

To Compare the Efficacy of Beta Agonist Ritodrine and Calcium Channel Blocker Nifedipine in the Management of Preterm Labour

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ABSTRACT

Aim: To compare the efficacy of beta agonist ritodrine and calcium channel blocker nifedipine in inhibiting uterine contractions for prolongation of pregnancy up to 48 hours, in patients with preterm labour.

Methods: This randomized clinical trial was conducted at Obstetrical & Gynaecological Department, Lady Aitchison Hospital, Lahore between six months from 8th July 2009 to 8th January 2010. One hundred and sixty patients with gestational age between 24 to 37 weeks were included. All patients were divided in 2 groups; group A (Inj. Ritodrine 2 ampules (100 mg) and group B (Tab. Nifedipine 20 mg). Each group comprised 80 patients..

Results: The mean age in group A was 27.7±3.8 years and 27.3±3.5 years in group B. The mean duration of pregnancy with dates in group A was 32.7±1.5 weeks and 32.5±1.7 weeks in group B. In group A, 67 (83.7%) patients in whom duration of treatment and delivery was more than 48 hours and in group B, there were 73 (91.2%) patients. In group A, 67 (83.7%) patients, in whose the treatment was effective and in group B, there were 73 (91.2%) patients.

Conclusion: Both the treatment modalities are effective, but nifedipine is significantly associated with a longer duration of postponement of delivery in comparison with ritodrine in the management of preterm labor.

Keywords: Efficacy, Preterm labour, Ritodrine, Nifedipine

INTRODUCTION

Preterm labour is spontaneous occurrence of regular uterine contractions productive of cervical changes that is dilatation and effacement after 24 weeks and prior to 37 completed weeks of gestation from 1st day of last menstrual period.¹ Preterm labour is a major cause of perinatal mortality and morbidity in developing countries.² Incidence of preterm labour is 12.5% in United States and 10.5% in Asian population³ and rate of premature births has increased by more than 33% in US since 1981.⁴ Its prevalence is affected by the way in which gestational age is assessed, by national differences in the registration of births and perceived viability of extremely preterm infants.⁵ Early detection and management are important steps in preventing preterm labour, which is leading cause of neonatal mortality and morbidity and accounts for 35% of all health care spending on the neonates. Preterm labour is diagnosed when there is persistence of at least two symptomatic uterine contractions in 10 minutes period, at least 50% cervical effacement and dilatation less than 4 cm with intact membranes⁶.

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Tocolytics in current use include beta agonists, calcium channel blockers, prostaglandin synthetase inhibitors nitric oxide donors and oxytocin receptor antagonists. Meta analyses has shown that beta adrenergic agents especially ritodrine are associated with a postponement of delivery for 48 hours in 76% of patients⁷ in comparison to nifedipine in 92% of patients.⁸ Ritodrine remains widely used and has been the most thoroughly evaluated. A recent cochrane review on preterm labour concluded that when tocolysis is indicated for preterm labour, calcium channel blockers are preferable to other tocolytic agents.⁹ Many developing countries are unable to cope with the health care costs associated with managing neonates that are born preterm, result in higher and often unacceptable neonatal morbidity and mortality. It has been widely recognized that its prevention and effective management will improve neonatal outcome and will have a profound effect on social and long term public healthcare costs.

PATIENTS AND METHODS

This randomized clinical trial was conducted at Obstetrical & Gynaecological Department, Lady Aitchison Hospital, Lahore between six months from 8th July 2009 to 8th January 2010. Patients aged 20 to 35 years, preterm labour between 24 to 37 weeks and singleton pregnancy of any gravity were

included. Those patients having premature rupture of membrane, antepartum haemorrhage, preterm labour with chorioamnionitis with prolonged rupture of membrane and cervical dilatation more than 4 cm were excluded from the study. One hundred and sixty patients were included and divided in two equal groups. In group A (80 patients) Inj. Ritodrine 2 ampules (100 mg) in 500 ml of 5% D/W with 4 drops/minute (0.05 mg/min) via continuous infusion was given and increased by 2 drops/minute every 15 minutes up to 12 drops/minute (0.15 mg/min) until contractions stopped or maternal heart rate reached more than 140 beats/minute followed by oral 10 mg tablet 6 hours before end of infusion. In group B (80 patients) Tab Nifedipine was given in 20 mg tablet initial dose followed by 20 mg every 6 hours until uterine contractions subsided. Variables like uterine contractions and cervical dilatation were recorded up to 48 hours. The efficacy of two groups was compared by applying Chi square test. P value ≤ 0.05 was considered as significant.

RESULTS

The age range between 20-35 years with mean age of the patients in group A was 27.7 ± 3.8 years and in group B was 27.3 ± 3.5 years (Table 1). The mean parity of the patients in group A was 1.9 ± 0.9 and in group B was 1.9 ± 0.8 (Table 2). The duration of pregnancy with dates between 28-36 weeks with mean in group A was 32.7 ± 1.5 weeks and in group B was 32.5 ± 1.7 weeks (Table 3). According to the efficacy of the treatment, in group A, there were 67 (83.7%) patients, in whose the treatment was effective and in group B, there were 73 (91.2%) patients in whose the treatment was effective. Statistically the difference was significant in efficacy of treatment ($P < 0.002$).

Table 1: Frequency and percentage of patients by age (n=160)

Age (years)	Group A		Group B	
	No.	%	No.	%
20 – 25	23	28.7	22	27.5
26 – 30	43	53.8	46	57.5
31 – 35	14	17.5	12	15.0

Table 2: Frequency and percentage of patients by parity (n=160)

Parity	Group A)		Group B)	
	No.	%	No.	%
0	20	25.0	19	23.7
1 – 2	34	42.5	45	56.3
3 – 4	18	22.5	12	15.0
5 – 6	8	10.0	4	5.0

Table 3: Frequency and percentage of patients by duration of pregnancy (n = 160)

Duration of pregnancy (weeks)	Group A		Group B	
	No.	%	No.	%
28 – 30	5	6.3	11	13.8
31 – 33	46	57.5	44	55.0
34 – 36	29	36.2	25	31.2

Table 4: Frequency and percentage of patients by efficacy of treatment (n = 160)

Efficacy	Group A		Group B	
	No.	%	No.	%
Yes	67	83.7	73	91.2
No	13	16.3	7	8.8

$\chi^2 = 10.7$ $P = 0.002$

DISCUSSION

Early detection and management are important steps in preventing preterm labour, which is leading cause of neonatal mortality and morbidity (such as respiratory distress, necrotizing enterocolitis, intraventricular hemorrhage and sepsis) and accounts for 35% of all health care spending on the neonates. Preterm labour is diagnosed when there is persistence of at least two symptomatic uterine contractions in 10 minutes period at least 50% cervical effacement and dilatation less than 4 cm with intact membranes.⁶

Tocolytics in current use include beta agonists, calcium channel blockers, prostaglandin synthetase inhibitors nitric oxide donors and oxytocin receptor antagonists. Meta-analysis has shown that beta adrenergic agents especially ritodrine are associated with a postponement of delivery for 48 hours in 76% of patients⁷ in comparison to nifedipine in 92% of patients.⁸ Ritodrine remains widely used and has been the most thoroughly evaluated. A recent Cochrane review on preterm labour concluded that when tocolysis is indicated for preterm labour, calcium channel blockers are preferable to other tocolytic agents.⁹

In the present study, the mean age of the patient's in group A was 27.7 ± 3.8 years and in group B was 27.3 ± 3.5 years. As compared with the study of Junejo et al⁵ the mean age of the patients in group A was 27.64 ± 6.06 years and in group B was 27.84 ± 6.16 years, which is almost same and comparable with our study. According to parity, the mean parity of the patients in group A was 1.9 ± 0.9 age in group B was 1.9 ± 0 . As compared with the study of Junejo et al⁵ the mean parity of the patients in group A was 2.34 ± 1.97 and in group B was 2.58 ± 1.99 , which is comparable with the present study. In the our study, the mean gestational age of the patients in group A was 32.7 ± 1.5 weeks and in

group B was 32.5±1.7 weeks. As compared with the study of Junejo et al⁵ the mean gestational age of the patients in group A was 31.9±2.4 weeks and in group B was 32.3±2.7 weeks, which is comparable with our study. In another study conducted by Elliott et al¹⁰ the mean gestational age of the patients was 33.2±2.2 weeks, which is also consistent with the present study.

Laohapojanart et al¹¹ reported that safety and efficacy of oral nifedipine versus terbutaline injection in preterm labour and found that nifedipine was effective for prolongation of delivery for 48 hours in 85% of patients. While in the present study nifedipine was found effective for prolongation of delivery for 48 hours in 91.2% patients, which is almost same and comparable with the above study. In another study conducted by Kupfermanc et al¹² the delivery was delayed for 48 hours, seven days, and until the 36th week of gestation in 83%, 67% and 50%, respectively of women in the nifedipine group, compared with 77%, 63% and 43% respectively, of women in the ritodrine group. The proportion of women who had not been delivery at 48 hours was 84.9% in the atosiban group and 86.8% in the ritodrine group. At 7 days 73% women had still not been delivered in both the atosiban and 76% in ritodrine groups. Ritodrine was comparable in clinical effectiveness to atosiban therapy. Neonatal morbidity, which was similar between the two treatment arms, was apparently related to the gestational age of the infant rather than to the exposure to either tocolytic agents.¹³

REFERENCES

1. Danielian P, Hal M. The epidemiology of preterm labour and delivery. Cambridge: Cambridge University Press; 2008.
2. Ghazi A, Jabbar S, Siddique NM. Preterm labour – still birth a challenge. Pak J Surg 2006;22:22-6.
3. Committee on understanding premature birth and assuring healthy outcomes. Preterm Birth: Causes, consequences and prevention. Washington, DC: The National Academies Press; 2006.
4. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Kirmeyer S. Births: final data for 2004. Natl Vital Stat Rep 2006;55(1):1-101.
5. Junejo J, Mumtaz F, Unar BA. Comparison of Salbutamol and Nifedipine as a Tocolytic agent in the treatment of preterm labour. JLUMHS 2008; 12: 115-9.
6. Van De Water M, Kessel ET, De Kleine MJ, Oei SG. Tocolytic effectiveness of nifedipine versus ritodrine and follow-up of newborns: a randomised controlled trial. Acta Obstet Gynecol Scand 2008;87(3):340-5.
7. Iqbal J, Nausheen F, Bhatti FA. Management of preterm labour. Ann King Edward Med Coll 2004; 10: 423-6.
8. Lyell DJ, Pullen K, Campbell L, Ching S, Druzin ML, Chitkara U, et al. Magnesium sulfate compared with nifedipine for acute tocolysis of preterm labor: a randomized controlled trial. Obstet Gynecol 2007;110(1):61-7
9. Al-Qaqa K, Al-Awaysheh F. Neonatal outcome and prenatal antibiotic treatment in premature rupture of membranes. Pak J Med Sci 2005; 21:441-4
10. Elliott JP, Bergauer NK, Jacques DL, et al. Pregnancy prolongation in triplet pregnancies. oral vs continuous subcutaneous terbutaline. J Reprod Med 2001; 46(11) :975-82.
11. Laohapojanart N, Soorapan S, Wacharaprechanont T, Ratanajamit C. Safety and efficacy of oral nifedipine versus terbutaline injection in preterm labor. J Med Assoc Thai 2007;90(11):2461-9.
12. Kupfermanc M, Lessing JB, Yaron Y, Peyser MR. Nifedipine versus ritodrine for suppression of preterm labour. Br J Obstet Gynaecol 1993;100(12):1090-4.
13. Moutquin JM, Sherman D, Cohen H, Mohide PT, Hochner-Celnikier D, Fejgin M, et al. Double-blind, randomized, controlled trial of atosiban and ritodrine in the treatment of preterm labor: a multicenter effectiveness and safety study. Am J Obstet Gynecol 2000;182(5):1191-9.