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A comparative study of oral salbutamol versus oral nifedipine for prevention of pre term labour

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Abstract
Objective: To conduct a comparative study between use of salbutamol versus nifedipine by oral route in prevention of preterm labor
Method: The study was conducted in the Department of Obstetrics and Gynaecology, M.G.M. Medical College and M.Y. Hospital, Indore (M.P.) during the period from August 2015 to August 2016.
Results and Conclusion: Nifedipine was found to be better tocolytic than salbutamol as it prolonged the pregnancy for more than 48 hrs. in which period steroids could be administered to patient in labor and hence the chances of respiratory distress syndrome in neonate could be reduced, and there were lesser side effects with use of nifedipine with no serious maternal adverse effects which makes it one of the best tocolytics to be used in pregnancy.

Keywords: preterm, salbutamol, nifedipine, tocolysis, steroid, neonatal outcome

Introduction
Preterm birth is the leading cause of perinatal morbidity and mortality worldwide. Preterm birth may be defined as birth between the age of viability and 37 completed weeks of gestation [1]. The lower limit of gestation is not uniformly defined; whereas in developed countries it has been brought down to 20 weeks, in developing countries it is 28 weeks.
The incidence of preterm birth ranges from 5% to 8% in most developed countries, but it is still increasing worldwide [2], attributed to the rise in multiple gestation from assisted reproductive techniques, better dating scans and iatrogenic deliveries.
Preterm birth accounts for 75% of neonatal deaths and 50% of long-term morbidity, including respiratory disease and neurodevelopmental impairment [3].
Preterm labour and delivery are among most challenging obstetric complications encountered. The rate of foetal morbidity can be reduced with early and accurate diagnosis of pre-term labour, intervention to delay preterm labour (tocolysis) for buying for the administration of corticosteroids.
Both oral nifedipine and oral salbutamol are commonly used as tocolytic agents.

Material and Methods
Study Design and study population
The present study entitled "Comparative Study between Use of Salbutamol Versus Nifedipine by Oral Route in Prevention of Preterm Labour" was conducted in the Department of Obstetrics and Gynaecology, M.G.M. Medical College and M.Y. Hospital, Indore (M.P.) during the period from August 2015 to August 2016.
This is a prospective comparative study performed on 200 pregnant female patients admitted in Obstetrics and Gynaecology Department. 100 patients would be given oral salbutamol and 100 patients would be given oral nifedipine randomly.

- **Group A:** Oral salbutamol 8 mg dose then repeated 6 hourly (if contraction persists) maximum till 24 hrs, (maximum 32mg/day).
- **Group B:** 20 mg oral Nifedipine initially followed by 10 mg at 4 hourly intervals for 48 h. If contractions persisted at 90 min, the first 10 mg dose was started at the same time.

Inclusion criteria

- Pregnant females between 28 weeks to 36 weeks 6 days of gestation.
- Normotensive females
- Primigravida and second gravida patients

Exclusion Criteria

- Pregnant females <28 and >36 weeks 6 days of gestation
- Pregnant females with gestational hypertension, pre-eclampsia, and eclampsia, antepartum haemorrhage, Intrauterine foetal demise.
- Pregnant females with chronic medical ailments (heart disease, diabetes, jaundice, tuberculosis, asthma, glaucoma)
- Hypersensitivity to salbutamol (β2 sympathomimetic drugs) or to nifedipine (calcium channel blockers)
- Third / fourth gravida, patients with bad obstetrical history.

Study Procedure

- On admission, a thorough assessment of the woman included:
- History-particularly relating to rupture of the membranes, contractions and Gestational age, confirmed by her L.M.P. and any available previous ultrasound data.
- General Examination- particularly temperature, blood pressure, pulse rate.
- Per abdomen examination-uterine tone and tenderness, amniotic fluid volume and fetal size and presentation.
- Vaginal examination - a speculum examination shall be performed with full aseptic technique and not touching the cervix with the speculum. If the cervix is closed Digital examination shall be avoided unless the cervix cannot be adequately visualised.
- Tocolytics are given and then monitoring is done half hourly, for maternal pulse, BP and respiratory rate until the contractions cease.
- All women with preterm labour were investigated for infection by complete hemogram, urine and vaginal swab culture. Antibiotics were provided to cases having significant pathogen count in urine or vaginal culture accordingly.

Data analysis

Statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%).

Significance is assessed at 5% level of significance. Mann Whitney U test has been used to find the significance of study parameters on ordinal scale between two groups and Chi-square test has been used to find the significance of study parameters on categorical scale between two groups.

The Statistical software namely Win-pepi and SPSS 10.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

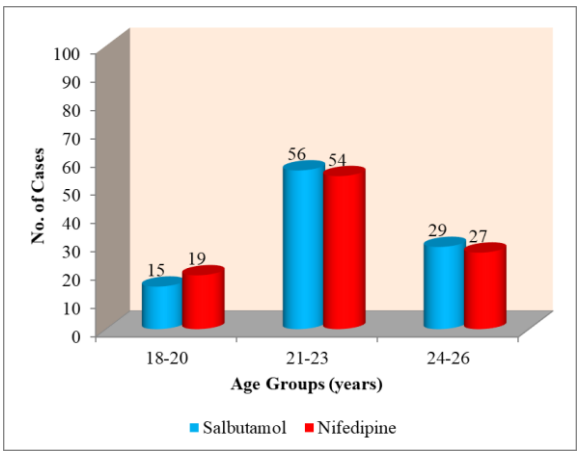
Table 1: Distribution of cases according to demographic factors

Parameter	Distribution Amongst Subjects (%)	
Age	18-20	17.0
	21-23	55.0
	24-26	28.0
Occupation	House Wife	60.0
	Laborers	25.0
	Service	11.6
	Tailor	1.7
	Teacher	1.7
Literacy	Literate	37.7
	Illiterate	62.3
Socio Economic Status	Lower	36.7
	Middle	35.0
	Upper Middle	*28.3*
Parity	Nulliparous (G1P0 & G1P0+1)	*86.5*
	Primi(G2P1L1)	*13.5*

Table 2: Age wise Distribution

Age (years)	Salbutamol	Nifedipine
18-20	15%	19%
21-23	56%	54%
24-26	29%	27%
Total	100%	100%

p value was obtained as 0.522. In both groups maximum number of patients were in age group 21-23 yrs. of age, and since p value is not significant hence both the groups are comparable.



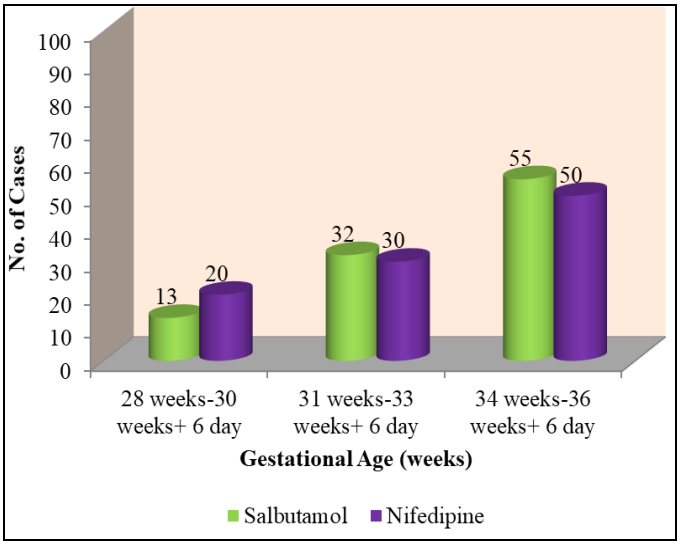
Graph 1: Age wise Distribution

Table 3: Gestational age and Parity wise distribution

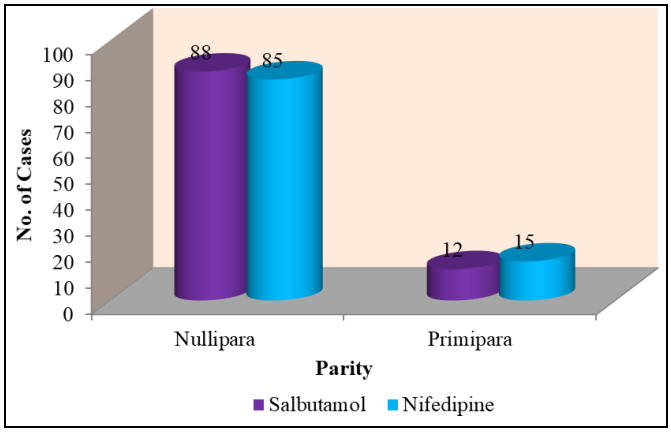
Gestational Age	Salbutamol	Nifedipine
28 weeks-30 weeks+ 6 day	13%	20%
31 weeks-33 weeks+ 6 day	32%	30%
34 weeks-36 weeks+ 6 day	55%	50%
Total	100%	100%
Parity		
Nullipara (G1P0 + G2P0+1)	88%	85%
Primipara (G2P1L1)	12%	15%
Total	100%	100%

Gestational age-p value was obtained as 0.258. Maximum number of patients in both groups belonged to gestational age group of 34-36 weeks 6 days, since the p value is not significant hence the groups are comparable.

Parity wise distribution-p value was obtained as 0.535.Maximum number of patients were nulliparous in both the groups, since p value is not significant, hence the groups are comparable.



Graph 2: Gestational Age wise Distribution



Graph 3: Parity wise Distribution

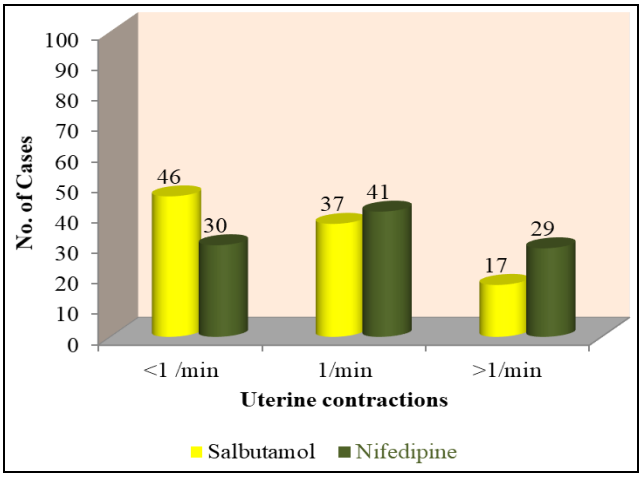
Table 4: Uterine contractions and cervical dilatation on admission

Uterine contractions	Salbutamol	Nifedipine
<1 /min	46%	30%
1/min	37%	41%
>1/min	17%	29%
Total	100%	100%
Cervical dilatation		
<2 cm	48%	36%
2-3 cm	38%	37%
>3 cm	14%	27%
Total	100%	100%
Cervical effacement		
<20%	52%	41%
20-50%	33%	34%
>50%	15%	25%
Total	100%	100%

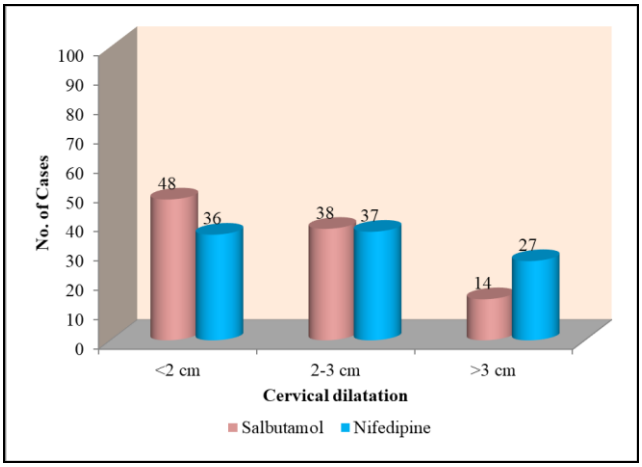
Uterine contractions on admission: p value was obtained as 0.01.'P' value is significant and hence women having a greater number of uterine contractions received nifedipine as compared to salbutamol.70% of women were having uterine contractions one per minute, or more than one per minute who were given nifedipine (Group A), as compared to 54% women in Group B.

Cervical dilation on admission: p value was obtained as 0.02.'P" value is significant and hence nifedipine was given to women with more cervical dilatation as compared to those who were given salbutamol.

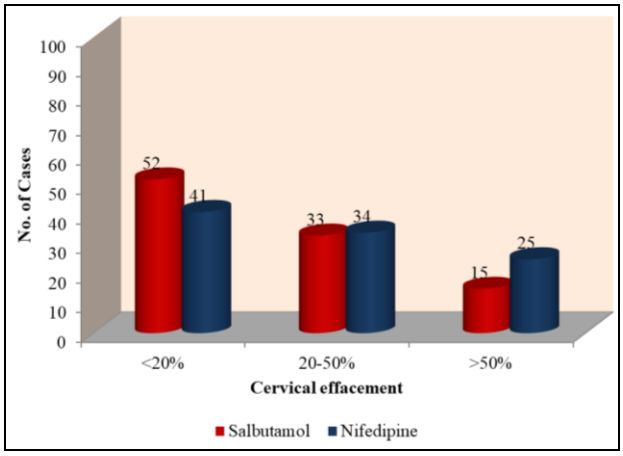
Cervical effacement at the time of admission: p value was obtained as 0.055. Group A had cervical effacement of <20% in 52% of patients, whereas in Group B 41% had cervical effacement of <20%. p value is not significant and hence there was no significant difference in cervical effacement in both the groups at the time of giving tocolytic



Graph 4: Uterine contractions on admission



Graph 5: Cervical dilatation at the time of admission



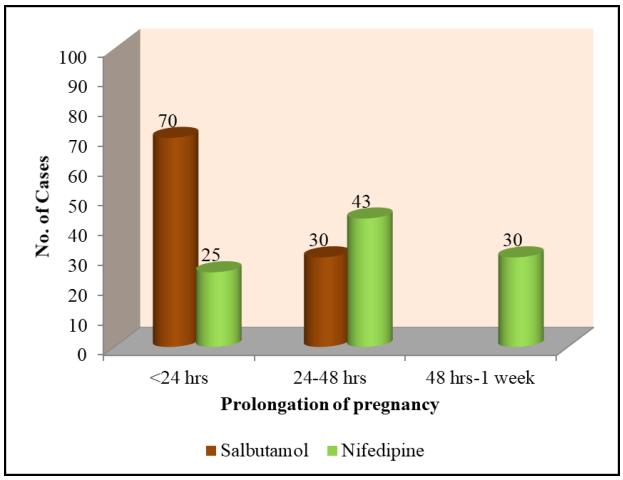
Graph 6: Cervical effacement at the time of admission

Table 5: Prolongation of pregnancy and outcome of pregnancy

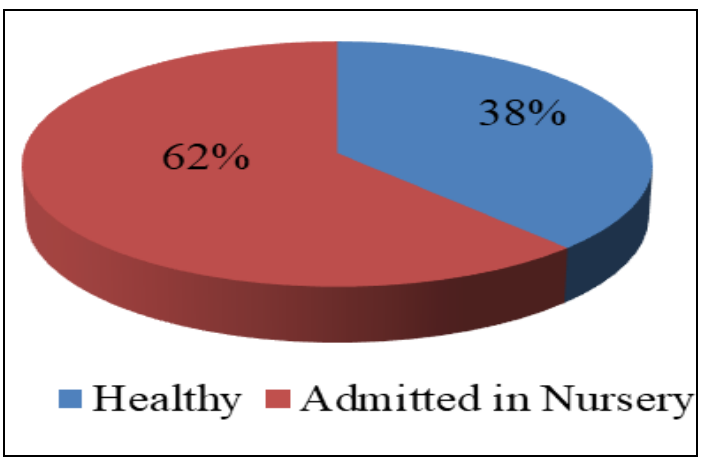
Prolongation	Salbutamol	Nifedipine
<24 hrs.	70%	25%
24-48 hrs.	30%	43%
48 hrs-1 week	-	30%
Total	100%	100%
Neonatal outcome		
Healthy	38%	49%
Admitted in Nursery	62%	50%
Total	100%	100%

Prolongation of pregnancy: p value was obtained as <0.001
30% of women in Group B had prolongation of labour for 48 hrs to 1 week while no one in Group A had this much prolongation of pregnancy. 70% of women in Group A delivered within 24 hrs of giving salbutamol.' P' value is significant and hence nifedipine was better and had better efficacy in prolongation of pre term labour than salbutamol.

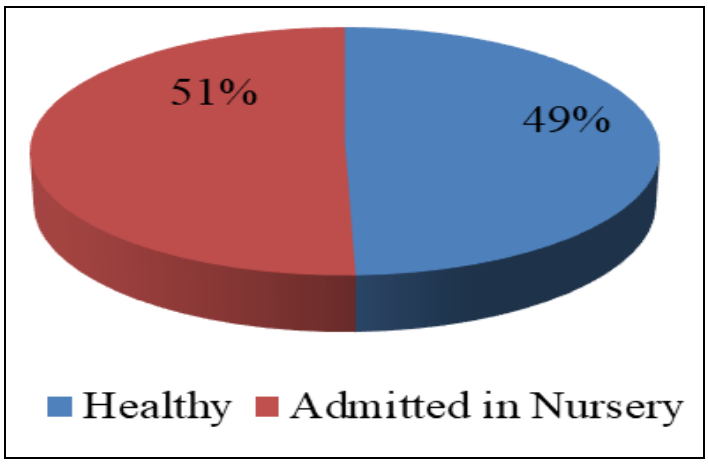
Neonatal outcome: 'P' value was obtained as 0.10 .
62% in group A and 50% in group B had their babies admitted in nursery.
'P' value is not significant and hence, admission to nursery of the new-born carries no remarkable statistical difference in use of these two drugs. However, outcome of babies from nursery was not included in our study.



Graph 7: Prolongation of pregnancy



Salbutamol



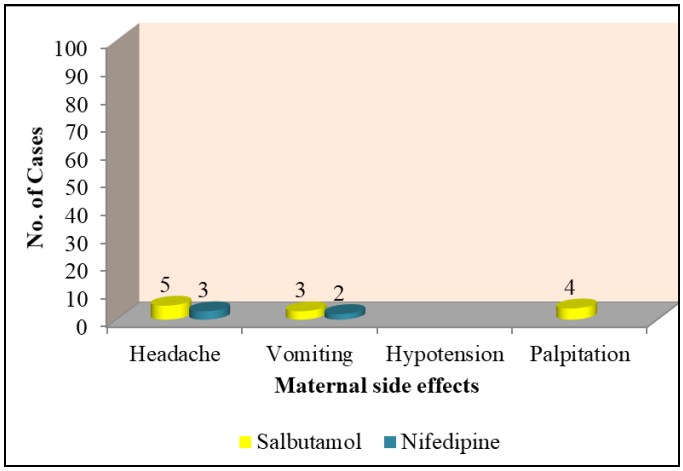
Nifedipine

Graph 8: Neonatal outcome

Table 6: Maternal side effects

Maternal side effects	Salbutamol	Nifedipine
Headache	5%	3%
Vomiting	3%	2%
Hypotension	-	-
Palpitation	4%	-
Total	12%	5%

p value was obtained as 0.07.



Graph 9: Maternal side effects

Discussion

Preterm birth is not singularly the consequence of preterm labour. There are three major etiological factors such as preterm rupture of membranes (25%), spontaneous preterm labour in pregnancy with intact foetal membranes (50%), complication of pregnancy that severely jeopardize foetal and maternal health (25%), and the life style factor. Approximately two thirds of all preterm births occur spontaneously. Preterm birth[4] is classified in mild preterm (32-36 weeks), very preterm (28-31 weeks) and very extremely preterm (<28 weeks).

Preterm delivery before 34 weeks gestation account for 75% cases of neonatal mortality, and mortality rate from 32 weeks of gestation are similar to those at term [5]. Various drugs have been used in inhibiting pre-term labour with the aim of tocolytic therapy to prolong gestation long enough till maturation of foetus is completed. This is done to delay delivery for at least 48 hours so that corticosteroid administration is effective or for transfer of patient to tertiary care centre with neonatal intensive care facility.

Total 200 patients were divided into two groups of 100 each.
Group A - oral salbutamol as tocolytic was given.
Group B - oral nifedipine as tocolytic was given.

Age

In our study, highest number of patients in Group A (56%) were in 21-23 years age group and lowest number (15%) among 18-20 years of age and in Group B highest number of patients (54%) were in 21-23 years age group and lowest number (19%) among 18-20 years of age.

Mean age in group A was 22.65±1.87 (21-24 years) and in group B, 22.44±1.93 (20-24 years) which is comparable to the study of Ghazi A, *et al*. [6]

Our study was in similarity with the study of Lockwood CJ *et al* [7] who found the increased risk of preterm delivery in women <20 years and over 35 years of age. But our study was in contrast to the Iqbal J *et al*, [8] where no patient was below the age of 20 years.

Parity

Mean parity in group A was 1.12±0.32 and in group B was 1.15±0.35

In our study, most of the patients were of low parity which is contradictory to the results found in study of Copper L *et al*, [9] where incidence of preterm labour was high in multi-para.

Gestational age

In our study mean gestational age in group A was 33.87±2.26 (31-35 weeks) and in group B, 33.29±2.32 (31-35 weeks), which is comparable to the study by Weerakul W *et al* [10], where mean gestational age was 31.7±1.8.

Prolongation of Pregnancy

In our study 70% of females who were given salbutamol were delivered within 24 hrs of giving the drug which proves it to be a less effective drug and this is comparable to other studies, whose results were 85%, 86% and 81% respectively [9-11]

In our study labour was prolonged for 24-48 hrs in 30% of patients who received salbutamol while in none of the females it was prolonged for 48 hrs-1 weeks.

Whereas, labour was prolonged for 48 hrs-1 week in 30% of females who were given oral nifedipine and hence proving it to be a better tocolytic than salbutamol. In 43% of patients labour was prolonged for 24-48 hrs and 25 % of women were delivered within 24 hrs.

Perinatal outcome

In group A 62% of babies were admitted in nursery as compared to 50% in group B, but this difference was statistically not significant (Pearson's chi square test was applied) and hence there was no difference in admission of new born babies to nursery in group A and group B, but the outcome of babies after admission to nursery was not included in our study (how many certified and how many were handed over as healthy), which is comparable to two studies [12, 13].

Side effects

In our study 12% of patients in Group A experienced side effects of which 4% experienced palpitations whereas in group B only 5% patients experienced side effects (3% headache, 2% vomiting) of which no one experienced any serious side effect which is comparable to study by Kiran K Malik [15] None of our patient had pulmonary edema but on re-view of literature one case of pulmonary edema among 582 women was reported when treated with beta-agonist by Ferguson JE *et al*. [14] This is possibly because of small sample size. Most common side effect in Group B was headache, and in group A was palpitations and headache [15].

Conclusion

Prediction and prevention of preterm labor is not possible despite extensive research on the subject. Nifedipine was found to be better tocolytic than salbutamol as it prolonged the pregnancy for more than 48 hrs. in which period steroids could be administered to patient in labor and hence the chances of respiratory distress syndrome in neonate could be reduced, and there were lesser side effects with use of nifedipine with no serious maternal adverse effects which makes it one of the best tocolytics to be used in pregnancy as compared to other conventional tocolytics.

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