Original Article

Comparison of Efficacy of Transpermal Nitroglycyrine Patch and Intravenous Ritodrine in Preterm Labor

Summaira Hamza[1], Kanta Ahuja[2] and Umair Asghar[3]

ABSTRACT

Objective: To compare the QT dispersion for coronary artery disease in cardiac stress test by transesophageal atrial pacing in patients with coronary heart disease.

Study Design: Randomized control trial study.

Place and Duration of Study: This study was conducted at Bolan Medical College Hospital Quetta from 1st July 2012 to 30th Jun 2013.

Materials and Methods: Sample size of 58 cases were included in the study through non-probability, purposive sampling. The informed consent and demographic details were noted and the patients underwent through tocolytic trial either by i/v ritodrine or transdermal nitroglycerine patch. The data was analyzed by using SPSS-10 software. Both groups were compared by using chi-square test taking p-value≤0.05 as significant.

Results: In Nitroglycerine group, there were 20 (69%) cases in which effectiveness of drug was achieved while in Ritodrine group, there were 23 (79.3%) cases in which effectiveness of drug was achieved. The difference between both study groups was insignificant (p-value = 0.368). There were 3 patients who complaint about headache, out of which there were 2 (6.9%) cases belonged to nitroglycerin group while 1 (3.4%) cases belonged to ritodrine group. There were 13 patients who complaint about tachycardia, 1 patient who complaint about breathlessness and 2 patients in which hypotension was observed. All these cases belonged to ritodrine group.

Conclusion: The efficacy of both drugs almost equal, the side effects of ritodrine were more severe and there were more cases who complaint about side effects. Hence nitroglycerine patch is effective drug with less side effects, as a result is more appropriate to manage patients with preterm labour.

Keywords: Preterm labor, Progesterone therapy, Efficacy, Gestational age

Citation of article: Hamza S, Ahuja K, Asghar U. Comparison of Efficacy of Transpermal Nitroglycyrine Patch and Intravenous Ritodrine in Preterm Labor. Med Forum 2016;27(11):41-44.

INTRODUCTION

Preterm labour refers to onset of labor after the gestation of viability, i.e. 20-28 weeks of gestation and before 37 completed weeks. Preterm labour occurs in 7-12% of all deliveries but accounts for over 85% of perinatal morbidity and mortality.[1,2] Mortality rates are 90% at 23 weeks dropping to 2% at 34 weeks.[3] To delay the delivery by use of tocolytic therapy is to administer corticosteroids to reduce respiratory distress and also to decrease incidence of intrauterine hemorrhage, necrotizing enterocolitis, patent ductus arteriosus and in utero safe transfer to a tertiary care unit.[4]

[1.] Department of Obs. & Gynae, Boland Medical College Hospital Quetta
[2.] Department of Obs. & Gynae, Gambat Institute of Medical Sciences Gambat
3. East Medical Ward, Mayo Hospital, Lahore

Correspondence: Dr. Summaira Hamza, Assistant Professor of Obs. & Gynae, Boland Medical College Hospital Quetta
Contact No: 0332-3007349
Email: summairahamza@gmail.com

Received: August 14, 2016; Accepted: September 25, 2016

Currently used tocolytic agents are β mimetics (ritodrine), Ca channel blocker, magnesium sulphate, prostaglandin synthesis inhibitors, glyceryl trinitrates, and nitroglycerine oxytocin antagonists. No one is still very effective but some have significant adverse effects and some has less.[5]

One of β mimetic used as tocolytic agent is ritodrine as it acts on β2 receptor of uterus which causes uterine relaxation and prolongs gestational age but has significant adverse effects like tachycardia, pulmonary edema and cardiac arrhythmias.[6] Another agent that is nitroglycerine in the form of a dermal patch is also used as a tocolytic agent. It has minimal adverse effects and is relatively safe.[7] When both ritodrine and nitroglycerine are compared for prolongation of pregnancy till 48 hours, ritodrine group is more effective 73.3%[8] than nitroglycerine patch 35.3%.[9]As for as side effects are concerned nitroglycerine patch has less side effects in terms of tachycardia 5%7, headache 28%,[10] chest pain 0%[11] while ritodrine has tachycardia 48%, headache 23% and chest pain 10%.[1]

The incidence of preterm labor is very high about 10%[12] and also premature babies have high incidence of acute respiratory distress syndrome, intracranial hemorrhage, jaundice, long term morbidity and mortality.[4] This study help to highlight the comparison

of efficacy and adverse effects of tocolytic agents, i.e. intravenous ritodrine and transdermal nitroglycerine patch, in prolongation of pregnancy for 48 hours, hence administration of corticosteroids to mother.

MATERIALS AND METHODS

Total 58 patients of preterm labor; 29 patients in each group i.e.in intravenous ritodrine group and transdermal nitroglycerine group keeping level of significance at 5%, power of test 90%. Anticipated population proportion ingroup receiving ritodrine is 0.7338, anticipated population proportion receiving nitroglycerine patch as 0.3539. All patients presenting with preterm labour, i.e. more than24 weeks and less than 37 weeks of gestation. This study was Randomized control trial Sample Technique was used Purposive non probability technique. Data was collected by taking history and examining the patients who got admission through emergency or OPD in the Department of Gynae Unit-III SPH Quetta with complaints of labour pain, meeting the inclusion criteria. The purpose and procedure of the study was explained to the patient. After discussing risks and benefits of the trial with the patient, informed consent was taken and the patients underwent through tocolytic trial either by intravenous ritodrine or transdermal nitroglycerine patch. Both type of trials are authentic and practiced in various centers, so two groups A & B of patients were selected one group was given transdem1al nitroglycerine patch and the second was given intravenous ritodrine. The first patient was given two performed labeled chits and requested to pick one and placed in group A. The rest of the patients were distributed between two groups having comparable age, parity and gestational age to minimize the effect of confounders. A preformed proforma was used to record the information about the patients, efficacy and adverse effects of the drugs used. Data was analyzed on computer using SPSS version10. Efficacy, i.e. time of prolongation of pregnancy was analyzed by calculating mean±SD of time prolongation in two groups was calculated. Applying t-test was test difference of mean time prolonged in two groups. P≤O.05 was taken as significant. Frequency of adverse effect like maternal tachycardia, headache and chest pain was analyzed difference of frequencies was tested statistically by applying chi square test $p<0.05$ was taken significant. For age of patients and gestational age mean±SD was calculated.

RESULTS

The mean age of all females was 31.66±6.34years with minimum and maximum age of females was 17years and 41years respectively. The mean age of females in nitroglycerine group was 32.24±6.59years while mean age of females in ritodrine group was 31.07±6.14years. The mean gestational age was 32.53±1.72 weeks with minimum and maximum gestational age of 28 weeks and 35 weeks respectively. The mean gestational age in nitroglycerine group was 32.45±2.01 weeks while mean gestational age in ritodrine group was 32.62±1.40 weeks (Table 1). There were 6 (10.3%) females who presented during gestational age of 28-29 weeks, 4 (6.9%) females presented during gestational age of 30-31 weeks, 29 (50%) females presented during gestational age of 32-33 weeks while 19 (32.8%)females presented during gestational age of 34-35 weeks (Table 2). There were 12 (20.7%) females who had parity 1-2, 27 (46.6%) females had parity 3-4, 14 (24.1%) females had parity 5-6, 3 (5.2%) females had parity 7-8 and only 2 (3.4%) females had parity 9-10 (Table 3). In Nitroglycerine group, there were 20 (69%) cases in which effectiveness of drug was achieved while in 9 (31%) cases effectiveness could not be achieved. In Ritodrine group, there were 23 (79.3%) cases in which effectiveness of drug was achieved while in 6 (20.7%) cases effectiveness could not be achieved.

Table No.1: Descriptive statistics of Age (Years), gestational age (weeks) and Distribution of females according to gestational age of Patients (n=58)

Descriptive statistics	Group	
	Nitroglycerine	Ritodrine
Age (years)	32.24±63.59	31.07±6.14
Gestational age(weeks)	32.45±2.01	32.62±1.40

Table No.2: Distribution of females according to gestational age [weeks] (n=58)

Gestational age (weeks)	No.	%
28-29	6	10.3
30-31	4	6.9
32-33	29	50.0
34-35	19	32.8

Table No.3: Distribution of Parity of females (n=58

Parity	No.	%
1--2	12	20.7
3--4	27	46.6
5--6	14	24.1
7--8	3	5.2
9--10	2	3.4

Table No.4: Comparison of efficacy achieved in both groups N=58

Effectiveness	Study Group		Total
	Nitrogly-cerine	Ritodrine	
Yes	20 (69.0%)	23 (79.3%)	43 (74.1%)
No	9 (31.0%)	6 (20.7%)	15 (25.9%)
Total	29 (100%)	29 (100%)	58 (100%)

Chi-square = 0.809, p-value = 0.368 (Insignificant)

Table No.5: Comparison of side effects in both groups N=58

Complications	Study groups		p-value	Significance
	Nitroglycerine (n=29)	Ritodrine (n=29)		
Headache	2 (6.9%)	1 (3.4%)	0.553	Insignificant
Tachycardia	0 (0%)	13 (44.8%)	0.000	Significant
Breathlessness	0 (0%)	1 (3.4%)	0.313	Insignificant
Hypotension	0 (0%)	2 (6.8%)	0.150	Insignificant

Inritodrine group, there were more cases in which effectiveness was achieved although the difference between both study groups was insignificant (p-value = 0.368) [Table 4]. There were 3 patients who complaint about headache, out of which there were 2 (6.9%) cases belonged to nitroglycerin group while 1 (3.4%) cases belonged to ritodrine group. The difference was insignificant. There were 13 patients who complaint about tachycardia, out of which there was no (0%) cases belonged to nitroglycerin group while 13 (44.8%) cases belonged to ritodrine group. The difference was highly significant and showing more severe side effect of ritodrine. There was 1 female who complaint about breathlessness and she belonged to ritodrine group. There were 2 females in which hypotension was observed. Both cases belonged to ritodrine group (Table 5)

DISCUSSION

Preterm labor represents a major obstetrical complication which is associated with adverse perinatal and neonatal outcomes. Its clinical significance is reflected by the fact that, it is responsible for the 74% of perinatal morbidity, even though it complicates only 7–12% of pregnancies. Factors traditionally associated with PL and delivery includes maternal characteristics (such as age, smoking, parity, history of PL, uterine anomalies and medical disorders), multiple gestation, pregnancy complications, and others.[13,14,15]

Pretermlabor is a challenging situation which requires a delicate judgment regarding the appropriate management. The use of tocolytics is associated with numerous and serious maternal, fetal and neonatal side effects, long hospitalization and questionable benefits. In addition, clinical experience has shown that preterm labour frequently progresses to true labor and delivery, irrespective of any conservative management. Digital assessment of the cervix is traditionally used to assess women presenting with threatened or true preterm labour, but various studies have shown the subjectivity of the assessment, which usually underestimates the true anatomic length of the cervix.[16,17]

Commonly used drugs in tocolysis are beta sympathomimetic (ritodrine, salbutamol and terbutaline), cyclooxygenaseinhibitors (indomethacin), calcium channel blockers (nifidipine), nitric oxide donors and oxytocin antagonist (atosiban).[18] In our study, we included total 58 pregnant females with the mean age of 31.66±6.34years. The mean age of females in nitroglycerine group was 32.24±6.59years while mean age of females in ritodrine group was 31.07±6.14years.All the females presented with preterm labor during mean gestational age of 32.53±1.72 weeks. There were 6 (10.3%) females who presented during gestational age of <30 weeks while 52 (89.7%) females presented during gestational age of >30 to 35 weeks.

Tocolytic drugs have been tried for long and even GTN is not a new drug as more than 100years ago nitric oxide donor was used in pregnancy.[19] GTN is convenient in its application and patientsthemselves can have control on symptoms as the patch canbe applied and removed as required and due to shorter half-lifeof GTN, patches have been found to be safe andeffective even at higher doses while treating serious patientsof angina as well.[20]

In Nitroglycerine group, there were 20 (69%) cases in which effectiveness of drug was achieved while in Ritodrine group, there were 23 (79.3%) cases in which effectiveness of drug was achieved. Inritodrine group, there were more cases in which effectiveness was achieved although the difference between both study groups was insignificant (p-value = 0.368).The significance level showed that both drugs are equally effective in controlling PTB. There were 3 patients who complaint about headache, 13 patients complaint about tachycardia, 1 female complaint about breathlessness andthere were 2 females, in which hypotension was observed. All cases belonged to ritodrine group, except 2 cases who had headache belonged to nitroglycerine group.

One randomized trial also compared the efficacy of nitroglycerine patch and i/v ritodrine HCl. The principal outcomes assessed were prolongation of pregnancy for 48 hours, 7 days and until 34 weeks of pregnancy & maternal side effects. Delivery of women was delayed for 48 h, 7 days and until 34 weeks gestation in 77.8%, 59.2% and 44.4% of women respectively treated with nitroglycerine compared with 73.3%, 56.7% and 43.3% respectively among women received ritodrine but the difference was insignificant as reported in our study. Average number of the side effects per patient was significantly (P <0.01) lower with nitroglycerine treatment than ritodine therapy. This study also concluded thatnitroglycerine was as effective as ritodrine in suppressing preterm labor. Its use was associated with less frequent side effects.[21]

Another study also reported that 92% patients benefitedfrom the nitroglycerine patch which is significantly higher than reported by other studies as well as ourswhich reported about 64% women had arrest of labour for a short term.[22,23]

Another study compared the efficacy of transdermal nitroglycerine and I/V ritodrine as tocolytics.The primary outcome was prolongation of gestation from entry to 37 weeks. Nitroglycerine and ritodrine

prolonged gestation by 74% of time to 37 weeks (difference nitroglecerine-ritodrine 0%). There was no significant difference in the proportion of women receiving nitroglycerine or ritodrine. No serious maternal side effects were reported for ritodrine or nitroglycerine. Authors concluded that no overall difference between nitroglycerine and ritodrine in the acute tocolysis of preterm labor but a suggested advantage of nitroglycerine over ritodrine in reducing preterm delivery rate. The maternal side effect profile and treatment discontinuation rates were fewer for nitroglycerine, suggesting it was a safer alternative to ritodrine.[24]

CONCLUSION

Through this study, it was concluded that efficacy of both drugs is almost equal but side effects of ritodrine are more severe and there were more cases who complaint about side effects. Thus nitroglycerine patch is effective drug with less side effects and thus is more appropriate to manage patients with preterm labour. Transdermal nitroglycerine patch is less effective than intravenous ritodrine incontrolling preterm labor but also has fewer side effects than ritodrine.

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Svigos JM, Robinson JS, Vigneswaran. Threatened and actual preterm labor including mode of delivery. High risk pregnancy. 3rd ed. Philadeiphia: Elsevier;2006.p.1304-20.
2. Mathews TJ, MacDorman MF. Infant mortality statistics from the 2004 period linked birth/infant death data set. Natl Vital Stat Rep 2007;55:1-32.
3. Hack M, Flannercy DJ, Schluchter M, Carter L, Borawaski E, Klein N. Outcomes in young adulthood of very low birth weight infants. N Engl J Med 2002;346:149-57.
4. Smith GN. What are the realistic expectations of tocolysis? BJOG. 2003;110:103-6.
5. Klam S, Leduc L. Management options for preterm labour in Canada. J Obstet Gynaecol Can 2004; 26:339-45.
6. Wani MP, Barakzai N, Graham I. Glyceryl trinitrate vs. ritodrine for the treatment of preterm labor. Int J Gynaecol Obstet 2004;85:165-7.
7. Malik M. Glyceryl trinitrate for treatment of preterm labour. Pakistan J Obstet Gynaecol 1999; 12:56-8.
8. Salem A. Efficacy and safety of glyceryl trinitrate versus ritodrine for preterm labor. Egyptian society of Obstet Gynaecol 2001;27:347-54.
9. Smith GN, Walker MC, McGrath MJ. Randomized, double-blind, placebo controlled pilot study assessing nitroglycerine as a tocolytic. BJOG 1999; 106:736-39.
10. Bujold E, Marquette GP, Ferreira E, Gauthier RJ, Boucher M. Sublingual nitroglycerin versus intravenous ritodrine as tocolytic for external cephalic version: A double-blinded randomized trial. Am J Obstet Gynecol 2003;188:1454-9.
11. El-Syed YY, Riley T, Holbrook RH, Cohen SE, Chitkara U, Druzin ML. Randomized comparison of intravenous nitroglycerine and magnesium sulfate for treatment of preterm labor. Obstet Gynaecol 1999;93:79-83.
12. Chohan A. Fundamentals of Obstetrics. 1st ed. Lahore: MAR Publication; 2005.p. 212.
13. Meis PJ, Michielutte R, Peters TJ, Wells HB, Sands RE, Coles EC, et al. Factors associated with preterm birth in Cardiff, Wales. I. Univariable and multivariable analysis. Am J Obstet Gynecol 1995; 173(2):590-6.
14. Satin AJ, Leveno KJ, Sherman ML, Reedy NJ, Lowe TW, McIntire DD. Maternal youth and pregnancy outcomes: middle school versus high school age groups compared with women beyond the teen years. Am J Obstet Gynecol 1994; 171(1):184-7.
15. DiFranza JR, Lew RA. Effect of maternal cigarette smoking on pregnancy complications and sudden infant death syndrome. J Fam Pract 1995; 40(4):385-94.
16. Andersen HF, Nugent CE, Wanty SD, Hayashi RH. Prediction of risk for preterm delivery by ultrasonographic measurement of cervical length. Am J Obstet Gynecol 1990;163(3):859-67.
17. Sonek JD, Iams JD, Blumenfeld M, Johnson F, Landon M, Gabbe S. Measurement of cervical length in pregnancy: comparison between vaginal ultrasonography and digital examination. Obstet Gynecol 1990;76(2):172-5.
18. Waheed A, Shami N. Preterm labour: effectiveness of transdermal glyceryl trinitrate patch. Prof Med J 2011;18(2):174-80.
19. Barnes F. Hour-Glass Contraction of the Uterus Treated with Nitrite of Amyl. Br Med J 1882; 1(1107):377.
20. Pittrof R, Lees C, Thompson C, Pickles A, Martin JF, Campbell S. Crossover study of glyceryl trinitrate patches for controlling pain in women with severe dysmenorrhoea. BMJ 1996; 312(7035):884.
21. Salem A. Efficacy and safety of glyceryl trinitrate versus ritodrine for preterm labor. Egyptian Soc Obstet Gynecol 2001;27(4-6):347-54.
22. Parveen S, Ainuddin JA, Naz S. Short term tocolytic efficacy of transdermal nitroglycerine. Med Chan 2010;16:152-4.
23. Shaikh S, Shaikh AH, Akhter S, Isran B. Efficacy of transdermal nitroglycerine in idiopathic pre-term labour. J Pak Med Assoc 2012;62(1):47-50.
24. Lees CC, Lojacono A, Thompson C, Danti L, Black RS, Tanzi P, et al. Glyceryl trinitrate and ritodrine in tocolysis: an international multicenter randomized study. GTN Preterm Labour Investigation Group. Obstet Gynecol 1999; 94(3):403-8.