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Which one is better for Tocolysis in Preterm Labor?: Oral Nifedipine vs Transdermal Nitroglycerin Patch

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ABSTRACT

Introduction: Preterm labour follows a spontaneous commencement of labour in two-thirds of preterm birth instances. Obstetricians must consider both treatment options for the management of preterm. The study was conducted to compare the tocolytic effects of oral nifedipine tablets and transdermal nitroglycerine patches in preterm labor.

Methodology: Cases with Singleton pregnancy, Pregnancy between 28 weeks to 36 completed weeks, and without contraindication for tocolysis were included in the study. Randomly assigned Nifedipine group received oral nifedipine (Tab Depin 10mg) and NTG group received transdermal nitroglycerine patch (Nitroderm 10). Progress was assessed for effect of drug for tocolysis.

Results: Both groups were comparable in terms of demographic variable, vital measures, bishop score and cervical dilatation at the time of reporting. Comparison of mean prolongation duration according to gestational age in both the study groups indicate that overall duration of prolongation was better in oral nifedipine. However, the differences were not statistically significant. Headache and hypotension were significantly higher in Nitroglycerine patch compared to oral nifedipine group. The treatment discontinuation was significantly higher in Nitroglycerine patch compared to oral Nifedipine.

Conclusion: Tocolytic effect of both, oral nifedipine and Nitroglycerine patch was statistically almost similar. However, considering the feasibility of application, availability, and cost of the drug, we recommend to use oral nifedipine for tocolysis over Nitroglycerine patch.

INTRODUCTION

Obstetricians all over the world struggle with preterm birth. Annually, 13 million infants are thought to be born around the world before 37 full weeks of pregnancy. [1] The primary factor in newborn morbidity and mortality is India is one of the top 10 nations in the world, accounting for 60% of preterm births worldwide, the survey said. [2] Preterm labour follows a spontaneous commencement of labour in two-thirds of preterm birth instances. [3] The cause of preterm labour is still unknown in roughly 45%–50% of instances. As a result, measures aimed at prevention have not been very successful, although preterm labour arrest remains urgently necessary. Obstetricians must consider both treatment options for the management of pre-

term labour and the problem of the survival of the premature newborn. [4]

Threatened preterm labour is the term used when uterine contractions are felt without a cervical shift. Preterm labour is associated with a number of high-risk factors, including previous preterm births, low socioeconomic status, maternal age of less than 18 or more than 40, premature rupture of the membranes, spontaneous second trimester abortions, uterine causes, and the presence of a retained intrauterine device. Tocolytic therapy aims to delay uterine contractions, lengthen pregnancy, and avoid preterm birth. The ability to offer steroid therapy and the ability to move the woman to a higher centre prior to delivery for improved neonatal care are the main benefits of tocolysis. Calcium channel blockers, nitric oxide donors, progesterones, beta-adrenergic agonists, prostaglandin synthetase inhibitors, oxytocin receptor antagonists, and magnesium salts are examples of tocolytics now in use. [5]

The current pharmaceutical measures are especially intended to halt uterine activity at the myocyte level. Nitroglycerin, also known as glyceryl trinitrate in some countries; Nitroglycerin Skin Patch (GTN) It is a very volatile, low-molecular-weight nitrate compound also referred to as a "nitro vasodilator." The liver has a high first-pass inactivation rate for the medication nitroglycerine. A glutathione-dependent organic nitrate reductase in the liver quickly breaks down the active ingredient. The medicine can be used transdermally to prevent it. [6] The amount of nitroglycerin in this transdermal administration method is 25 mg. It has a 10 cm2 medication release area and disperses 5 mg of nitroglycerin over the course of 24 hours. As a nitric oxide donor nitroglycerin stimulates guanyl cyclase and boosts the production of cyclic 3-guanosine monophosphate (cGMP), which relaxes smooth muscles. To keep the uterus dormant, nitric oxide concentration rises during pregnancy and production falls during labour, which explains how nitroglycerin can stop preterm labour. Nifedipine is a derivative of pyridine. The most popular calcium channel blocker used for tocolysis is nifedipine. The plasma membrane's voltage-dependent calcium channels are blocked by nifedipine. Additionally, it increases calcium outflow from the cell and inhibits intracellular calcium release from sarcolemma reserves. Myometrial relaxation is the result of decreased intracellular free calcium, which inhibits the phosphorylation of the calcium-dependent MLCK (Myosin Light Chain Kinase). Tocolytic therapies have been attempted with varying degrees of success to prevent premature deliveries. Efforts have been undertaken to develop a procedure that is the least burdensome, has the fewest adverse effects, and enables patients to stay mobile. The purpose of the study is to compare the tocolytic effects of oral nifedipine tablets and transdermal nitroglycerine patches in preterm labor.

OBJECTIVES

The study was conducted to compare the tocolytic effects of oral nifedipine tablets and transdermal nitroglycerine patches in preterm labor.

METHODOLOGY

The study was conducted in KIMS hospital, Karad which is a tertiary care health care institute proving services to nearby urban and rural area. Pregnant women visiting obstetrics and gynecology department of the hospital with preterm labour constitute the study population. This was a single centre hospital-based randomized control study conducted in patients admitted at KIMS, Karad over a period of 18 months from November 2020 to May 2022.

Sample size calculation: According to research conducted by Nidhi Sharma et al[7] the estimated sample size calculated by percentage of women delivering after 48 hours after receiving tab oral nifedipine (P_0) and percentage of women delivering by receiving nitroglycerine patch (P)

$$N = 2 \times \left(\frac{z_{1-\alpha} + z_{1-\beta}}{\delta_0}\right)^2 \times PP_o \times (1-P)(1-P_o)$$

Where N is size per group; P is the response rate of standard treatment group; P_0 is the response rate of new drug treatment group; $z_{1-\alpha}$ is the standard normal deviate for a one or two sided α; $z_{1-\beta}$=the power of the study; and δ_0 is a clinically acceptable margin.

The calculated sample size for each group n= 57 which was rounded to 60. Thus the final sample size for the study was 120 and this was divided into 2 groups. Group 1 Oral nifedipine group with sample size 60 and Group 2 Nitroglycerine patch group with sample size 60.

Eligible candidates for the study admitted in the maternity ward of hospital.

Inclusion criteria: Cases with Singleton pregnancy, Pregnancy between 28 weeks to 36 completed weeks, and without contraindication for tocolysis were included in the study.

Exclusion criteria: Any cases with cervical dilatation more than 4cm, severe Pre-Eclampsia/Imminent Eclampsia, hypotension (BP less than 90mm systolic/less than 60mm diastolic), intra uterine fetal demise, antepartum hemorrhage, ruptured membranes or signs/symptoms of chorioamnionitis, cardiac disease, known tocolytic exposure during current pregnancy, fetal malformation and severe intra uterine growth restriction was excluded.

Randomization: All eligible cases giving informed consent were assigned to any of two study groups using computer-generated random numbers with equal probability of selection in either group.

Data Collection

Gestational age was be determined by the date of last menstrual period (LMP) with a reliable menstrual history, an early urine pregnancy test and/or an ultrasound prior to 20 weeks of gestation. A demographic profile, detailed history with complete general physical examination including per abdominal examination and sterile per speculum examination to assess cervical dilatation and to exclude any rupture of membranes was done. After randomization, patients were divided in two groups: group A was received Oral Nifedipine, and group B was received Transdermal Nitroglycerine Patch. Blood pressure, pulse rate and uterine contractions were recorded hourly for the first 12 hours and then 4 hourly for next 60 hours in both the groups. Patients in both groups received injection dexamethasone for fetal lung maturity.

Group A: Oral Nifedipine

Nifedipine group received oral nifedipine (Tab Depin 10mg). They were given tablet nifedipine 30mg oral as loading dose. If contractions persist after sixty minutes, additional oral dose of 10mg was given. If labor was suppressed after first/second dose, a maintenance dose of 10 mg orally every 6 hours was be given starting 6 hours following the loading dose and continued until 72 hours.

Treatment was discontinued, if there was fall of Bp less than 90/60mmhg, if the pulse rate is more than 100/mt, if the patient had premature rupture of membranes, or if there are persistent uterine contractions even after 72 hours

Group B: Transdermal Nitroglycerine Patch

NTG group received transdermal nitroglycerine patch (Nitroderm 10) which was applied on the abdomen. If contractions persist at end of 1 hour, an additional patch was applied. Not more than 2 patches was applied simultaneously (20 mg). At end of 24 hours, it was replaced by another patch for next 24hours. **Treatment was discontinued if p**atient complaining of any headache, hypotension less than 90/60mmhg, pulse rate more than 100/min, if the patient had premature rupture of membranes, or if there are persistent uterine contractions even after 48 hours.

Statistical Methods

Data was analyzed and appropriate statistical methods like frequency, percentage, Mean, Standard Deviation (SD), chi-square test, and 't' test were employed to analyze data throughout study.

Descriptive and inferential statistical analysis was carried out in the present study. Results on continuous measurements were presented on Mean ± SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 95 % level of significance. The following assumptions on data was made for the statistical analysis: Assumptions: 1. Dependent variables should be normally distributed, Samples drawn from the population should be random, Cases of the samples should be independent.

Student t test (two tailed, independent) was be used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups.

Ethical consideration

The prospective participants were explained about the purpose and nature of the study by me in the language he/she understands. A duly signed informed consent form was sought from the patient. The participant shall be recruited only after patient willingly signs the Informed Consent Form (ICF). Anonymity and confidentiality of the participant was maintained at all levels. The Participant was given the right to opt out of the study at any stage without having to give any reason. This was not jeopardizing his/her right to receive appropriate treatment and care. No Participant had to bear any extra cost exclusively for the purpose of this study. If extra cost is required to be incurred purely for the purpose of this study, it was borne by the investigator. Approval of "Institutional Ethics Committee" was sought before start of the study. I was committed to inform "Institutional Ethics Committee" about any change in study, protocol, or design in

advance for approval, however, no such instance arises during the course of the study.

RESULTS

Table 1 shows comparison of various obstetrical and clinical variables between the two study groups. The distribution of maternal age is almost similar in both the groups. The mean age in oral nifedipine group was 24.25±3.99 years whereas in Nitroglycerine patch group 24.20±2.63 years. The distribution of gestational age is almost similar in both the groups. The mean GA in oral nifedipine group was 32.65±1.33 weeks whereas in Nitroglycerine patch group 32.88±1.27 weeks. Here, 38 (63.33%) out of 60 in oral nifedipine group had single parity whereas in nitrogycerine patch group it was 34 (56.67%). 14 (23.33%) out of 60 in oral nifedipine group had second parity whereas in nitrogycerine patch group it was 16 (26.67%). The mean pulse rate in oral nifedipine group was 83.7±5.2 bpm whereas in nitrogycerine group it was 85.1±7.1 bpm. The mean Systolic blood pressure in oral nifedipine group was 112.7±8.8 mmHg whereas in nitrogycerine group it was 109.4±7.5 mmHg. The mean Diastolic blood pressure in oral nifedipine group was 70.4±9.3 mmHg whereas in nitrogycerine group it was 68.6±7.9 mmHg. The mean Bishop Score was 4.9±1.4 in oral nifedipine group whereas in nitroglycerine patch group it was 5.2±1.5. Out of 60 in oral nifedipine group, 30 (50%) cases were found 2 to 3 cervical dilation at the time of reporting followed by 20 (33.33%) were found 1 to 2. Out of 60 in nitroglycerine patch group, 34 (56.67%) cases were found 2 to 3 cervical dilations at the time of reporting followed by 19 (31.67%) were found 1 to 2. Comparison of all the variables between two groups showed that the p value is >0.05 indicating that there is no significant difference in both the study groups for the above-mentioned variables.

Table 1: Comparison of Obstetrical and clinical variables between two study groups

Background Variables	Oral Nifedipine (n=60) (%)	Nitroglycerine Patch (n=60) (%)	P value*
Maternal Age in years			
18-20	7 (11.67)	3 (5)	0.167
21-25	26 (43.33)	38 (63.33)	
26-30	23 (38.33)	18 (30)	
31-34	3 (5)	1 (1.67)	
>=35	1 (1.67)	0 (0)	
Mean age in years	24.25±3.99	24.20±2.63	
Gestational Age at the time of registration			
28-30 weeks	3 (5)	2 (3.33)	0.877
31-32 weeks	13 (21.67)	12 (20)	
33-34 weeks	35 (58.33)	34 (56.67)	
35-36 weeks	9 (15)	12 (20)	
Mean GA	32.65±1.33	32.88±1.27	
Maternal parity			
1	38 (63.33)	34 (56.67)	0.889
2	14 (23.33)	16 (26.67)	
3	6 (10)	7 (11.67)	
>3	2 (3.33)	3 (5)	
Vital Signs			
Pulse (bpm) (Mean ± SD)	83.7±5.2	85.1±7.1	0.22
SBP (mmHg) (Mean ± SD)	112.7±8.8	109.4±7.5	0.28
DBP (mmHg) (Mean ± SD)	70.4±9.3	68.6±7.9	0.255
Bishop score			
4-Jan	11 (18.33)	11 (18.33)	0.827
7-Apr	44 (73.33)	42 (70)	
10-Jul	5 (8.33)	7 (11.67)	
Mean Bishop Score	4.9±1.4	5.2±1.5	
Cervical Dilation at the time of reporting			
0-1 cm	5 (8.33)	4 (6.67)	0.828
1-2 cm	20 (33.33)	19 (31.67)	
2-3 cm	30 (50)	34 (56.67)	
3-4 cm	5 (8.33)	3 (5)	

Table 2: Comparison of outcome variables between two study groups

Outcome variable	Oral Nifedipine (n=60) (%)	Nitroglycerine Patch (n=60) (%)	P value
Prolongation of pregnancy (days)			
<2 days	18 (30)	23 (38.33)	0.628
2-7 days	35 (58.33)	31 (51.67)	
>7 days	7 (11.67)	6 (10)	
Mean Prolongation in days (up to 7 day f/up) according to GA at the time of reporting			
28-30 weeks	3.01±2.06	2.76±1.24	0.422
30-32 weeks	3.49±2.22	2.67±2.76	0.075
32-34 weeks	3.71±1.65	2.93±2.73	0.06
35-36 weeks	3.53±2.26	3.06±1.69	0.209
Complications			
Severe Headache	4 (6.67)	15 (25)	0.005
Tachycardia	16 (26.67)	5 (8.33)	0.001
Hypotension	2 (3.33)	8 (13.33)	0.047
Palpitation	4 (6.67)	2 (3.33)	0.402
Complications leading to treatment discontinuation			
Severe Headache	1 (1.67)	5 (8.33)	
Tachycardia	4 (6.67)	2 (3.33)	
Hypotension	1 (1.67)	5 (8.33)	
Palpitation	0 (0)	1 (1.67)	
Any complication	6 (10)	13 (21.67)	0.04

Table 2 shows comparison of various outcome indicators between two group after the intervention. More cases have more than 2 days of prolongation in oral nifedipine group compared to nitroglycerine patch group. However, the p value is >0.05 indicating that there is no significant difference in duration of prolongation in both the study groups. The mean prolongation days at 35-36 weeks of GA was 3.53±2.26 in oral nifedipine group whereas in nitroglycerine patch group it was 3.06±1.69. Comparison of mean prolongation duration according to gestational age in both the study groups indicate that overall duration of prolongation was better in oral nifedipine group compared to Nitroglycerine patch group. However, the differences were not statistically significant. Comparison of complications and their p values (<0.05) indicate that headache and hypotension was significantly higher in Nitroglycerine patch compared to oral nifedipine group. This also led to significantly higher discontinuation rate due to hypotension in Nitroglycerine patch group compared to oral nifedipine group. Tachycardia was significantly higher in oral nifedipine group compared to Nitroglycerine patch group with p value <0.01. In oral nifedipine group treatment was discontinued in one case due to severe headache, in four cases due to tachycardia, and in one case due to hypotension. In Nitroglycerine patch group treatment was discontinued in five cases due to severe headache, in two cases due to tachycardia, in five cases due to hypotension, and in one case due to palpitation. Out of 60 cases in oral nifedipine group in 6 cases treatment was discontinued while in Nitroglycerine patch group in 13 cases treatment was discontinued. This difference was statistically significant (p<0.05) indicating that treatment discontinuation was significantly higher in Nitroglycerine patch compared to oral Nifedipine.

Table 3: Comparison of cost of treatment in both the study groups

	Treatment details for each case	Approx Unit cost of medication	Mean Cost per case in the present study
Oral Nifedipine (n=60)	Cap Nifedipine 30mg loading dose followed by 10 mg 8 hourly for 3 days Requirement of Tablet range from 8 to 11 tablet.	Rs. 3.00 per 10mg tablet	Rs. 30.00 per patient with standard deviation of 2.12
Nitroglycerine Patch (n=60)	One or Two Nitroglycerine patches required	Rs. 65.00 per patch	Rs. 92.00 per patient with standard deviation of 10.37

P value <0.001 (unpaired t test)

Table 3 shows the cost of treatment and its comparison between two group. Oral nifedipine given 30 mg state orally followed by 10 mg every 8 hourly for two to three days. Each 10 mg tablet costs Rs. 3.00, So average cost of treatment per case was Rs. 30.00 (sd 2.12). Nitroglycerine patch cost around Rs. 65.00 per patch and each case required one or two patches. So, in the present study average cost per patient was Rs. 92.00 (sd 10.37). Application of unpaired t test gives p value <0.001 which indicates that the average cost of Nitroglycerine patch is significantly higher than oral nifedipine cost per patient.

DISCUSSION

Preterm labour is defined by the World Health Organization as the commencement of labour before 37 completed weeks (259 days) counting from the first day of the previous menstrual cycle. While the specific cause of preterm labour is still unknown, preterm deliveries are most usually caused by either a disease that causes uterine contractions or early or premature onset of regular physiological uterine contractions.[8]

Preterm birth accounts for 7–12% of pregnancies and causes up to 70–80% of infant morbidity and mortality, making it a severe public health concern.[9] Practically speaking, due to the recent rapid developments in feto-maternal medicine, survival outcomes are better in births that occur after 34 weeks of gestation.[10]

One of the best ways to lower preterm morbidity and death is to use tocolytics. They partially relax the uterus, which helps to extend the pregnancy by at least two to three days and gives enough time to administer four doses of corticosteroids that promote lung development and prevent respiratory distress syndrome in babies. To postpone labour, a variety of tocolytics with different mechanisms of action has been employed over time. Adverse effects of using medications like Isoxsuprine, Ritodrine, and Nifedipine include pulmonary oedema, arrhythmia, and myocardial ischemia in mothers, as well as neonatal hyperglycemia, hypokalemia, hypoglycemia, and paralytic ileus in the foetus.[10]

In the treatment of premature labour, transdermal Nitroglycerine patches are more efficient than oral nifedipine. The biggest issue in perinatal medicine is prematurity. For a number of reasons, the rate of prematurity has not decreased in recent years despite the availability of tocolytic drugs.[11] The management of premature babies may place a heavy psychological and financial burden on the families, having a significant psychosocial impact.[4]

In present study, the distribution of previous preterm delivery is almost similar in both the groups. Here majority of the cases were not found previous preterm delivery in both the groups. Only 4 (6.67%) cases out of 60 in oral nifedipine group were found previous preterm delivery whereas in nitrogycerine patch group it was 5 (8.33%). P value is >0.05 indicating that there is no difference in previous preterm delivery in both the study groups. It means that history of previous preterm delivery was almost similar in both the groups. In the study by Sharma N et al[7] (2019), 18.5% out of 51 cases in nifedipine group were found previous preterm delivery whereas 7 (14.2%) out of 49 cases in NTG group. There is no significance difference found in both study group. (p = 0.28) This result is similar to our research. Amorim et al[12] (2009) engaged 50 patients to test the effects of NTG as a therapeutic drug vs oral nifedipine. They discovered that the rates of preterm birth in the first 48 hours were 15.4% in the nitroglycerin group and 12.5% in the nifedipine group. The tocolytic effects of nifedipine and NTG were compared in 43 and 41 patients in each group, respectively, by Dhawle A et al[13] (2013). When compared to Nifedipine, they discovered that delivery within 48 hours was considerably higher with NTG (p=0.02).

NTG and nifedipine were compared in a randomised clinical trial by Kashanian et al[14] (2014). as a tocolytic agent. In comparison to the nifedipine group, more women in the NTG group delivered after 48 hours (52 women, or 86.7% vs. 41 women, or 68.3%, P=0.016), and after 7 days (47 women, or 78.3% vs. 37 women, or P=0.046). Neonatal weight and foetal outcomes like Apgar score were improved in the NTG group. Additionally, the NTG group had fewer admissions to the newborn intensive care unit (NICU) and shorter stays there. Both groups' negative impacts were comparable and barely noticeable. In their study, Balasubramani and Kamatchi[4] also found that nifedipine group preterm labour was 22% and NTG group preterm labour was 18%. 18% of participants in the nifedipine group and 20% of patients in the NTG group had a prior history of abortion. No statistically significant difference was identified between the 32.2% of patients in the nifedipine group and the 13.3% of patients in the NTG group who had a prior history of abortion, according to Kashanian et al[15] They also noted a history of premature labour in 6.7% of

the nifedipine group's patients and 5% of the NTG group's patients.

In present study, 17 (28.33%) cases out of 22 in oral nifedipine group were found Caesarean delivery followed by 5 (8.33%) were found Normal vaginal delivery. In nitrogycerine patch group out of 26 cases, 22 (36.67%) were found Caesarean delivery followed by 4 (6.67%) were found Normal vaginal delivery. P value is >0.05 indicating that there is no difference in mode of delivery in previous pregnancy in both the study groups. It means that mode of delivery was almost similar in both the groups. In the study by Kashanian et al[15] (2005), out of 25 cases in nifedipine group 12 (20%) cases were found normal vaginal delivery whereas in NG group it was 6 (10%). Out of 25 cases in nifedipine group 13 (21.7%) cases were found Caesarean delivery whereas in NG group it was 7 (11.7%). There no significance difference found in the both the study groups.

In present study, the mean pulse rate in oral nifedipine group was 83.7±5.2 bpm whereas in nitrogycerine group it was 85.1±7.1 bpm. The mean Systolic blood pressure in oral nifedipine group was 112.7±8.8 mmHg whereas in nitrogycerine group it was 109.4±7.5 mmHg. The mean Diastolic blood pressure in oral nifedipine group was 70.4±9.3 mmHg whereas in nitrogycerine group it was 68.6±7.9 mmHg. P value are >0.05 indicating that there is no difference in pulse and blood pressure measurements in both the study groups. It means that pulse; SBP and DBP were nearly similar in both the study groups. In the study by Sharma N et al (2019) [7], the mean pulse rate in nifedipine group was 84.6±5.2 bpm whereas in nitrogycerine group it was 86.2±6.8 bpm. The mean Systolic blood pressure in oral nifedipine group was 114.9±9.5 mmHg whereas in nitrogycerine group it was 111.6±8.5 mmHg. The mean Diastolic blood pressure in oral nifedipine group was 72.6±9.1 mmHg whereas in nitrogycerine group it was 69.3±8.6 mmHg. P value was 0.06. Therefore, there is no difference in pulse and blood pressure measurements in both the study groups.

In present study, the mean Bishop Score was 4.9±1.4 in oral nifedipine group whereas in nitroglycerine patch group it was 5.2±1.5. Mean Bishop Score was slightly higher in nitroglycerine patch group compared to oral nifedipine group; however, the p value is >0.05 indicating that there is no significant difference in Bishop score in both the study groups. There is no significance difference found in Bishop Score in the study by Sharma N et al (2019)[7]. (p= 0.98). This result is comparable with our study. In present study, out of 60 in oral nifedipine group, 30 (50%) cases were found 2 to 3 cervical dilation at the time of reporting followed by 20 (33.33%) were found 1 to 2. Out of 60 in nitroglycerine patch group, 34 (56.67%) cases were found 2 to 3 cervical dilation at the time of reporting followed by 19 (31.67%) were found 1 to 2. Comparison of cervical dilatation at the time of reporting for the study showed that the p value is >0.05 indicating that there is no significant difference in cervical dilatation at the time of reporting in both the study groups. In the study by Kaur P et al (2021)[16], found different results from our study. At >3 cm cervical dilation the mean prolongation of pregnancy in NTG group was 2.11±0.32 days whereas in nifedipine group it was 3.6±1.97 days. (p= 0.0030) This result was statistically significant. Balasubramani and Kamatchi[4] and Dhawle et al[13] had also discovered similar outcomes. According to Dhawle et al., nifedipine was substantially more successful at extending pregnancy compared to NTG when the cervical dilation was 3 cm (5.00 ± 5.45 days versus 0.56 ± 0.53 days; P = 0.015). Similar findings were made by Balasubramani and Kamatchi,[4] who discovered that when the cervix was dilated by 2 cm, the mean prolongation was 11 days in the nifedipine group and 4 days in the NTG group. The mean prolongation with Group I was 3.2 days and with Group II was 2.8 days when the cervical dilatation was 3 cm (P = 0.0458, significant).

In present study, the distribution of prolongation of pregnancy days was almost similar in both the groups. Here 35 (58.33%) out of 60 cases in oral nifedipine group were found 2 to 7 days requirement for prolongation of pregnancy whereas in nitroglycerine patch group it was 31 (51.67%). More cases have more than 2 days of prolongation in oral nifedipine group compared to nitroglycerine patch group. However, the p value is >0.05 indicating that there is no significant difference in duration of prolongation in both the study groups. Similar result found in the study by Sharma N et al (2019) [7]. Both the medications found same impact on prolongation of pregnancy for longer than 48 hours (52.9 in nifedipine group and 53.1% in NTG group, p= 0.99) and for longer than 7 days (13.7% in the Nifedipine group and 14.3% in the NTG group, p=0.94). Kaur P et al (2021) [16] discovered a difference in the mean length of pregnancy between the two study groups that was statistically significant.

In present study, the mean prolongation days at 28-30 weeks of GA was 3.01±2.06 in oral nifedipine

group whereas in nitroglycerine patch group it was 2.76±1.24. The mean prolongation days at 35-36 weeks of GA was 3.53±2.26 in oral nifedipine group whereas in nitroglycerine patch group it was 3.06±1.69. Comparison of mean prolongation duration according to gestational age in both the study groups indicate that overall duration of prolongation was better in oral nifedipine group compared to Nitroglycerine patch group. However, the differences were not statistically significant. In study by Kaur P et al (2021)[16], both in NTG Group and nifedipine Group, the mean length of the pregnancy varied significantly with gestational age upon admission. The mean prolongation in NTG Group was 2.79±1.41 days and in nifedipine Group it was 3.70±1.77 days when the gestational age was between 32.1 and 34.0 weeks. There was a statistically significant difference between them. In the study by Sharma N et al (2019)[7], the mean GA at delivery in nifedipine group was 33.1±1.5 weeks whereas 33.1±1.1 weeks in NTG group. (P= 0.42)

In present study, out of 60 cases in oral nifedipine group common complications were 16 (26.67%) tachycardia, 4 (6.67%) headache and 4 (6.67%) palpitation. Out of 60 cases in nitroglycerine patch group common complications were 15 (25%) headache, 8 (13.33%) hypotension, 6 (10%) cases were discontinued the treatment due to hypotension and 5 (8.33%) were found tachycardia. In the study by Sharma N et al (2019)[7], out of 51 cases in nifrdipine group 4(7.8%) were found birth asphyxia whereas 1 (2%) in out of 49 cases in NTG group. (p=0.36) Death cases in nifedipine group were 2 (3.9%). In the study by Kaur P et al (2021)[16], out of 50 cases in NTG group common complications were headache 21 (42%), Tachycardia 10 (20%), Hypotension 1 (2%) and Palpitation 3 (6%). Out of 50 cases in nifedipine group common complications were headache 3 (6%), Tachycardia 14 (28%), Hypotension 2 (4%) and Palpitation 5 (10%). The NTG group (42%) experienced headaches more frequently than the nifedipine group (6%). 20% of the women in Group A and 28%, 4%, and 10% of the women in Group B, respectively, had tachycardia, hypotension, and palpitations. Similar to our study, Dhawle et al [13] found that the overall incidence of adverse events was 48.7% with NTG against 34.88% with nifedipine. With NTG, headache rates were substantially higher (41.5% vs. 4.7%). Between the two groups, there was no difference in the frequency of tachycardia or palpitations.

Except for headache, which affected roughly 30% of patients receiving nitroglycerine and 8.3% of patients receiving nifedipine, there was no statistically significant difference in the frequency of adverse effects reported by patients in the study by Amorim et Al. [12] In Amorim et al (2009)[12] study, both drugs were found to be almost equally efficacious. Headache was significantly more in NTG group than nifedipine (30.8% versus 8.3%, p=0.04).

When compared to ritodrine, the incidence of side effects with nifedipine was reported to be much lower (18.9% versus 36%) by Papatsonis et al. [17]

In contrast to atosiban, which had a side effect rate of 17.5%, nifedipine was related with side effects in 40% of patients, according to Kashanian et al. [15] They also discovered that 27.7% of people taking nifedipine developed hypotension.

The most frequent side effects of nifedipine, in contrast to these trials, were headache (32%), followed by palpitations (8%) and hypertension (8%), according to Yasmin et al.[18] With 48% of patients reporting no side effects, the NTG patch had a better adverse effect profile. However, headache (32%) was the most common complaint with it.

The American College of Obstetricians and Gynaecologists endorses the short-term (up to 48 hours) prolonging of pregnancy with beta-adrenergic agonist therapy, calcium channel blockers, or NSAIDs in order to facilitate the delivery of prenatal steroids. Tocolytic treatment does not, however, directly improve new-born outcomes.[19]

Additionally, it should be remembered that tocolysis is utilized for preterm infants who are already likely to be brought to the NICU for prematurity and disorders associated to prematurity, yielding higher likelihood of nursery admission than term infants. An economic analysis of the trial was conducted as a secondary analysis. Oral nifedipine is less expensive than the more expensive transdermal nitroglycerine.

CONCLUSION

In this study there was no significant difference in the base line indicators and obstetrical history like age of mother, gestational age, parity, history of previous abortion, history of previous preterm delivery, previous cesarean delivery between study group which receive oral nifedipine and the group which receive nitroglycerine patch.

Baseline vital indicators like pulse, systolic and diastolic blood pressure were also similar in both the study groups. There is no significant difference in

Bishop's score and cervical dilatation at the time of reporting in both the study groups.

Duration of Prolongation of pregnancy was slightly better in oral nifedipine group compared to nitroglycerine patch; however the difference was statistically non-significant.

Complications like headache and hypotension were significantly higher in Nitroglycerine patch group while Tachycardia was significantly higher in oral nifedipine group. Significantly higher discontinuation rate due to hypotension was reported in Nitroglycerine patch group compared to oral nifedipine group.

So, finally we can conclude that tocolytic effect of both, oral nifedipine and Nitroglycerine patch was statistically almost similar. However, considering the feasibility of application, availability, and cost of the drug, we recommend to use oral nifedipine for tocolysis over Nitroglycerine patch.

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