

Compare the Effectiveness of Transdermal Nitro-Glycerine Versus Oral Nifedipine for Acute Tocolysis in Preterm Labour

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ABSTRACT

Objective: The aim of this study is to compare the efficacy of transdermal nitro-glycerine versus oral nifedipine for acute tocolysis in preterm labour.

Study Design: Randomized, Control trial

Place and Duration: Conducted at Khattak Medical Center Dabgari Garden Peshawar for duration of one year from 1st August 2019 to 31st July 2020.

Methods: Total 126 patients of preterm labor were presented in this study. Patients were aged between 18-40 years. Patients were equally divided into two groups A and B. Patients of group A received transdermal nitro-glycerine while Group B received oral nifedipine for acute tocolysis. Within 48 hours, failure of tocolysis was observed while effectiveness was observed after 48 hours to 10 days and greater than 10 days. Complete data was analyzed by SPSS 22.0 version.

Results: Mean age of the patients in group A was 29.96 \pm 4.32 years with mean BMI 25.70 \pm 4.12 kg/m² and mean age among patients of group B was 28.78 \pm 9.48 years with mean BMI 25.68 \pm 8.21 kg/m². Mean gestational age at admission in group A was 32.34 \pm 1.68 whereas in group B it was 32.12 \pm 1.52 weeks. At time delivery mean gestational age in group A was 37.52 \pm 2.86 and in group B was 36.18 \pm 1.45. Frequency of failure was lower in group A as compared to Group B within 48 hours and prolongation of delayed delivery was greater in group A 18.45 \pm 1.68 days as compared to group B 15.94 \pm 4.22 days.

Conclusion: We concluded in this study that nitroglycerine was more effective for prolongation of delayed delivery in preterm labor as compared to oral nifedipine.

Keywords: Tocolysis, Nitroglycerine, Rifedipine, Preterm labour

INTRODUCTION

Preterm delivery tends to be one of the biggest causes of perinatal death and long-term illness. The overall perinatal death is due to over 70% of preterm birth. Preterm birth, including deteriorating neurodevelopment abilities, impedance of learning, visual problems, and secondary long-term health effects, is also a major contributor of neonatal morbidity¹.

The association of premature work with motherly and obstetrical complications and the resulting premature membrane rupture could render the premature birth rate significantly below current levels more difficult for the work to achieve.³ However, premature births due to preterm spontaneous labour without any obvious medical or obstetrical complications may be treatable with Several approaches have been used, such as preterm birth, progesterone treatment, infection treatment and tocolytic therapy^{2,3}, for patients with risk of preterm birth.

Around 40,45% of preterm deliveries come on preterm labor⁴. The focus of preterm labour is on tocolytic therapy to help boost the maturity of the foetal lung and transfer the mother to a tertiary treatment centre with a neonatal intensive care unit the administration of antenatal corticosteroids (NICU). The ideal tocolytic agent for the typical pathway of parturition should be simple to handle, effective to prevent preterm birth and capable of enhancing neonatal effects, with very few maternal, foetal and neonatal side effects and without long-term adverse effect.⁵

The new update of the Cochrane review on transdermal nitroglycerin for the preterm laboratory coverage involved four randomized controlled trials involving a total of 436 patients.⁶ This analysis found that the normal use of nitric oxide donor (mainly transdermal nitroglycerin) in preterm work care was insufficient evidence for this study. However, in 2002 literature investigations were undertaken, on which this analysis was based. Further randomized, controlled studies have been conducted to test transdermal nitroglycerin, which justifies re-evaluating the effectiveness and safety of this agent. A large range of uterine contractions have been used to counteract^{3,10} inhibitors^{11,12}, calcium channel blocker,^{5,13} oxytocin-receptor antagonists,^{9,13} oxytocin-receptor blocker and nitric oxide donor^{14,15,31,14,21}. Calcium channel blockers.

MATERIAL AND METHODS

This randomized control trial study was conducted at Khattak Medical Center Dabgari Garden Peshawar for duration of one year from 1st August 2019 to 31st July 2020 and comprised of 126 patients. Patients detailed demographics including age, sex and body mass index were recorded after taking written consent. Patients with cardiac disease, fetal malformation, severe intra uterine growth restriction, ruptured membranes were excluded from this study.

Patients of preterm labour were equally (n=63) divided in two groups. In group A nitroglycerine was given

to the patients whereas in group B, nifedipine was provided. Prolongation of delayed delivery was recorded after 48 hours to 10 days and after 10 days. Failure of tocolysis was recorded within 48 hours. T test and chi square were used to compare effectiveness of prolongation delayed delivery between both groups. Complete data was analyzed by SPSS 22.0 version.

RESULTS

Mean age of the patients in group A was 29.96 ± 4.32 years with mean BMI 25.70 ± 4.12 kg/m² and mean age among patients of group B was 28.78 ± 9.48 years with mean BMI 25.68 ± 8.21 kg/m². Mean gestational age at presentation in group A was 32.34 ± 1.68 but in group B it was 32.12 ± 1.52 weeks. At delivery mean gestational age in group A was 37.52 ± 2.86 and in group B was 36.18 ± 1.45 . (table 1)

Table 1: Baseline detailed characteristics of enrolled cases

Variables	Group A(n=63)	Group B(n=63)
Mean Age (years)	29.96 ± 4.32	28.78 ± 9.48
Mean BMI (kg/m ²)	25.70 ± 4.12	25.68 ± 8.21
Mean gestational age at start (weeks)	32.34 ± 1.68	32.12 ± 1.52
Mean gestational age at delivery (weeks)	37.52 ± 2.86	36.18 ± 1.45

Prolongation of delayed delivery was greater in group A 18.45 ± 1.68 days as compared to group B 15.94 ± 4.22 days. Within 48 hours failure of tocolysis in group A was 8 (12.7%) but in group B it was 28 (44.4%). In group A effectiveness in delayed delivery after 48 hours to 10 days were 30 (47.62%) and after 10 days 25 (39.7%) but in group B 48 hours to 10 days it was 16 (25.4%) and after 10 days 18 (28.6%) patients were delayed. (table 2)

Table 2: Effectiveness in prolongation of delayed delivery among both groups

Variables	Group A	Group B
Failure	8 (12.7%)	28 (44.4%)
48hours -10days	30 (47.62%)	17 (27%)
>10days	25 (39.7%)	18 (28.6%)
Mean time (days)	18.45 ± 1.68	15.94 ± 4.22

Significantly no difference was observed at neonatal outcomes. At birth 40 (63.5%) cases in group A had weight less than 2.5kg but in group B 36 (57.14%) cases had weight less than 2.5kg. Birth asphyxia was among 4 (6.35%) cases in group A while in group B it was 5 (7.94%). 6 (9.5%) cases of group A admitted in NICU and 7 (11.11%) cases of group B. (table 3)

Table 3: Comparison of neonatal outcomes among both groups

Variables	Group A	Group B
Weight <2.5kg at birth	40 (63.5%)	36 (57.14%)
Birth asphyxia	4 (6.35%)	5 (7.94%)
NICU admission	6 (9.5%)	7 (11.11%)

DISCUSSION

The primary aim is to offer antenatal corticosteroid time those results in decreased neonatal morbidity and mortality. The authors find that pregnancy is prolonged for >2 days in this study. In the group nitroglycerin and nifedipine, the rate of premature delivery within 48 hours

was 12.7% and 44.4%. After 48 hours -10 days the effectiveness of nitroglycerine groups was greater 47.62% as compared to nifedipine group 27%. These results were comparable to the many previous studies.^{16,17}

For 43 and 41 patients in each group, Dhawle A et al. compared the tocolytic impact of nifedipine and NTG. In contrast to Nifedipine, delivery within 48 hours was considerably greater with NTG ($p=0.02$). In both groups neonatal findings were identical as seen in the present study for their average birth weight, need and length of neonatal intensive care. [18] Kashanian et al. conducted a randomized clinical trial that was to be used to equate NTG with nifedipine. In the NTG Community, more women were administered after 48 hours (52 women (86.7%) versus 41 (68.3%), $P=0.016$) and 7 days (47 (78.3%) versus 37 (61.7%) versus $P=0.046$) relative to women from the Nifedipine group. The fetal results such as Apgar, the neonatal weight of the NTG category were higher. In the NTG community, the admission and time of the NICU in neonatal intensive care (NICU) was also decreased. Related and minor adverse effects occurred in both classes.¹⁹ Neonatal weight less than 2.5kg, birth asphyxia and NICU were recorded for our research.

Delayed in delivery after 10 days were effectively greater in nitroglycerine group 39.7% as compared to nifedipine group 28.6%. Papatsonis et al, nifedipine was found to delay childbirth beyond 7 & 14 days in 72.1% and 64.7% patients respectively, compared to 50% and 40.7% prolongation in the ritodrine group.²⁰

CONCLUSION

We concluded in this study that nitroglycerine was more effective for prolongation of delayed delivery in preterm labour as compared to oral nifedipine.

REFERENCE

- Slattery MM, Morrison JJ. Preterm delivery. *Lancet*. 2002;360(9344):1489-97.
- Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller AB, et al. Born too soon: the global epidemiology of 15 million preterm births. *Reprod Heal*. 2013;10(1):S2.
- Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Spong CY, Dashe JS, Williams Obstetrics 24th ed. New York: McGraw Hill Medical Publishing Division; 2014:829-861.
- Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008;371:75-84.
- Conde-Agudelo A, Romero R, Kusanovic JP. Nifedipine in the management of preterm labor: a systematic review and metaanalysis. *Am J Obstet Gynecol*. 2011;204:134. e1-20.
- Duckitt K, Thornton S. Nitric oxide donors for the treatment of preterm labour. *Cochrane Database Syst Rev*. 2002;3:CD002860.
- Moutquin JM, Sherman D, Cohen H, Mohide PT, Hochner-Celnikier D, Feigin 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;182:1191-9.
- Anotayanonth S, Subhedar NV, Garner P, Neilson JP, Harigopal S. Betamimetics for inhibiting preterm labour. *Cochrane Database Syst Rev*. 2004;4:CD004352.
- Terrone DA, Rinehart BK, Kimmel ES, May WL, Larmon JE, Morrison JC. A prospective, randomized, controlled trial of high and low maintenance doses of magnesium sulfate for acute tocolysis. *Am J Obstet Gynecol*. 2000;182:1477-82.

10. How HY, Zafaranchi L, Stella CL, Recht K, Maxwell RA, Sibai BM, et al. Tocolysis in women with preterm labor between 32 0/7 and 34 6/7 weeks of gestation: a randomized controlled pilot study. *Am J Obstet Gynecol.* 2006;194:976–81.
11. Stika CS, Gross GA, Leguizamon G, Gerber S, Levy R, Mathur A, et al. A prospective randomized safety trial of celecoxib for treatment of preterm labor. *Am J Obstet Gynecol.* 2002;187:653–60.
12. Sawdy RJ, Lye S, Fisk NM, Bennett PR. A double-blind randomized study of fetal side effects during and after the short-term maternal administration of indomethacin, sulindac, and nimesulide for the treatment of preterm labor. *Am J Obstet Gynecol.* 2003;188:1046–51.
13. Papatsonis DN, Van Geijn HP, Dekker GA. Nifedipine as a safe and effective tocolytic agent in the treatment of preterm labor. *Am J Obstet Gynecol.* 2000;183:513–4.
14. Romero R, Sibai BM, Sanchez-Ramos L, Valenzuela GJ, Veille JC, Tabor B, et al. An oxytocin receptor antagonist (atosiban) in the treatment of preterm labor: a randomized, double-blind, placebo-controlled trial with tocolytic rescue. *Am J Obstet Gynecol.* 2000;182:1173–83.
15. Thornton S, Goodwin TM, Greisen G, Hedegaard M, Arce JC. The effect of barusiban, a selective oxytocin antagonist, in threatened preterm labor at late gestational age: a randomized, double-blind, placebo-controlled trial. *Am J Obstet Gynecol.* 2009;200:627. e1–10.
16. Amorim MM, Lippo LA, Costa AA, Coutinho IC, Souza AS. Transdermal nitroglycerine administration versus oral nifedipine for tocolysis: A randomized clinical trial. *Rev Bras Ginecol Obstet.* 2009;31:552- 8.
17. Jamil M, Abid R, Basharat A, Kharunisa. Transdermal Nitro-Glycerine Versus Oral Nifedipine for Acute Tocolysis in Preterm Labour: A Randomised Controlled Trial. *J Soc Obstet Gynaecol Pak.* 2020; Vol 10(1):26-29.
18. Dhawle A, Kalra J, Bagga R, Aggarwal N. Nifedipine versus nitroglycerin for acute tocolysis in preterm labour: a randomised controlled trial. *Int J Reprod Contracept Obstet Gynecol.* 2013;2:61-6.
19. Kashanian M, Zamen Z, Sheikhsari N. Comparison between nitroglycerin dermal patch and nifedipine for treatment of preterm labor: a randomized clinical trial. *J Perinatol.* 2014;34(9):683-7.
20. Papatsonis DN, Van Geijn HP, Adèr HJ, Lange FM, Bleker OP, Dekker GA. Nifedipine and ritodrine in the management of preterm labor: a randomized multicenter trial. *Obstet Gynecol* 1997;90:230-234.