*Med. J. Cairo Univ., Vol. 86, No. 5, September: 2733-2740, 2018*
www.medicaljournalofcairouniversity.net

# A Comparative Study between the Efficacy of Ritodrine Hydrochloride Versus Nitroglycerin Patch as a Short Term Tocolysis

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## Abstract

*Background:* Preterm birth continues to be a problem for obstetricians. Preterm birth complicates 8-10% of birth. Although the causes of preterm labour are not well understood, the burden of preterm birth is clear. The majority of neonatal deaths and over one third of infant deaths are linked to preterm birth. Methods to detect preterm labour at early stage include ultrasound examination of cervix and detection of biochemical markers of preterm labour in blood, saliva and cervicovaginal secretion. Given the methods to predict and prevent preterm birth are imperfect, attention focuses on the treatment of women admitted with preterm labour.

*Aim of the Work:* The aim of the study to compare the safety and efficacy of transdermal nitroglycerine patch versus ritodrine hydrochloride in treatment preterm labour.

*Patients and Methods:* This retrospective study was included 50 cases of threatened preterm labour attending the Obstetrics and Gynecology Department of Tanta University Hospital who were involved in this study. Woman were randomly divided in this retrospective study into two groups: Group 1: Included twenty five (25) patient, they received B-sympathomimetc ritodrine (yutopar). Ritodrine was giving in dose of: 150mg in 500ml saline infusion starting dose is 0.05mg/min this to be increased 0.05mg/min every 10-15 minutes (1ml contain 0.3mg and 1ml about 16 drops so 0.05mg about 3 drops) until a dose that provide tocolytic effect is reached or maternal tachycardia above 130 beats/minute occur. Group 2: Included twenty five (25) patients treated with 10mg nitrodermal patch directly applied on the abdominal skin.

*Inclusion Criteria:* Pregnant woman in the age of 20-35 years, gestational age between 28-34 weeks, body mass index (25-30), singleton pregnancy, uterine contraction 2 per 10 minutes or 4 per 20 minutes, cervical dilatation 3 centimeters, effacement up to 80%, intact membranes and primigravida or multigravida.

*Exclusion Criteria:* Fetal problems: Fetal congenital anomalies, fetal growth restriction and fetal distress. Maternal problems: "Medical problems": Chronic hypertension, chronic renal disease, cardiac disease, diabetes mellitus, contraindication to beta agonists, non-steroidal anti-inflammatory drugs and other tocolytics, cigarette smoker, anemia (HB less than 10mg/dl), thyroid disorders, maternal tachycardia ."Obstetric problems": Preeclampsia, polyhydraminos and oligohydraminos, ante-partum hemorrhage and rupture of membranes and Chorioamnionitis. All patients were subjected to thorough history taking with special emphasis on gestational age (in weeks), history of medical disease) and clinical examination regarding blood pressure and body mass index. Obstetrical abdominal ultrasound was done for gestational age (BPD, AC, FL), amniotic fluid, viability. Routine investigations as fasting blood sugar blood group and Rh factor, blood urea, creatinine, haemoglobin concentration and analysis of urine albumin, sugar, microscopy, culture and sensitivity.

*Results:* Equal percentage in cases which delivered in the same day and not responding to the drugs only 2 cases in each group present 8.0%. In the next day 3 cases delivered in group 1 present 12.0% and 1 case in group 2 present 4.0%. The delivery in the first 48 hours present failure rate of the drug, in our study the failure rate was 20% in group 1 and 12% in group 2. Labour by 7 day occur in 2 cases in each group presenting 8.0% in each group. Labour by 14 day occurred in 2 cases in group 1 and 1 case in group 2 presenting 8% and 4% respectively. Labour at 32 week occurred in 3 cases in group 1 and 2 cases in group 2 presenting 12% and 8% respectively. Labour at 34 week occurred in 4 cases in each group presenting 16% to each group. Labour at 37 week occurred in 6 cases in group 1 and 8 cases in group 2 presenting 24% and 32% respectively. Labour by 32 week occurred in 6 cases in group 1 and 2 cases in group 2 presenting 24 and 8 respectively. Labour by 34 week occurred in 2 cases in group 1 and 3 cases in group 2 presenting 8% and 12% respectively. Labour by 37 week occurred in 4 cases in group 1 and 6 cases in group 2 presenting 16% and 24%.

*Conclusion:* Both glyceryltrinitrate and ritodrine were comparable in prolongation of gestation in patients in preterm labour, both in duration and in terms of success. The advantages of glyceryltrinitrate patch over ritodrine are lesser side effects and simplicity of administration and it also allows the patient to remain ambulatory.

***Key Words:*** *Nitroglycerine – Ritodrine – Preterm labour.*

## Introduction

**PRE-TERM** labour is defined as the onset of labour after the age of viability (20-24) and before

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37 completed weeks of pregnancy and its incidence is 6-10% of all births in developed countries [1]. It is common in patients with low body weight, low stature, smokers and lower social classes [2]. Risk factors that have been linked to pre-term delivery include cervical incompetence, haemorrhage like abruptio placenta, genital tract infection like bacterial vaginosis, hormonal changes due to maternal or foetal stress, multifoetal pregnancy and previous history of pre-term labour [3]. Complications of prematurity account for more than 70% of foetal and neonatal deaths annually in babies without anomalies [4]. The treatment includes bed rest, hydration and sedation, the measures that are commonly used are tocolytic drugs, corticosteroids and antibiotics. Tocolytics are pharmacological agents that relax the uterine myometrium and inhibit uterine contractions leading to abolition of preterm labour. They act through a variety of mechanisms to decrease the availability of intracellular calcium ions leading to inhibition of actin-myosin interaction. Though, use of tocolytic drugs has become controversial, they should still be considered if the few days gained would be put to good use such as completing a course of corticosteroids or in-utero transfer [5]. They are not recommended after 34 weeks gestation and currently there is no consensus regarding the lower gestational limit at which they could be used [6]. Many tocolytic drugs have been developed and used and several experimental drugs are being evaluated. Beta sympathomimetics, calcium channel blockers, magnesium sulphate, oxytocin antagonists, prostaglandin synthetase inhibitors, nitric oxide and combination of these drugs have been used for tocolysis [5]. Future research is needed for development of drugs with more utero selectivity and fewer side effects. Recently, nitric oxide donors have been found to be potent uterine relaxants in vitro and transdermal nitroglycerine has been reported to be safe for the mother and the fetus [7]. Nitroglycerine (nitric oxide donors) may be an-effective choice as a tocolytic agent due to its safety profile with infrequent maternal and foetal side effects [7].

*Aim of the work:*

The aim of the study to compare the safety and efficacy of transdermal nitroglycerine patch versus ritodrine hydrochloride in treatment preterm labour.

## Patients and Methods

This retrospective study included 50 case of threatened preterm labour attending the Obstetrics and Gynecology Department of Tanta University Hospital involved in this study.

*Inclusion criteria:* Pregnant woman in the age of 20-35 years, gestational age between 28-34 weeks, body mass index (25-30), singleton pregnancy, uterine contraction 2 per 10 minutes or 4 per 20 minutes, cervical dilatation 3 centimeters, effacement up to 80%, intact membranes and primigravida or multigravida.

*Exclusion criteria:* Fetal problems: Fetal congenital anomalies, fetal growth restriction and fetal distress.

*Maternal problems:* "Medical problems": Chronic hypertension, chronic renal disease, cardiac disease, diabetes mellitus, contraindication to beta agonists, non-steroidal anti-inflammatory drugs and other tocolytics, cigarette smoker, anemia (HB less than 10mg/dl), thyroid disorders, maternal tachycardia. "Obstetric problems": Preeclampsia, polyhydraminos and oligohydraminos, ante-partum hemorrhage and rupture of membranes and chorioamnionitis. All patients were subjected to thorough history taking with special emphasis on gestational age (in weeks), history of medical disease and clinical examination regarding blood pressure and body mass index. Obstetrical abdominal ultrasound was done for gestational age (BPD, AC, FL), amniotic fluid, viability. Routine investigations as fasting blood sugar blood group and Rh factor, blood urea, creatinine, haemoglobin concentration and analysis of urine albumin, sugar, microscopy, culture and sensitivity.

Woman were randomly divided in this prospective study into two groups: Group 1: Includes twenty five (25) patient, they received B-sympathomimetc ritodrine (yutopar). Ritodrine was giving in dose of: 150mg in 500ml saline infusion starting dose is 0.05mg/min this to be increased 0.05mg/min every 10-15 minutes (1ml contain 0.3mg and 1ml about 16 drops so 0.05mg about 3 drops) until a dose that provide tocolytic effect is reached or maternal tachycardia above 130 beats/minute occur. Group 2: Includes twenty five (25) patients treated with 10mg nitrodermal patch directly applied on the abdominal skin. If after one hour no reduction of uterine contractions, an additional patch can be applied (10mg) at the same time for 24 hours. All patient will received 3 doses 8mg/8 hours dexamethasone intramuscular.

## Results

There was no statistical significant differences between the two studied groups according to age, BMI, parity, previous preterm labour, uterine contraction, cervical dilatation, gestational age on admission and gestational age on delivery. Also

when compare the 2 studied group it was found there was no statistical significant differences between the two studied groups according to fetal weight.

Table (1): Changes in maternal Heart Rate (HR) in both group before treatment and after 15m, 30m, 1h, 6h, 12h and 24h after treatment.

| HR (in min) | Range | Mean±SD | *t*-test | *p*-value |
|---|---|---|---|---|
| *On admission:* | | | | |
| Group 1 | 68-88 | 77.32±6.12 | 0.026 | 0.873 |
| Group 2 | 68-90 | 77.04±6.16 | | |
| *After 15m:* | | | | |
| Group 1 | 72-96 | 83.88±6.43 | 9.419 | 0.004* |
| Group 2 | 70-92 | 78.56±5.81 | | |
| *After 30m:* | | | | |
| Group 1 | 78-96 | 88.72±5.41 | 28.360 | 0.001 * |
| Group 2 | 72-92 | 80.04±6.09 | | |
| *After 1 h:* | | | | |
| Group 1 | 80-100 | 92.32±4.64 | 55.737 | 0.001 * |
| Group 2 | 72-92 | 81.00±5.99 | | |
| *After 6h:* | | | | |
| Group 1 | 84-102 | 95.04±4.17 | 96.242 | 0.001 * |
| Group 2 | 73-94 | 81.04±5.79 | | |
| *After 12h:* | | | | |
| Group 1 | 82-102 | 95.76±4.05 | 89.762 | 0.001 * |
| Group 2 | 73-96 | 83.04±5.35 | | |
| *After 24h:* | | | | |
| Group 1 | 84-102 | 96.48±3.38 | 85.597 | 0.001 * |
| Group 2 | 78-94 | 85.28±5.02 | | |

*p*-value >0.050 non significant.
*p*-value <0.050 significant*.

*This table show:* Group (1): On admission maternal heart rate ranged between 68-88, after giving the drug (Ritodrine) our study show there was increase in MHR.

As by estimation MHR after 15min it was ranged between 72-96/min, then after 30min ranged between 78-96/min, then after 1h ranged between 80-100/min, then after 6h ranged between 84-102/min, then after 12h ranged between 82-102/min and after 24h ranged between 84-102/min. So this values show gradual increase which became statistically significant after 15min.

*Group (2):* On admission maternal heart rate ranged between 68-90, after giving the drug (Nitroglycerine) our study show there was increase in MHR after 1h.

As by estimation MHR after 15min it was ranged between 70-92/min, then after 30min ranged between 72-92/min, then after 1h ranged between 72-92, then after 6h ranged between 73-94/min, then after 12h ranged between 73-96/min and after 24h ranged between 78-94/min. So this values show gradual increase in MHR which became statistically significant after 1h.

*Conclusion:* When compare the 2 studied group it was found MHR after treatment was significant higher in group 1 than group 2. (Table 1).

Table (2): Changes in Mean Arterial Pressure (MAP) mmHg before treatment and after 15m, 30m, 1h, 6h, 12h and 24h after treatment.

| Mean arterial pressure (mmHg) | Range | Mean±SD | *t*-test | *p*-value |
|---|---|---|---|---|
| *On admission:* | | | | |
| Group 1 | 76-110 | 95.16±8.71 | 1.154 | 0.288 |
| Group 2 | 73-116 | 92.08±11.39 | | |
| *After 15m:* | | | | |
| Group 1 | 73-106 | 90.44±8.08 | 0.012 | 0.988 |
| Group 2 | 70-112 | 90.48±10.72 | | |
| *After 30m:* | | | | |
| Group 1 | 71-102 | 88.04±8.27 | 0.429 | 0.516 |
| Group 2 | 72-110 | 89.80±10.59 | | |
| *After 1h:* | | | | |
| Group 1 | 72-100 | 86.16±7.98 | 1.073 | 0.305 |
| Group 2 | 70-110 | 88.96±10.91 | | |
| *After 6h:* | | | | |
| Group 1 | 70-99 | 83.84±8.05 | 1.671 | 0.202 |
| Group 2 | 70-106 | 87.12±9.81 | | |
| *After 12h:* | | | | |
| Group 1 | 70-97 | 83.00±7.76 | 1.217 | 0.275 |
| Group 2 | 70-106 | 85.80±10.05 | | |
| *After 24h:* | | | | |
| Group 1 | 70-95 | 82.04±7.26 | 1.512 | 0.225 |
| Group 2 | 70-100 | 85.04±9.80 | | |

*This table show:* Group (1): On admission the mean arterial blood pressure (MAP) ranged between 76-110, after giving the drug (Ritodrine) our study show there was decrease in MAP after 15min.

As by estimation MAP after 15min it was ranged between 73-106mmHg, then after 30min ranged between 71-1 02mmHg, then after 1h ranged between 72-100mmHg, then after 6h ranged between 70-99mmHg, then after 12h ranged between 70-97mmHg and after 24h ranged between 70-95 mmHg. So this values show gradual decrease in MAP which became statistically significant after 15min.

*Group (2):* On admission the mean arterial blood pressure (MAP) ranged between 73-116 mmHg, after giving the drug (Nitroglycerine) our study show there was decrease in MAP after 12h.

As by estimation MAP after 15min it was ranged between 70-112mmHg, then after 30min

ranged between 72-110mmHg, then after 1h ranged between 70-1 10mmHg, then after 6h ranged between 70-106mmHg, then after 12h ranged between 70-106mmHg and after 24h ranged between 70-100mmHg. So this values show decrease in MAP which became statistically significant after 12h.

*Conclusion:* When compare the 2 studied group it was found there was no significant statistical difference between two studied groups (Table 2).

Table (3): Changes in Fetal Heart Rate (FHR) before treatment and after 15m, 30m, 1h, 6h, 12h and 24h after treatment.

| FHR (min) | Range | Mean±SD | *t*-test | *p*-value |
|---|---|---|---|---|
| *On admission:* | | | | |
| Group 1 | 126-150 | 138.12±7.18 | 0.114 | 0.737 |
| Group 2 | 125-150 | 137.44±7.08 | | |
| *After 15m:* | | | | |
| Group 1 | 130-152 | 141.08±6.61 | 2.054 | 0.158 |
| Group 2 | 126-150 | 138.36±6.81 | | |
| *After 30m:* | | | | |
| Group 1 | 132-154 | 144.16±6.32 | 6.154 | 0.0 17* |
| Group 2 | 128-150 | 139.68±6.45 | | |
| *After 1 h:* | | | | |
| Group 1 | 136-155 | 146.68±5.57 | 11.579 | 0.001* |
| Group 2 | 128-152 | 140.76±6.69 | | |
| *After 6h:* | | | | |
| Group 1 | 140-157 | 149.64±4.79 | 21.128 | 0.001* |
| Group 2 | 130-154 | 141.64±7.27 | | |
| *After 12h:* | | | | |
| Group 1 | 142-158 | 151.76±4.66 | 24.787 | 0.001* |
| Group 2 | 132-156 | 143.24±7.18 | | |
| *After 24h:* | | | | |
| Group 1 | 148-160 | 153.88±3.93 | 38.228 | 0.001* |
| Group 2 | 132-156 | 143.60±7.33 | | |

*This table show:* On admission the FHR ranged between 126-1 50\Min, after giving the drug (Ritodrine) our study show there was increase in FHR after 30min.

As by estimation FHR after 15min it was ranged between 130-152/min, then after 30min ranged between 132-154/min, then after 1h ranged between 136-155/min, then after 6h ranged between 140-157/min, then after 12h ranged between 142-158/min and after 24h ranged between 148-160/min. So this values show gradual increase in FHR which became statistically significant after 30min.

*Group (2):* On admission the FHR ranged between 125-150/min, after giving the drug (Nitroglycerine) our study show there was increase in FHR after 1h.

As by estimation FHR after 15min it was ranged between 126-150/min, then after 30min ranged between 128-150/min, then after 1h ranged between 128-152/min, then after 6h ranged between 130-154min, then after 12h ranged between 132-156/min and after 24h ranged between 132-156/min. So this values show gradual increase in FHR which became statistically significant after 1h.

*Conclusion:* When compare the 2 studied group it was found FHR after treatment was significant higher in group 1 over course of treatment than group 2 (Table 3).

Table (4): Fate of the drug in both groups according to onset of labour.

| Delivery | Group 1 | Group 2 | $\chi^2$ | *p*-value |
|---|---|---|---|---|
| *In same day:* | | | | |
| N | 2 | 2 | 0.0 | 1.0 |
| % | 8.0% | 8.0% | | |
| *In next day:* | | | | |
| N | 3 | 1 | 1.087 | 0.297 |
| % | 12.0% | 4.0% | | |
| *By 7D:* | | | | |
| N | 2 | 2 | 0.0 | 1.0 |
| % | 8.0% | 8.0% | | |
| *By 14D:* | | | | |
| N | 2 | 1 | 0.355 | 0.552 |
| % | 8.0% | 4.0% | | |
| *At 32W:* | | | | |
| N | 3 | 2 | 0.222 | 0.637 |
| % | 12.0% | 8.0% | | |
| *At 34W:* | | | | |
| N | 4 | 4 | 0.0 | 1.0 |
| % | 16.0% | 16.0% | | |
| *At 37W:* | | | | |
| N | 6 | 8 | 0.397 | 0.529 |
| % | 24.0% | 32.0% | | |
| *By 32W:* | | | | |
| N | 6 | 2 | 2.381 | 0.123 |
| % | 24.0% | 8.0% | | |
| *By 34W:* | | | | |
| N | 2 | 3 | 0.222 | 0.637 |
| % | 8.0% | 12.0% | | |
| *By 37W:* | | | | |
| N | 4 | 6 | 0.501 | 0.480 |
| % | 16.0% | 24.0% | | |

*This table show:* Equal percentage in cases which delivered in the same day and not responding to the drugs only 2 cases in each group present 8.0%. In the next day 3 cases delivered in group 1 present 12.0% and 1 case in group 2 present 4.0%. The delivery in the first 48 hours present

failure rate of the drug, in our study the failure rate was 20% in group 1 and 12% in group 2. Labour by 7 day occur in 2 cases in each group presenting 8.0% in each group. Labour by 14 day occurred in 2 cases in group 1 and 1 case in group 2 presenting 8% and 4% respectively. Labour at 32 week occurred in 3 cases in group 1 and 2 cases in group 2 presenting 12% and 8% respectively. Labour at 34 week occurred in 4 cases in each group presenting 16% to each group. Labour at 37 week occurred in 6 cases in group 1 and 8 cases in group 2 presenting 24% and 32% respectively. Labour by 32 week occurred in 6 cases in group 1 and 2 cases in group 2 presenting 24 and 8 respectively. Labour by 34 week occurred in 2 cases in group 1 and 3 cases in group 2 presenting 8% and 12% respectively. Labour by 37 week occurred in 4 cases in group 1 and 6 cases in group 2 presenting 16% and 24%.

*Conclusion:* By comparing the two studed group there was no significant statistically difference between the both groups (Table 4) & Fig. (1).

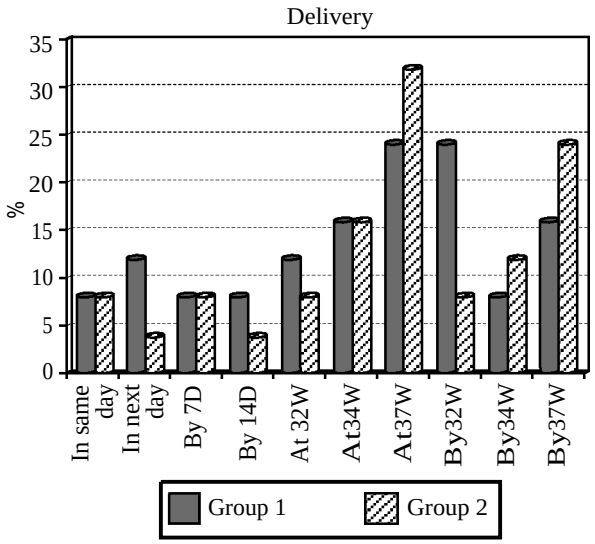


Fig. (1): There was no significant statistically difference between the both groups according to the gestational age in delivary.

When compare the 2 studied group it was found that group 1 showed significantly higher percentage of cases suffering from palpitation, tachycardia and chest pain than group 2. Group 2 showed significantly higher percentage of cases suffering from headache than group 1. When compare the 2 studied group it was found there was no statistical significant differences between the two studied groups in fetal side effect Fig. (2).

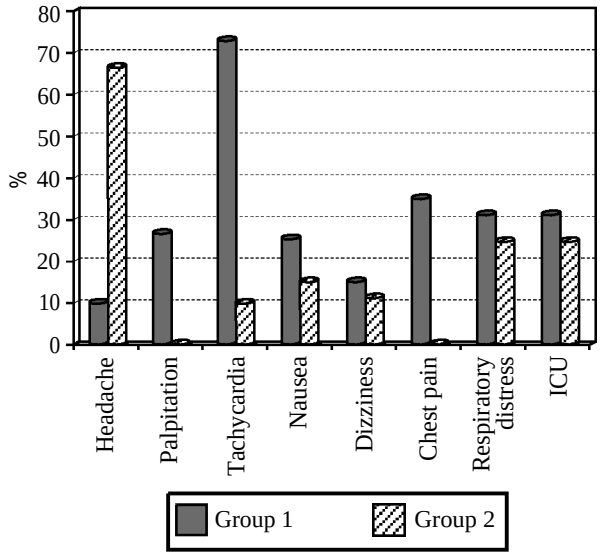


Fig. (2): There was no statistical significant differences between the two studied groups according to fetal weight.

## Discussion

Preterm labour is characterized by observable uterine contractions of at least one every 10 minutes of sufficient magnitude to effect progressive cervical dilatation up to 2cm, cervical length less than 1 cm or rupture of membranes. Intervention with tocolytics remain a dilemma, due to non-availability of a wide spectrum of pharmacological agents **[8]**. Existing drugs have relatively short duration of action, lack utero-specificity, have poor efficacy and are often associated with potentially serious maternal and fetal adverse effects. Tocolytics delay PTL long enough for corticosteroids to induce fetal lung maturation or allow mother's transportation to a tertiary care centre but they have not been shown to greatly improve neonatal outcomes **[8]**.

In the present study we aimed to compare the safety and efficacy of transdermal nitroglycerine patch versus ritodrine hydrochloride in treatment of preterm labour we included 50 patients with threatened preterm labour were divided into two group group 1 received ritodrine hydrochloride and 2 received nitroglycerin patch.

In the current study we found that there was no statistical significant differences between the two studied groups as regard age, parity, BMI, previous preterm labour, cervical dilatation, uterine contractions, gestational age on admission and gestational age on delivery.

In agree with our study a RCT by Jain C et al., **[8]** comparing the Glyceryl trinitrate patch versus intravenous ritodrine for tocolysis in pre-term

labour they found that The mean age of both groups were comparable at 23.72 in group I and 23.88 in group II, 48% in both groups were nulliparous with no statistical difference between both the groups regarding parity. No statistical significance was noted amongst the two groups with respect to history of previous abortions and preterm deliveries [8].

As regard to Singh N et al., study comprised of a total of 200 cases of preterm labour. Out of these, 60 patients were treated with ritodrine, 50 with isoxsuprine, 30 with nifedepine, 30 with glyceryltrinitrate and 30 with magnesium sulphate showed no significant differences between studied groups and demographic data and this agree with our result [9]. In RCT by Jain C et the difference was not statistically significant ($p$=0.07) and this in consistent with our result.

Counter with our study they disagree with our study in that they showed that the mean gestational age at delivery was 34.97 in GTN group as compared to 33.24 weeks in Ritodrine group which is statistically significant ($p$=0.0004) [8].

In agreement with our result Smith GN et al., study found that there was no difference in mean GA at randomization but in contrast there was a difference in mean GA at delivery ($p$.04) between the 2 groups (the GTN group compared to placebo) [10].

In our study there was no statistically significant in prolongation of gestation by 48 hours which achieved in 42/50 patients, 20 patients in group 1 (GTN) 80% as compare to 22 patients seen in group 2 (Ritodrine) 88%. Also there was no significant after 7 days between the both groubs, 72% of cases continued over a week in group 1 (GTN) compare to 80% of cases in group 2 (Ritodrine).

In counter with our study RCT by Jain C et al., comparing the Glyceryl trinitrate patch versus intravenous ritodrine for tocolysis in pre-term labour they found that there was statistically not significant. Prolongation of gestation by 48hrs was considered successful tocolysis which was achieved in 41/50 patients (82%) combined, 22 patients (88%) in group I (GTN) as compared to 19 (76%) seen in group II (IV Ritodrine). $p$-value –0.23 showed no statistical significance. 88% patients had pregnancy prolongation by 48 hours, 72% over a week and 44% continued over 37 weeks in GTN group compared to 76%, 54%, and 20% in Ritodrine group [8].

In Wani et al., study on 403 women, 132 were randomly assigned to receive GTN (ns67) or ritodrine (ns65) using. The women in the two groups had similar characteristics. The GTN group was more likely than the ritodrine group to deliver after 34 and 37 weeks' gestation and had fewer infants below 2500g whose admission rate to neonatal intensive care was halved [11].

Also Jain et al., showed that GTN group showed higher success rate as compared to Ritodrine group (88% versus 76%) as opposed to study conducted by Lees CC et al., who showed that Ritodrine may be more effective (84% vs. 90% for GTN and Ritodrine). Both the Jain C et al., study and Lees CC et al., concluded that both drugs were equally effective in prolongation of gestation reported by Lees et al., [12]. The difference was not statistically significant.

Nankali et al., showed that the average prolongation of the pregnancy in the GTN group ranged from 9.5 days in the study conducted by Bisits on PROM and fibronectin positive women [13] to 20.9 days [10] 34 days [14] and 42 days [12] in studies where their inclusion criterion was uterine contractions.

In the current study as regard maternal outcome and side effect we found that when compare the 2 studied group it was found MHR after treatment was significant higher in group 1 than group 2. When compare the 2 studied group it was found there was no significant statistical difference between two studied groups as regard Mean Arterial Pressure (MAP).

In agree with our study Nankali et al., showed that regarding incidence of complications, despite minor differences in the drug and placebo groups, only headache had a statistically significant difference. In the GTN group, Systolic Blood Pressure (SBP) and mean arterial blood pressure (MAP) showed a significant drop after the use of medication. Moreover, the Maternal Heart Rate (MHR) indicated a significant increase. Moreover, the differences were compared between the mean values measured before and after use of patch in the drug and placebo groups. There was a significant difference between the mean systolic blood pressure, mean arterial blood pressure and maternal heart rate in the drug and placebo groups [15].

In our study when compare the 2 studied group it was found that group 1 showed significantly higher percentage of cases suffering from palpitation, tachycardia and chest pain than group 2. But

group 2 showed significantly higher percentage of cases suffering from headache than group 1.

In agree with us conde-agudelo et al., revealed that treatment with transdermal nitroglycerin was associated with a significant decrease in the rates of maternal tachycardia, flushing, palpitations, nausea/vomiting, chest pain, dyspnea, discontinuation of treatment because of adverse events and fetal tachycardia, and a significant increase in the rates of headache and hypotension **[16]**.

As regard to Jain et al., they showed that among studied patients 7 (28%) patients had headache relieved with simple analgesics and few patients had cutaneous reaction in the form of erythematous rash and burning sensation in GTN group. Comparatively the Ritodrine group had severe adverse effects requiring discontinuation of therapy in 8%. Tachycardia >110min was seen in 60% of cases, palpitations in 20%, nausea and vomiting in 24% and dizziness in 8% but serious adverse effects like pulmonary edema and hypotension was not observed **[8]**.

In agree with us Rowlands et al., **[17]**, Lees et al., **[12]** reported 3.12% and 3% cases complaining of giddiness and Lees et al., reported 7.69% patients developing hypotension for which the patch had to be removed. Ritodrine, a nonselective, beta adrenergic receptor stimulator may act on beta receptors of the heart thus producing significant maternal adverse effects like tachycardia, atrial flutter, insufficiencies, arrhythmias and ischemia **[18]**.

In the current study as regard fetal outcome and fetal side effect we found that when compare the 2 studied group it was found FHR after treatment was significant higher in group 1 over course of treatment than group 2. Group (1): There was 7 (28%) fetus suffered from respiratory distress and 7 (28%) cases needed Intensive Care Unit (ICU).

Group (2): There was 5 (20%) fetus suffered from respiratory distress and 5 (20%) cases needed Intensive Care Unit (ICU). when compare the 2 studied group it was found there was no statistical significant differences between the two studied groups, when compare the 2 studied group it was found there was no statistical significant differences as regard fetal weight between the two studied groups. $p$-value=0.109.

In a agreement with our result Conde-agudelo et al., meta analysis showed that there were no significant differences between the groups in the risk of neonatal morbidity, although a significant reduction was seen in the risk of admission to NICU and use of mechanical in the transdermal nitroglycerin group compared with the β2-adrenergic-receptor agonists group **[18]**.

Another study by Jain et al., revealed that no case of fetal distress was detected in in GTN Group as compared to 4 (16%) in Ritodrine. There was no case of intra uterine death or Stillbirth in either groups. Birth weight in GTN group was found to be better with 10 neonates having birth weight >2.5kg as compared to only 2 in Ritodrine group. Mean birth weight was higher in GTN group (2.36 kg versus 2.05kg) as compared to Ritodrine group **[8]**.

*Conclusion:*

Both glyceryltrinitrate and ritodrine were comparable in prolongation of gestation in patients in preterm labour, both in duration and in terms of success. The advantages of glyceryltrinitrate patch over ritodrine are lesser side effects and simplicity of administration and it also allows the patient to remain ambulatory.

## References

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# دراسة مقارنة بين فعالية ريتودرين هيدروكلوريد مقابل التصحيح النتروجلسرين بإعتباره حل المخاض قصير الأجل

يستمر الحمل الطبيعى من ٣٧ إلى ٤٢ أسبوعا، بعد العد من اليوم الأول لآخر دورة شهرية. يسمى الحمل الذى يستمر إلى ما بعد ٣٧ أسبوعا بالحمل الكامل. يتم تعريف الولادة المبكرة بأنها المخاض الذى يبدأ قبل الأسبوع ٣٧ من الحمل. حوالى ١٢ بالمائة من الأطفال الرضع فى الولايات المتحدة يولدون قبل الأوان، ٨٠ فى المائة من هؤلاء يعزى إلى الولادة المبكرة نتيجة إنفجار الأغشية الجنينية قبل الأوان أو بدون سبب. أما النسبة المتبقية والبالغة ٢٠ فى المائة فهى الولادة المبكرة المخططة التى يتم إجراؤها لمشاكل الأم أو الجنين التى تمنع المرأة من الإستمرار فى حملها بأمان. يحدث المخاض قبل الأوان عندما تؤدى التقلصات النتظمة إلى فتح عنق الرحم قبل الإسبوع ٣٧ من الحمل. يجب أن يستمر الحمل الكامل لمدة ٤٠ أسبوعا تقريبا. إذا كانت إنقباضات الرحم تؤدى إلى الولادة قبل الأوان، فإن الطفل سيولد فى وقت مبكر. تحدث الولادة المبكرة، كلما زادت المخاطر الصحية على الطفل. تحتاج هذه الأطفال إلى رعاية خاصة فى وحدة العناية المركزة للولدان. فى حين أن السبب المحدد للولادة المبكرة غالبا ما يكون غيرا واضح، فإن بعض عوامل الخطر قد تزيد من إحتمالات الولادة المبكرة. يمكن أن تحدث الولادة قبل الأوان أيضا فى النساء الحوامل دون عوامل خطر معروفة. ومع ذلك، فمن الجيد أن تعرف ما إذا كان معرضا لخطر الولادة المبكرة وكيف يمكن أن تساعد فى الوقاية منها.

من أسباب الولادة المبكرة: تاريخ من جراحة عنق الرحم، مثل LEEP أو خزعة المخروط. أن تكون حاملا بتوأم والعدوى فى الأم أو فى الأغشية المحيطة بالطفل أو بعض العيوب الخلقية فى الرضيع أو إرتفاع ضغط الدم فى الأم أو كيس الماء ينفجر مبكرا أو الكثير من السائل الأمينوسى أو الثلث الأول من النزيف.

معايير الإستبعاد: مشاكل بالجنين: تشوهات الأجنة أو تأخر فى نمو الجنين أو إضطراب فى الوظائف الحيوية للجنين.

مشاكل بالأم: مشكلات طبية: الإرتفاع المزمن بضغط الدم أو الأمراض الكلوية المزمنة أو أمراض القلب أو مرضى السكر أو مرضى الأنيميا أو أمراض بالغدة الدرقية أو إرتفاع معدل ضربات القلب أو موانع لإستخدام محفزات المستقبلات بيتا.

الوسائل: التاريخ المرضى والفحص السريرى والتحاليل والأشعة: سكر عشوائى بالدم/فصيلة الدم ومعامل رساس/يوريا وكرياتين/همجلوبين/أشعة تلفزيونية لتحديد كمية الماء حول الجنين وتشوهات الأجنة وعمر الحمل/تحليل بول كامل.

تقسيم المرضى على مجموعتين: المجموعة الأولى: تحتوى هذه المجموعة على ٢٥ مريضة سوف يتم علاجها بالريتودرين هيدروكلوريد عن طريق التسرب الوريدى حيث يتم إضافة ١٥٠ميلى جرام من الريتودرين إلى ٥٠٠مللى محلول ملح، وبعد توقف الإنقباضات يعطى البروجستيرون المهبلى.

المجموعة الثانية: تحتوى هذه المجموعة على ٢٥ مريضة يتم علاجها بواسطة لاصقة النيتروجلسرين بتركيز ١٠مللى جرام حيث يتم وضعها على بطن السيدة وإذا لم يتوقف إنقباض الرحم خلال ساعة سوف يتم إضافة لاصقة أخرى لمدة ٢٤ ساعة.

الإستنتاج: كان كلا لاصقة النيتروجلسرين وعقار الريتودرين هيدروكلوريد متشابهين فى إطالة فترة الحمل عند الجوامل التى تعانى من الولادة المبكرة، سواء من حيث المدة أو من حيث النجاح. لكن اسبتت لاصقة النيتروجلسرين إنها أقل فى الآثار الجانبية عن عقار الريتودرين هيدروكلوريد.