلية المشيمية البشرية (9.4٪) مقارنة بمجموعة كبريتات المغنيسيوم (6.7٪). كان متوسط المدة بالساعات من وقت بدء العلاج بكبريتات المغنيسيوم إلى تثبيط التقلص (2.9 ± 0.08) أقل من مجموعة المعالجة هرمون الغدد التناسلية المشيمية البشرية (3.11 ± 0.13). كان التأثير الجانبي الأكثر شيوعًا لـ كبريتات المغنيسيوم هو العطش (50٪) ، ارتفاع الحرارة (46.67) ، آلام الرأس (30٪) ، الدوخة (30٪) ، بينما لا توجد آثار جانبية بين مجموعة هرمون الغدد التناسلية المشيمية البشرية باستثناء حالة واحدة مشكو منها من آلام في الرأس (3.13 ٪) .

تم الاستنتاج الى ان كبريتات المغنيسيوم أفضل من هرمون الغدد التناسلية المشيمية البشرية في ايقاف المخاض مع عدم ، وبتأثير أسرع من هرمون الغدد التناسلية المشيمية البشرية ولكن لها آثار جانبية أكثر لدى الامهات اكثر من هرمون الغدد التناسلية المشيمية البشرية.

1. Introduction

Preterm labor and delivery continue to take an important space in the obstetrical interest and research society because of the community health issue they persist to generate. Existing treatment for preterm labor at top delay delivery for 48 h, through which time glucocorticoids can be administered to promote fetal lung maturity and so reduce the probability or severity of intraventricular haemorrhage, respiratory distress syndrome, neonatal death, necrotising enterocolitis, and length of neonatal hospital stay [1]. Recently there are no unanimous protocols for the treatment of preterm labor and the treatment of preterm labor persists an issue of contentious [2]. So, obstetrician should detect and treat preterm labor amid essential controversy over the efficiency of therapeutic and preventive modalities [3,4]. Corticosteroids, tocolytics and to some degree antibiotics have all been found to have a function to play in the treatment. Magnesium sulphate therapy has been utilized as a tocolytic in obstetric practice in American since the 1960 [5]. The guide that supports its utilization for tocolysis is weak. Magnesium ions do prevent myometrial contractility in vitro, perhaps by suppression of myometrial calcium channels. However randomized trials demonstrate that it is no better than placebo at postponing delivery of preterm [6]. Magnesium sulfate lowers calcium levels in uterine muscle cells since calcium is necessary for muscle cell to contract, this is thought to relax uterine muscle[17]. Complications correlated with the utilization of magnesium sulfate include vomiting and nausea. headache and hypotension, and the more severe influence of pulmonary edema and respiratory depression. Because magnesium sulfate crosses the placenta, fetal side effects involve reduced lethargy and muscle tone [8]. The aim of the study was to compare the efficacy as well as adverse effects of human chorionic gonadotropin hormone and magnesium sulphate.

2. Patients and Methods

This study was designed as a comparative single blind randomized clinical trial from 1st of April, 2020 to end of August, 2020 included pregnant women with preterm labor, who were admitted to Salah Al Din General Hospital, in Tikrit city were invited to participate. Sixty two cases who consented (Informed written consent was obtained from all the patients)

were randomly allocated to 2 different intervention groups, named A and B. Group A and B consisted of 30 and 32pregnant women, respectively.

Data were collected utilizing full history taking and questionnaire, and clinical examination. Information included the demographic information, parity , age and gestational age, information about side effect of the drugs, complications of pregnancy, obstetrical history, drug side effect information, and information of clinical examination. Examination of the vital signs of the mother, contractions and fetal heart rats using manual procedure or Cardiotocography (CTG). Gestational age was determined by last menstrual period and first trimester ultrasound dating.

2.1. Preterm Labor Diagnosis

Preterm labor diagnosis was made in women between 28 weeks and 36 weeks + 6 days of gestation if contractions of the uterus at a frequency of four contractions per 20 min or eight contractions per 40 min and were associated. The cases placed in the lateral recumbent posture and externally observed for contractions and fetal heart rats using manual procedure or Cardiotocography (CTG). If contractions of uterus were existing at minimum every 15 min, a bolus infusion of glucose water intravenously of 500 mL of was administered. This rapid intravascular expansion can reduce the contractions of an irritable uterus and help the obstetrician distinguish this condition from preterm labor. By this mode cases could be included.

2.2. Exclusion criteria

1. Abnormal vaginal bleeding
2. Premature rupture of membrane.
3. Cervical dilatation more than 3 cm
4. Diabetes mellitus,
5. Maternal cardiorespiratory diseases,
6. Maternal infections,
7. Genitourinary infections,
8. Chorioamnionitis,
9. Pelvis and fetal anatomical anomalies,
10. Uterine anomalies,
11. Preeclampsia, eclampsia or gestational hypertension,
12. Fetal disorders like fetal distress, IUGR.
13. Polyhydramnios.

2.3. Management of involved cases

All cases were admitted in labour room and their Hemoglobin concentration, general urine examination, blood group and Rh, blood sugar was investigated. In order to enhance fetal lung maturation, Betamethasone 12mg every 24 hrs was prescribed for two days. In order to prevent any streptococcal infection in neonates in both group Erythromycin was given as 500mg twice per day for 5 days.

2.4. Group A

Patients of group A (30 patient) received an intravenously loading dose of 4 g (1 g/min) Magnesium sulphate. A continual infusion of 2 g/hr was then administrated. The infusion was continued until 12 h of uterine quiescence is done .

All of the patients were under monitoring in the hospital until 24 h of the end of drug infusion. Patients were under control until the end of pregnancy.

In this study data such as maternal. Gestational age when the diagnosis of preterm labor was done, delay of labor due to management protocols, complications frequency in both groups were registered.

2.5. Group B

For patients of group B (32 women), HCG (Human Chorionic Gonadotropin) was administered in an initial dose of 5000 IU intramuscular injection. Then 10000 IU of HCG in 500 mL of normal saline was administered by the order of 20 drops per minute intravenously. The protocol was continued until the time that contractions discontinued. Half hourly assessment of uterine contractions, maternal vital signs, fetal heart rate monitoring was done.

Patient was kept under monitoring 24 hrs after cessation of uterine contractions and arrest of labor. Follow up was done in antenatal clinics. At each visit blood pressure, pulse rate and fetal heart rate were recorded. Preterm labor's signs and symptoms were reviewed. At the delivery time, weeks of gestation and neonatal weight were identified to calculate duration of prolongation of pregnancy.

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2.6. Statistical analysis

Results were analyzed using descriptive statistics, distributional indices. Independent t-test was occupied to compare maternal age, gravidity, time of admission and neonatal birth weight between two groups.

3. Results

Most of the preterm cases enrolled in the study was (30-31 wk), MgSO4 12(40%), HCG 12(37.5%), followed by (32-33 wk), MgSO4 10(33.3%), HCG 12(37.5%), this relation was statistically not significant as shown in Table 1.

Table 1. The distribution of the patient according to study group and gestational age

Gestational age in week	Study Group		Total
	Group A (MgSO4)	Group B (HCG)	
< 28 wk	2	2	4
	6.70%	6.30%	6.50%
28-29 wk	2	2	4
	6.70%	6.30%	6.50%
30-31 wk	12	12	24
	40.00%	37.50%	38.70%
32-33 wk	10	12	22
	33.30%	37.50%	35.50%
34-37 wk	4	4	8
	13.30%	12.50%	12.90%
Total	30	32	62
	100.00%	100.00%	100.00%

X2=0.117, df=4,Pvalue >0.05 NS

The time was calculated by hours from the point at which the treatment started til the suppression of contractions. Analysis of the timeline show that 13(43.3%) of the MgSO4 group respond within 2.9 hours, while HCG group most of them respond within 3.1 hours, this relation was statistically significant (p value < 0.05), as shown in Table 2

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Table 2:The association between onset time for contraction suppression and type of treatment.

time for suppression of contraction in hours	Study Group		Total
	Group A (MgSO4)	Group B (HCG)	
2.8	9	1	10
	30.00%	3.10%	16.10%
2.9	13	5	18
	43.30%	15.60%	29.00%
3	6	0	6
	20.00%	0.00%	9.70%
3.1	2	15	17
	6.70%	46.90%	27.40%
3.2	0	5	5
	0.00%	15.60%	8.10%
3.3	0	6	6
	0.00%	18.80%	9.70%
Total	30	32	62
	100.0%	100.0%	100.0%

X2=36.87, df=5, p value < 0.05 significant

Delay of Labor for ≥21 day was higher among HCG group 22(68.8%) than among MgSO4 group 18(60%), and delivery within <2 days was higher among HCG group 3(9.4%) than among MgSO4 group 2(6.7%), this relation was statistically not significant (p value > 0.05), as shown in table 4

Table 4. The association between duration of delayed labour and type of treatment.

Days of delayed labour	Study Group		Total
	Group A (MgSO4)	Group B (HCG)	
< 2	2	3	5
	6.70%	9.40%	8.10%
2 day	4	4	8
	13.30%	12.50%	12.90%
3-7 day	2	1	3
	6.70%	3.10%	4.80%
7-13 day	2	1	3
	6.70%	3.10%	4.80%
14-20 day	2	1	3
	6.70%	3.10%	4.80%
≥21 day	18	22	40
	60.00%	68.80%	64.50%
Total	30	32	62
	100.00%	100.00%	100.00%

X2=1.57, df=5, p value > 0.05 not significant (Likelihood Ratio)

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The mean duration in hours from time of start of treatment with Magnesium sulphate to the contraction suppression was (2.9±0.08) lower than of the HCG treatment group (3.11±0.13), this relation was statistically significant (P value <0.05), as shown in figure 1.

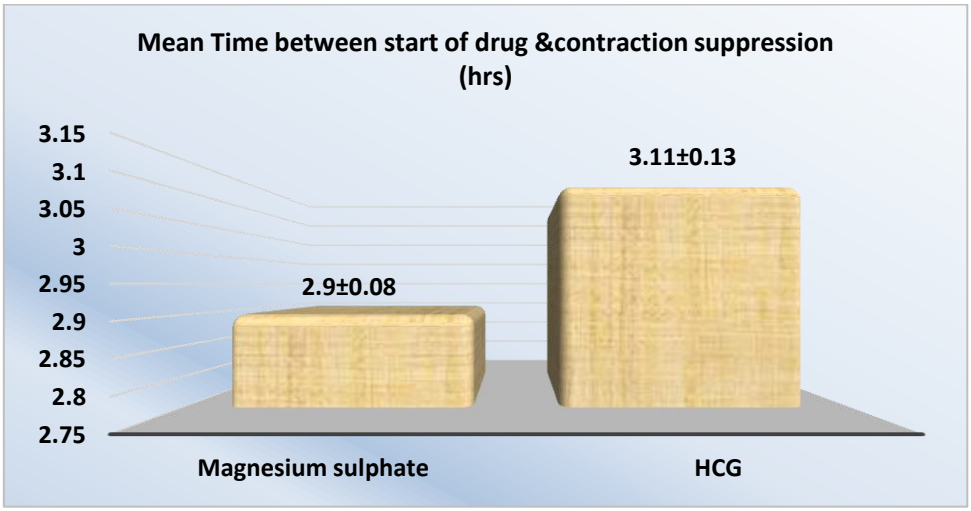

Figure 1: The mean duration from start of the treatment to the contraction suppression (hr)

The commonest side effect of MgSO4 was thirst 15(50%),hyperthermia 14(46.67), and head ache 9(30%), dizziness 9(30%), while there is no side effect among HCG group except single case complained of head ache 1(3.13), as shown in table 5.

Table 5: The distribution of the side effects according to type of treatment

Complaints of patients	Group A (MgSO4)		Group B (HCG)	
	Frequency	Percent	Frequency	Percent
Headache	9	30.00	1	3.13
Dizziness	9	30.00	0	0
Thirst	15	50.00	0	0
Nausea and vomiting	6	20.00	0	0
Hyperthermia	14	46.67	0	0

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4. Discussion

The current study revealed that the analysis of study groups that treated with Magnesium sulphate (MgSO4) (30 patient), and those treated with HCG (32 patient), show that there is no difference among both groups regarding age, parity, gestational age. This goes in accordance with Sakhavar N who found that most factors in the Magnesium Sulfate group and HCG group were the same including: parity of mothers, history of urinary infection, interval between previous and present delivery, history of preterm labor and abortion, duration and interval of contractions[9] Also agrees with Goswami P who found that the demographic characteristics in both the study groups were similar, including maternal age, parity, gestational age, education and socioeconomic factors [10]. The current study revealed that the most of the preterm cases enrolled in the study was (30-31 wk), MgSO4 (40%), HCG (37.5%), followed by (32-33 wk), MgSO4 (33.3%), HCG (37.5%). This goes in accordance with Goswami P [10] who found that the mean gestational age at the time of enrollment was (31.22 wks & 30.93wks), in women receiving H.C.G. & Magnesium sulphate respectively. Maximum cases were enrolled between gestational ages (30-31) wk 6 days i.e. 36.25%) . Also Nemani S *et al* 2018 [11] found that (66.7%)respond within 2 hrs, and lower than what found by Kawagoe Y *et al* (100) the time taken for uterine quiescence was 6.22 hrs. HCG group most of them respond within 3.1 hour, this goes in accordance with Prakriti Goswami, and Veena Agrawal who studied only HCG effect in 2015 found that the mean duration between initiation of treatment and suppression of contractions after HCG treatment was 3.1±0.12 hrs [10]. The current study revealed that the delay of labour for ≥21 day was higher among HCG group (68.8%) than among MgSO4 group (60%), and delivery within <2 days was higher among HCG group (9.4%) than among MgSO4 group (6.7%). This indicates the both these drugs have similar efficacy with respect to mean prolongation of pregnancy and it is higher among HCG group. This goes in accordance with Goswami P who found that Mean prolongation of pregnancy in H.C.G. group was 31.4 days & in Magnesium sulphate group was 30.33 days. Also Goswami P found the average rate of labour within 48 hrs after beginning of treatment, in the H.C.G. group was 8% (4 out of 50) and in the Magnesium sulphate group was 6.67% (2 out of 30). Lorzadeh N *et al*., in their study found that delivery was delayed for 48 hrs in 90.3% of women receiving H.C.G. The mean birth weight in their study was 2334 gm, which is almost similar to that found in our study. No adverse

maternal/neonatal side effects were observed by them [13]. The current study revealed that the commonest side effect of MgSO4 was thirst (50%),hyperthermia (46.67), and head ache (30%), dizziness (30%), while there is no side effect among HCG group except single case complained of head ache (3.13). This goes in accordance with Goswami P who found that none of the patients receiving H.C.G. had any complaints. All 30 women receiving Magnesium sulphate had one or another complaint from side effects of drugs [14] Sakhavar N, found that the their findings indicate that the ability of HCG in suppression of preterm labor is similar to Magnesium Sulfate however, maternal tormenting side effects of Magnesium Sulfate was 100% while it was nil for HCG. [15]. Al-Saffar IY, and Salih HI [16] conducted a study, using H.C.G., on 57 women with preterm labour in Bhagdad, concluded that H.C.G. exhibits potent tocolysis, thereby prolonging pregnancy durations in women with preterm labour, without causing any adverse maternal/neonatal side effects.

5. Conclusions

1. Delay of Labour for ≥21 day was higher among HCG group than among MgSO4 group,
2. The mean duration in hours from time of start of treatment with Magnesium sulphate to the contraction suppression was lower than of the HCG treatment group.
3. The commonest side effect of MgSO4 was thirst, hyperthermia, and head ache, dizziness.
4. There was no side effect among HCG group except single case complained of head ache.
5. H.C.G. exhibits potent tocolysis with no maternal & neonatal side effects. Further studies need to be done to establish the role of H.C.G. in suppression of preterm labour.
6. Magnesium sulphate is better than H.C.G., as it has statistically significant, faster onset of action.

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