SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 7.
Issue: 1
Page N. 09-14
Year: 2023

Original Article www.wjahr.com

A STUDY FOR COMPARISON BETWEEN THE EFFICACY OF NIFEDIPINE AND RITODRINE MATERIALS IN SUPPRESSION OF PRETERM LABOUR

Dr. Yousef Samoua*, Prof. Dr. Hasan Saleh and Prof. Dr. Safa Salman

Professor Supervisor[2], Professor Supervisor Assiciated[3]
Department of Obstetrics and Gynecology, Tishreen University, Faculty of Medicine, Lattakia, Syria.

Received date: 29 October 2022 **Revised date:** 19 November 2022 **Accepted date:** 09 December 2022

***Corresponding Author: Dr. Yousef Samoua**

Department of Obstetrics and Gynecology, Tishreen University, Faculty of Medicine, Lattakia, Syria.

ABSTRACT

Objective: The aim of this study was to compare between the efficacy of Nifedipine and Ritodrine in suppression of preterm labour and to compare their side effects of the mother and the neonate. Patients and Methods: Case_Control study was conducted for the period one year (June 2021 – June 2022) at Tishreen University Hospital in Lattakia _ Syria. The study included 80 pregnant women with preterm labour who were divided into group A (Cases): included 40 pregnant women with preterm labour who were given Ritodrine, and group B (Control): 40 pregnant women with preterm labour who were given Nifedipine. Results: Suppression of preterm labour for 48 hours was better in Nifedipine group than Ritodrine (87.5 % vs 67.5%, p:0.03). Fetus age had no role in influencing the results $p>0.05$ counter to bishop score which had important role in influencing the results $p<0.05$ and when comparing the side effectsof each group, Ritodrine achieved more side effects than Nifedipine and we stopped the therapy because of severe side effects in Ritodrine group, palpitation (42.5%Ritodrine vs 7.5%Nifedipine), dyspnea (5%Ritodrine vs 0% Nifedipine), nausea and vomiting (10% Ritodrine vs 0% Nifedipine), tachycardia of the fetus (40%Ritodrine vs 0% Nifedipine) however headache (20%Nifedipine vs 0%Ritodrine), Flare (5%Nifedipine vs 0%Ritodrine) with $p<0.05$, headache and flare were simple side effects and didn´t require to stop the treatment with Nifedipine so side effects in Ritodrine group were more serious than Nifedipine one, and when comparing side effects of these drugs on the neonates we found that there was no difference between these drugs on (median fetus age, median neonate weight, ARDS in the neonate, neonate death): median fetus age (35.3 w Nifedipine vs 34 w Ritodrine, $p>0.05$), median neonate weight (2050gm Nifedipine vs 1900gm Ritodrine, $p>0.05$), ARDS in the neonate (12.5%Nifedipine vs 17.5%Ritodrine, $p>0.05$), neonate death (10%Nifedipine vs 15%Ritodrine, $p>0.05$) however the neonate´s needing for NICU was less in Nifedipine group thanRitodrine one: NICU (50% Nifedipine vs 65% Ritodrine, $p<0.05$). Conclusion: Nifedipine was betterin suppression of preterm labour and achieved less side effects than Ritodrine.

KEYWORDS: Preterm Labour, Nifedipine, Ritodrine.

INTRODUCTION

Preterm labour is defined as regular uterus contractions which cause increased dilation in the cervix after 20 weeks of pregnancy and up to 36,6 weeks. It´s considered as one of serious conditions that faces Obstetritions and Gynecologists nowadays because of its serious side effects on the neonate and the mother and her psychological health. The rate of preterm labour increased during last decades worldwide although of the development in the modern techniques around delivery, and this increasing in preterm labour due to increasing in obstetrical interventions, improvement in diagnostic tools of preterm labour and the increasing in using ultrasound to confirm the age of pregnancy and to measure the length of cervix. There is difference in the incidence of preterm labour according to patient origin which is 9.9% in White American, 17.6% in Black, 12.2% Original American people, 11.2 % in Spanish and 7.4% in Asian. Risk factors and causes of preterm labour include: smoking, alcohol, cocaine, low weight of the woman before pregnancy and low weight gain during pregnancy, vaginal sepsis, asymptomatic bacteriuria, domestic violence, stress, low socioeconomic status,

chronic medical conditions like autoimmune conditions, diabetes, kidney disease, heart disease, hypertention, anemia, previous preterm labour, PPROM, multiple pregnancy, no antenatal care, previous cervicalinjury as a result of (surgery - cone biopsy - LEEP…..), IVF, polyhydramnios, uterus anomaly, placenta previa and placenta abruptio. Preterm labour can cause significant maternal and neonatal complications: most common side effect on the mother is psychological sequelae and the other maternal complications depend on medical treatment (long time bed rest, side effects of the medications). Neonatal outcomes include IUGR, ARDS, intraventricular haemorrhage, opened PDA, necrotizing enterocolitis, retinopathy, hyper bilirubinemia, increasing sensitivity for sepsis, anemia, chronic pulmonary diseases, retardation of the psychomotor development. Signs and symptoms of preterm labour include: painful or painless uterus contractions, pelvic pressure, watery or blood vaginal discharge and low back pain. Several studies have compared between Nifedipine and Ritodrine in suppression of preterm labour. Therefore, the objective of this review was to determine differences between these two drugs (there efficacy, and there side effects on the neonate and the mother).

Patients and Methods: This is a (Case-Control) study of a group of pregnant women with preterm labour attending department of obstetrics and gynecology at Tishreen University Hospital in Lattakia – Syria during one year period (June 2021 – June 2022). The inclusion criteria were: Fetus age between (24-36.6)w according to LMP and/or ultrasound with preterm labour, existing of 4 uterus contractionsat least in 20 minutes observations or 8 contractions at least in 60 minutes observations, cervical dilation (2-4)cm, cervical length < 20 mm according to vaginal ultrasound, cervical effacement ≥ 80%with no ruptured membrane. The exclusion criteria were: severe pregnant disease which prevent continuing pregnancy (severe heart disease, renal failure…), advanced labour (dilation>4 cm), fetal abnormalities didn´t correspond with life, fetal death, amniotic sepsis, severe conditions related to pregnancy (active bleeding, severe preeclampsia…), multiple pregnancy, PPROM, any contraindication for Nifedipine or Ritodrine, pregnants who used labour suppressants in last 2 days before coming to hospital. The following data were collected: History, general physical examination, abdominal examination, vital signs, observation of uterus contraction, cervical examination to determine cervical dilation and effacement and bishop score, vaginal ultrasound to measure cervical length, abdominal ultrasound to determine number of fetuses and mode of presentation, fetus age, blood samples for (CBC, glucose, CRP) and urinalysis, we gave the patients Dexamathazone 6mg/12hrs (4 doses IM) or Betamethazone 12mg/24hrs (2 doses IM) for gestational age < 34 weeks however for gestational age ≥ 34 weeks we gave Dexamethazone or Betamethazone just if the patient didn´t take it before, we gave the patients Ampicillin 1gm/6hrs as prophylaxis from B streptococcus and if extrauterus sepsis exist we gave Cephalosporin to patients. Then we gave the patients Nifedipine or Ritodrine according to group attached with patient (Case or Control), success treatment: suppression of uterus contraction for 48 hours or more with no severe side effects causing stopping of treatment, failure treatment: still existing contractions although of using maximum dose of drug or occurrence of severe side effects causing stopping of treatment, drugs doses: Nifedipine: primary dose 10mg orally every 20 minutes up to 3 doses then (10-20)mg every (4-8)hours orally, Ritodrine: venous infiltration (primary dose 50mcg/min or 3-4 drops/min from solution which its concentration 300mcg/min and it will be increased around 50mcg/min every 15 minutes and the maximum dose is 300 mcg/min = 24 drops/min. This study was performed following the Declaration of Helsinki.

Statistical Analysis: Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations(SD), median, frequency and percentages. To examine the relationships and comparisons between the two groups, chi-square test was used or Fisher exact test if it need. Independent t-student test was used to compare 2 independent groups. All the tests were considered significant at a 5% type I error rate ($p<0.05$), ß:20%, and power of the study: 80%.

RESULTS

A total of 80 pregnant women with preterm labour who admitted to the department of obstetrics and gynecology from June 2021 to June 2022 were included in the study. Ages range from (27 – 28) years (mean 27.5 years). women were divided into two groups: group (A) (Cases): included 40 pregnant women with preterm labour who were given Ritodrine, and group (B) (Control): 40 pregnant women with preterm labour who were given Nifedipine. The baseline characteristics of the participants were comparible between groups and didn´t influence the results as shown in (Table 1).

Table 1:

Standard deviation	median	Nifedipine group	Ritodrine group	
		40	40	Number of patients
0.25	30.3	30.5 weeks	30.1weeks	Median gestational age
0.13	5.85	5.7	6	Median Bishop score
27 Mode	27.5	27	28	Median patients´ age
	22.8	21.6%	23.7%	Primigravida ratio

As shown in (Table 2), suppression of pretem labour for 48 hours succeed in 27 patients (67.5%) and failed in 13 patients (32.5%) in group (A) and the causes of failed suppression were side effects of the drug (5 patients) (12.5%) and not responsing to treatment (8 patients) (20%), and the suppression of preterm labour for 48 hours succeed in 35 patients (87.5%) in group (B) and failed in 5 patients (12.5%) with Pvalue: 0.003 < 0.05

Table 2:

p.value	Nifedipine	Ritodrine	
	40	40	Number of patients
0.003	35(87.5%)	27(67.5%)	Treatment success
0.003	5(12.5%)	13(32.5%)	Failure treatment

And when comparing results according to gestational age, we divided each group to 3 subgroups, subgroup l: gestational age between (24 – 27.6) weeks and subgroup ll: gestational age between (28 – 32.6) weeks and subgroup lll: gestational age between (33 – 36.6) weeks and we found these results in

Table 3:

percentage %	Treatment failure	Percentage %	Treatment success	Number ofpatients	Group According togestational age	Drug
%36.4	4	%63.6	7	11	l	Ritodrine
%29.5	5	%70.5	12	17	ll	
%33.4	4	%66.6	8	12	lll	
%14.3	2	%85.7	12	14	l	Nifedipine
%12.5	2	%87.5	14	16	ll	
%10	1	%90	9	10	lll	

And when application statistical scale ANOVA on the results in (Table 3) we found Pvalue > 0.05 and we accepted the hypothesis saying that there is no influences of gestational age on the treatment.

And when comparing the results according to Bishop Score, we divided each group to 3 subgroups, subgroup 1: bishop score from (0-2), subgroup 2: Bishop score from (3-6), subgroup 3: Bishop score ≥ 7, and we found these results in (Table 4).

Table 4:

Percentage%	Treatment failure	Percentage%	Treatment failure	Number of patients	Group	Drug
%23.1	3	%76.9	10	13	1	Ritodrine
%33.4	6	%66.6	12	18	2	
%44.5	4	%55.5	5	9	3	
%0	0	%100	12	12	1	
%5.9	1	%94.1	16	17	2	
%18.2	2	%81.8	9	11	3	Nifedipine

And when application statistical scale ANOVA on the results in (Table 4), we found Pvalue < 0.05 and we accepted the hypothesis saying that Bishop score influences on the results and when Bishop score increases, the suppression of preterm labour fails.

And when comparing the side effects of the drugs on the mothers we found the results in (Table 5), and Ritodrine achieved severer and more side effects than Nifedipine and we stopped the therapy because of severe side effects in Ritodrine group, palpitation (42.5%Ritodrine vs 7.5%Nifedipine), dyspnea (5%Ritodrine vs 0% Nifedipine), nausea and vomiting (10% Ritodrine vs 0% Nifedipine), tachycardia of the fetus (40%Ritodrine vs 0% Nifedipine) however headache (20%Nifedipine vs 0%Ritodrine), Flare (5%Nifedipine vs 0%Ritodrine) with p<0.05, headache and flare were simple side effects and didn´t require to stop the treatment with Nifedipine so side effects in Ritodrine group were more serious than Nifedipine one.

Table 5:

Nifedipine		Ritodrine		Side Effect
percentage%	Patient number	percentage%	Patient number	
7,5%	3	42,5%	17	palpitation
-	-	5%	2	dyspnea
20%	8	-	-	Headache
5%	2	-	-	flare
-	-	10%	4	Nausea &vomiting
-	-	40%	16	Tachycardia of the fetus

And when application statistical scale on the results we found Pvalue < 0.05 and we accepted the hypothesis saying that Ritodrine side effects are severer and more than Nifedipine.

And when comparing the side effects on the neonate we found the results in (Table 6) and there was no difference between these drugs on (median fetus age, median neonate weight, ARDS in the neonate, neonate death): median fetus age (35.3 w Nifedipine vs 34 w Ritodrine, p>0.05), median neonate weight (2050gm Nifedipine vs 1900gm Ritodrine, p>0.05), ARDS in the neonate (12.5%Nifedipine vs 17.5%Ritodrine, p>0.05), neonate death (10% Nifedipine vs 15%Ritodrine, p>0.05) however the neonate´s needing for NICU was less in Nifedipine group than Ritodrine one: NICU (50% Nifedipine vs 65% Ritodrine, p<0.05).

Table 6:

p.value	Nifedipine	Ritodrine	
> 0.05	35,3 w	34 W	Median gestational age
> 0.05	2050g	1900g	Median neonatal weight
< 0.05	(%50)20	(%65)26	NICU
> 0.05	(%12,5)5	(%17,5)7	ARDS
> 0.05	(%10)4	(%15)6	Neonatal death

DISCUSSION

In this study we applicated 2 drugs on preterm labour patients (Nifedipine and Ritodrine) and we compare between efficacy of these drugs in suppression of preterm labour and the side effects of thesedrugs on the mothers and the neonates, and we found that Nifedipine is better than Ritodrine in suppression of preterm labour and less side effects on the mother and the neonate. The accurate surveillance during application of the drugs blocked drugs toxicity and any threatening for the pregnant lives and any severe complication like (pulmonary edema, heart failure …) which warrant admissionthe patient in the ICU. In this study, we found that Bishop score influences the results and when Bishop score increases, the suppression of preterm labour fails and we found that gestational age doesn´t influence the treatment. In a study of Kupfermic and Ferguson they found that Nifedipine is better than Ritodrine in suppression of preterm labour like our study. In expirement of Meta Analysis in 2 different studies, they compare between Nifedipine and Ritodrine, the first study (Oei SG, et al) involved 9 expirements on (607) patients and the second one (Tsatsaris V, et al) involved also 9 expirements on (679) patients; they found that Nifedipine is better than Ritodrine in suppression of preterm labour more than 48 hours (RR = 1.13) with less ARDS and less needing for admission of theneonate in NICU and less other side effects on the neonate. the study of King and his partners,involved 11 expirements on (870) patients, Nifedipine was better than Ritodrine in suppression ofpreterm labour during 48 hours (RR = 0.77), and this is compatible with our study. Kupfermic andFerguson and Meyer noticed that using Nifedipine is less side effects on the mother than Ritodrine andthis is compatible with our study. Ferguson stopped the treatment in 3 patients due to chest pain in Ritodrine group. Papaison in his study found decreasing in admission in NICU in Nifedipine group which is compatible with our study. Maitra in his study found that Abgar score and ARDS in theneonate didn´t have

been affected in both groups which is compatible in our study, and Nifedipine didn´t have any influence on the heart rate contrary to Ritodrine which made it faster.

In summary, Nifedipine is better than Ritodrine in suppression of preterm labour and less side effects on the mother and the neonate.

REFERENCES

1. Lyell DJ, Pullen K, Campbell L, et al: Magnesium sulfate compared with nifedipine for acute tocolysis of preterm labor: a randomized controlled trial. Obstet Gynecol, 2007; 1108: 61.
2. Hobel C, Culhane J: Role of psychosocial and nutritional stress on poor pregnancy outcome. J Nutr, 2003; 133: 1709S.
3. Tsatsaris V, et al. Tocolysis with nifedipine or beta adrenergic agonists: a meta analysis obstet gynecol, 2001.
4. Grimes DA, Nanda K: Magnesium sulfate tocolysis: time to quit. Obstet Gynecol, 2006; 108: 986.
5. Williams obestatrics 25th edition, 2012; 814.
6. Lockwood CJ: Sress-associated preterm delivery: the role of corticotropin releasing hormone. Am J Obstet Gynecol, 1999; 100: 1090-4.
7. Kupferminc M, Lessing JB, Yaron Y, et al. Nifedipine versus Ritodrine for suppression preterm labour. Br J Obstet Gynecol. 1993; 100: 1090-4.
8. Songthamwat S, Na Nan C Effectiveness of nifedipine in threatened preterm labor: a randomized trial. Int J Womens Health, 2009 Jun 15; 10: 317-323. doi: 10.2147/IJWH.S159062. eCollection, 2005.
9. Stiles AD: Prenatal corticosteroids-early gain, long-term questions. N Engl J Med, 2007; 357: 1248.
10. Van De Vater; Tocolytic Effectiveness of Nifedipine verses Ritodrine and follow up of newborns; Arandomised controlled trials…et alActa Obstetric Gynecol scand, 2008.
11. Seema BN, Tejaswi V. Pujar, Comparison of safety, efficacy and perinatal outcome of isoxsuprineand nifedipine in women with preterm labour, International Journal of Reproduction, Contraception, Obstetrics and GynecologySeema BN et al. Int J Reprod Contracept Obstet Gynecol, 2000 Feb; 6(2): 400-403.
12. Prerna Jain, Supriya Suman, Comparative study of nifepidine and isoxsuprine in suppression of preterm labour, International Journal of Reproduction, Contraception, Obstetrics and GynecologyJain P et al. Int J Reprod Contracept Obstet Gynecol, 2003 Nov; 5(11): 3754-3757.
13. Goldenberg RL: The management of preterm labor. Obstet Gynecol, 2002; 100: 1020.
14. Varner MW, Epslin MS: Genetic factors in preterm birth-the future. BJOG, 2005; 112(Suppln1): 28.
15. Abd Almawla; Nifedipine Verses Ritodrine for suppression of Preterm labor and analysis of side Effects et al, 2001.
16. Flenady V, Wojcieszek AM Calcium channel blockers for inhibiting preterm labour and birth. Cochrane Database Syst Rev., 2001 Jun 5; (6): CD002255. doi: 10.1002/14651858.CD002255.pub2
17. Mathews TJ, Mac Dorman MF: Infant mortality statistics from the 2009 period linked birth/infant death data set. Natl Vital Stat Rep, 2013; 61(8): 1.
18. Salim R, Grami G, Zohar N, et al: Nifedipine compared with atosiban for treating preterm labor: a randomized controlled trial. Obstet Gynecol, 2012; 120(6): 1323.
19. Gajer P, Brotman RM, Bai G, et al: Temporal dynamics of the human vaginal microbiota. Sci Transl Med, 2012; 4(132): 132ra52.
20. Grobman WA, Thom EA, Spong CY, et al: 17alpha-Hydroxyprogesterone caproate to prevent prematurity in nulliparas with cervical length less than 30 mm. Am J Obstet Gynecol, 2012; 207(5): 390e.
21. American College of Obstetricians and Gynecologists: Management of preterm labor. Practice Bulletin No., 1998; 127.
22. American College of Obstetricians and Gynecologists: Prediction and prevention of preterm birth. Practice Bulletin No. 130, October 2012.
23. Papatsonis DNM, Blaker OP, Vangeijn HP, et al. Nifedipine and Ritodrine in the management of preterm labour: RCT trial. Obstet Gynecol, 1997; 90.
24. Chao TT, Bloom SL, Mitchell JS, et al: The diagnosis and natural history of false preterm labor. Obstet Gynecol, 2011; 118(6): 1301.
25. Hassan SS, Romero R, Vidyadhari D, et al: Vaginal progesterone reduces the rate of preterm birth in women with sonographic short cervix: a multicenter, randomized, double- blind, Placebo-controlled trial. Ultrasound Obstet Gynecol, 2011; 38: 18.
26. Petraglia F, Imperatore A, Challis JRG: Neuroendocrine mechanisms in pregnancy and parturition Endocrine Rev, 2010; 31(6): 783.
27. Crowther CA, Doyle LW, Haslam RR, et al: Outcomes at 2 years of age after repeat doses of antenatal corticosteroids. N Engl J Med, 2007; 357: 1179.
28. Gibson CS, Maclennan AH, Dekker GA, et al: Genetic polymorphisms and spontaneous preterm birth. Obstet Gynecol, 2007; 109: 384.
29. Maitra N, Christian V, Verma RN, et al. Maternal and fetal cardiovascular side effects of Nifedipine and Ritodrine used as tocolysis. J Obstet Gynecol India, 2007; 57: 131-4.
30. Berghella V, Odibo AO, To MS, et al: Cerclage for short cervix on ultrasonograohy: meta-analysis of trials using individual patient-level data. Obstet Gynecol, 2005; 106(1): 181.
31. Yost NP, Bloom SL, Mclntire DD, et al: Hospitalization for women with arrested preterm labor: a randomized trial. Obstet Gynecol, 2005;

106: 14.
32. King JF, Flenady V, Papatsonis D, et al: Calcium Channel blockers for inhibiting preterm labor: asystematic review of the evidence and a protocol for administration of nifedipine. Aust N Z J Obstet Gynaecol, 2003; 43: 192.
33. Andrews WW, Sibai BM, Thom EA, et al: Randomized clinical trial of metronidazole plus erythromycin to prevent spontaneous preterm delivery in fetal fibronectin-positive women. Obstet Gynecol, 2003; 101: 847.
34. Oei SG, et al. Nifedipine versus ritodrine for suppression of preterm labor: a meta-analysis. Acta Obstet Gynecol Scand, 1999.
35. Ferguson JE II, Dyson DC, Schutz T, et al. A comparison of tocolysis with Nifedipine or Ritodrine: analysis of efficacy and maternal fetal and neonatal outcome. Am J Obstet Gynecol, 1990; 163: 105-12.
36. King J, Flenady V, Antibiotics for preterm labour with intact membranes: Cochrane Database Syst Rev, 2000; 2: CD000246.
37. Meyer WR, Randall HW, Graves WL. Nifedipine versus Ritodrine for suppressing preterm labour. J Reprod Med, 1990; 35: 649_53.