

Impact of Glyceryl Trinitrate Transdermal Patch on Mother and Foetus in Preterm Labour

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ABSTRACT

Objective: To determine impact of Glyceryl Trinitrate Transdermal Patch on mother and foetus in preterm labour.

Methods: This quasi-experimental study was conducted at the Gynae Unit-I of Lady Willingdon Hospital Lahore, from July 2009 to June 2010. 113 pregnant women at 28-34 weeks of gestation were recruited after they met the selection criteria based on non-probability consecutive sampling. 103 patients continued with trial while 10 patients did not follow up. Patients diagnosed with pre-term labour were given glyceryl trinitrate (GTN) 5 mg/12 hours transdermal patch which was applied on the anterior abdominal wall. The second patch of same dose was applied after 12 hours. The outcome measures were side effects observed in mother, babies born alive, birth weight of babies and apgar score.

Results: All the (100%) babies were born alive. Birth weight of more than 2.4kg was noted in 25 (24.3%) babies, while 55 (51.4%) were born with birth weight between 2.2 to 2.4kg. Twelve (14.6%) babies had weight of 1.9kg to 2.1kg and only 11(10.67%) had weight of less than 1.8kg. In the last group ten babies were born within 24 hours of the start of tocolytic, and died in their first week of life due to the refusal of the parents to stay in the neonatology ward for long enough and left against medical advice. Babies born with good apgar score were 82 (79.6%) The most common side effect noticed among the mothers was headache (11.3%) followed by hypotension (5.1%), dizziness (4.1%), flushing (4.1%) vomiting (3%) and irritation (0%) at patch site.

Conclusion: Glyceryl Trinitrate transdermal Patch is a safe tocolytic as not associated with adverse effects in mother and foetus.

Key words: preterm labour, Glyceryl Trinitrate Transdermal Patch, Foetomaternal outcome

INTRODUCTION

Preterm delivery is the major cause of perinatal morbidity and mortality world wide. Although many factors have been linked to preterm delivery, including infection, fetal abnormality and antepartum hemorrhage, no specific cause can be identified in more than one half of all cases¹. The use of tocolytic drugs has not significantly reduced the overall incidence of preterm deliveries, but these agents may reduce the proportion of deliveries within 48 hours of onset of preterm labor². This delay allows for administration of steroids, which induce fetal lung maturation, thereby reducing neonatal respiratory distress³. For treatment of preterm labour, a wide variety of tocolytic agents have been advocated like beta agonists, calcium channel blockers, prostaglandin synthetase inhibitors, magnesium sulphate and also oxytocin receptor antagonists⁴. Most of these drugs require strict monitoring of both mother and foetus due to their adverse effects while some are expensive and not available universally⁵.

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GTN skin patches have the attraction of convenience, potential effectiveness, low cost & few side effects. Several studies have reported varying degree of success with this approach of tocolysis^{6,7,8}. It is a vasodilator that is essential for maintenance of normal smooth muscle tone of uterus. There is now considerable evidence that nitric oxide is involved in the regulation of myometrial contractility during pregnancy, where nitric oxide donors have been applied on myometrium in vitro, inhibition of spontaneous and oxytocin-induced activity was found when amplitude or force of contraction was measured⁹. Pregnancy is prolonged by its direct effect on the uterine blood flow¹⁰. The evidence that glyceryl trinitrate's relaxant effect on uterine smooth muscle may be enhanced during pregnancy has raised interest in its use. Glyceryl trinitrate could also have fewer adverse effects on the mother and fetus than other tocolytic drugs available¹¹.

MATERIAL AND METHODS

This quasi experimental study was conducted in Gynae Unit 1, Lady Willingdon Hospital Lahore from July 2009-July 2010. A total of 113 women with pre-

term labour pains between 28-34 weeks gestation and those who fulfilled the inclusion/exclusion criteria, were recruited in the study by non-probability consecutive sampling after informed written consent. These women were admitted in labour room either from emergency or outpatient department. The inclusion criteria were: gestational age between 28-34 weeks, women in the age group of 20-35 years, women with parity up to four, singleton pregnancy, and patients with pre-term labour pains but intact membranes. The exclusion criteria were: history of hypertensive disorders and major cardiac disease, diabetes, poly hydramnios, cases of antepartum haemorrhage, foetal anomaly, foetal distress and intrauterine death, and uterine anomalies like bicornuate uterus or uterine fibroids.

Diagnosis of preterm labour was established by history (intermittent, regular and painful uterine contractions, at least one every 10min) and clinical examination (cervical dilatation more than 2cm but less than 4cm or cervical length less than 1cm). Women were explained about procedure details. Nitroglycerine patch of 5mg was applied over the anterior abdominal wall of patient. The second patch of same strength (5mg) was applied after 12 hours. The patients were given 500ml intravenous normal saline over 30 min as prophylaxis against potential GTN induced hypotension. Maternal blood pressure was monitored at every 15 min for 1 hour, & every 4 hours thereafter. Patients were given a course of steroids to enhance foetal lung maturity. The outcome measures were side effects observed in mother, babies born alive, birth weight of babies and apgar score. The women stayed in the ward for at least 48 to 72 hours to complete corticosteroid doses and were then discharged and counselled for follow-up. Data analysis was done with SPSS version 10.

RESULTS

The study initially recruited 113 patients with pre-term labour once they fulfilled the exclusion and inclusion criteria from July 2009 to June 2010. Ten patients did not continue with the trial. Hence, the results were based on 103 patients who were given 5mg GTN patch immediately and 5mg after 12 hours. All the (100%) babies were born alive. Birth weight of more than 2.4 kg was noted in 25 (24.3%), while 55 (51.4%) were born with birth weight between 2.2 to 2.4kg. Twelve (14.6%) babies had weight of 1.9kg to 2.1kg and only 11(10.67%) had weight of less than 1.8kg. In the last group ten babies were born within 24 hours of the start of tocolytic, and died in their first week of life due to the refusal of the parents to stay in the neonatology ward for long enough and left against medical advice. Babies born with good apgar

score were 82 (79.6%) The most common side effect noticed among the mothers was headache (11.3%) followed by hypotension (5.1%), dizziness (4.1%), flushing (4.1%) vomiting (3%) and irritation (0%) at patch site.

Table 1

Maternal Side Effects	No.	%age
Headache	11	11.3
Hypotension	5	5.1
Vomiting	3	3
Dizziness	4	4.1
Flushing	4	4.1
Local irritation	0	0

Table 2

Birth weight of baby	No.	%age
More than 2.4kg	25	24.3
2.2-2.4kg	53	51.4
1.9-2.1kg	15	14.6
Less than 1.8kg	11	10.67

DISCUSSION

The main aim of tocolytic therapy is to improve perinatal outcome by suppressing preterm labour¹². Though benefit of tocolytic agent in prolongation of gestation for 48 hrs is unlikely to improve neonatal outcome in terms of physical maturation but these golden hours used to optimized by in utero transfer of the mother to a tertiary care center with neonatal facilities & administration of antenatal corticosteroids¹³. Tocolytic drugs have been tried for long and even glyceryl trinitrate (GTN) is not a new drug as more than 100 years ago nitric oxide donor was used in pregnancy and was first reported in the British Medical Journal¹⁴. Glyceryl trinitrate is convenient in its application and cost effective also. In my study, the most common side effect noticed among the mothers was headache (11.3%) followed by hypotension (5.1%), dizziness (4.1%), flushing (4.1%) vomiting (3%) and irritation (0%) at patch site. These results are comparable to a study carried out at Larkana¹⁵. All the (100%) babies were born alive. Birth weight of more than 2.4kg was noted in 25 (24.3%), while 55(51.4%) were born with birth weight between 2.2 to 2.4kg. Twelve (14.6%) babies had weight of 1.9kg to 2.1kg and only 11(10.67%) had weight of less than 1.8kg. In the last group ten babies were born within 24 hours of the start of tocolytic, and died in their first week of life due to the refusal of the parents to stay in the neonatology ward for long enough and left against medical advice. Babies born with good apgar score were 82 (79.6%). These result are also comparable to a study carried out at Larkana¹⁵. One international trial found that the risk of

developing neonatal morbidity was reduced by 79% and more when mothers were treated with GTN.⁽¹⁷⁾ Another study suggested improved foetal outcome after GTN-induced pregnancy prolongation by confirming decrease in total vascular resistance in maternal and foetal vasculature¹⁷. Many comparative studies of GTN with magnesium sulphate, ritodrine & salbutamol conclude that GTN is safe & at least equivalent tocolytic^{18,19,20,21}.

Valuable results were achieved with the GTN. Its straightforward administration and safety suggests that it is alternative to other tocolytic agents, like salbutamol, ritodrine or calcium channel blockers for pre-term labour and could make a major involvement in the management of pre-term labour.

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