Comparison of the Efficacy of Progesterone and Nifedipine in Inhibiting Threatened Preterm Labor a Randomized Comparative Study

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Abstract: Preterm laboris a common obstetric problem. It is any birth that occurs before 37 completed weeks of gestation. The incidenceis between 5% and 10% in most developed nations. In 2009, 13 million babies were born preterm, 11 million in Africa and Asia and 500, 000 in the USA; the highest rates of preterm birth are in Africa (11.9%) and North American (10.6%). Aim of our study is to evaluate the efficacy of progesterone and nifedipine in treatment of threatened preterm labor, considering any fetal or maternal drawbacks caused by these medications. In our study, nifedipine was successful to inhibit contractions in threatened preterm labor about 78% (39/50 cases) but oral progesterone was successful to inhibit contractions in threatened preterm labor by 10% (5/50 cases) only. There was highly statistical significance in both groups with P value (0.001).

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1. Introduction:

Preterm birth is the leading cause of perinatal morbidity and mortality, and its prevention is an important healthcare priority ***(Wang et al., 2016)***. Preterm birth is the most common cause of death among infants worldwide; About 15 million babies are preterm each year (5% to 18 % of all deliveries). In many countries rates of premature births have increased between the 1990s and 2010 **(*Blencowe et al., 2012).*** Preterm birth causes over 70% of fetal death rates and approximately 50 % of neonatal neural deficits ***(Hwang et al., 2015)***. With the aim of prolonging gestation, improving neonatal outcomes, and reducing the burden of maternal and fetal complications, various approaches to the management of preterm labor have been extensively investigated ***(Romero et al.,2014)***. Complications from preterm births resulted in 0.74 million deaths in 2013 down from 1.57 million in 1990 ***(Abubakar et al., 2015).*** The chance ofsurvival at less than 23 weeks is close to zero, while at 23 weeks it is 15%, 24 weeks 55% and 25 weeks about 80% **(*Naghavi et al., 2015*).** The chance of survival withoutlong term difficultiesis less **(*Jarjour, 2015*).** The cause of preterm birth is often not known. Risk factors include diabetes, high blood pressure, being pregnant with more than one baby, being either obese or underweight, a number of vaginal infections, tobacco smoking and psychological stress, among others **(*Blencowe et al., 2012).*** In those at risk, the hormone progesterone, if taken during pregnancy, may prevent preterm birth, **P**rogesterone is useful in allowing pregnancy to reach its physiologicterm because at sufficient levels in the myometrium, it blocks the oxytocin effect of prostaglandin F2α and α-adrenergic stimulation and therefore, increases the α-adrenergic tocolytic response ***(Regmi et al., 2012).*** **C**alcium-channel Blockers interfere with the calcium ions transfer through the myometrial cell membrane, They decrease intracellular free calcium concentration and induce myometrial relaxation ***(Gáspár & Hajagos-Tóth, 2013)***. Nifedipine was first reported in 1980 in an observational study to be an effective tocolytic agent with minimal side effects ***(Flenady et al., 2014).*** Nifedipine is an efficient tocolytic agent, with an easy oral route of administration, few side effects and a low neonatal complications rate.

Objectives:

Our study is a comparative clinical trial. The objective of our study was to compare the efficacy of administration of progesterone and nifedipine therapy on inhibition of threatened preterm Labor.

2. Methods

one hundred (100) pregnant women selected on basis of being singleton pregnancy, gestational age between 28 and 34 weeks of gestation, intact membranes, no effacement and no dilatation. The pregnant women were randomly assigned in two groups (progesterone and nifedipine group), fifty (50) women in each group. Gestational age was calculated on the basis of the last normal menstrual period, and ultra sonographic examination. Medication started after observation of at least one uterine contraction in 10 minutes after examination taken at least an hour and administration of antenatal corticosteroids. The

pregnant ladies were showed how to use the medication and schedule of follow up. The primary outcome is the inhibition of threatened preterm Labor. Treatment continued to 48 hours to inhibit contractions. Successful treatment is defined as cessation of contraction observed 48 hours, and no further cervical changes, tocolytic failure mean persistent of symptomatic uterine contraction despite of maximal attainable dose of therapy, rupture of intact membrane or occurrence of sever side effect necessitating discontinuation of therapy.

3. Results

In our study, comparison of the studied groups as regards general data (maternal age, gestational age, parity, previous cesarean, previous preterm labor and rate of uterine contractions/10 minutes for an hour) there was no statistically significant difference between two groups. The success rate in nifedipine group was (78%) but in progesterone group was (10%) the P value (0.001) shows highly statistically significant difference. As regard to maternal heart rate, fetal heart rate and maternal mean blood pressure before and after administration of both drugs there was no statistically significant difference. As regards maternal complications in our study we found that in progesterone group there were 28(56%) have no complication, 8(16%) have tachycardia, 8(16%) have hypotension and 6(12%) have both; on the other hand in nifedipine group we found that 20(40%) have no complication, 7(14%) have tachycardia, 12(24%) have hypotension and 11(22%) have both; with the P value 0.299 which is statistically insignificant.

4. Discussion

Preterm birth is the leading cause of perinatal morbidity and mortality, and its prevention is an important healthcare priority ***(Wang et al., 2016*)**. Some interventions have been used to prevent preterm labor including good antenatal care, bed rest, and intravenous hydration seemed to improve outcome but there was no strong evidence supporting those intervention in preterm labor prevention ***(Davey et al., 2015).*** Only fetal fibronectin in cervical mucus and cervical length are used with good evidence based to predict preterm birth ***(van Baaren et al., 2014).*** However, threatened preterm Labor which is classified as regular uterine contractions, can progress to be preterm birth about 25% ***(Chawanpaiboon & Sutantawibul, 2012).***

progesterone and nifedipine were still the most promising medications with minimal side-effects. However, neither a study nor strong evidence which supported the use of both drugs to inhibit uterine contractions in threatened preterm labor **(*Chawanpaiboon et al., 2011).*** Synthetic Progesterone (dydrogesterone) is identical to the Progesterone produced by the placenta and corpus luteum and so is readily metabolized and associated with minimal side effects ***(Salehpour et al., 2013*)**.

In our study there was no statistically significant difference between both groups as regarding to maternal age, gestational age and parity similar to the study of **Chawanpaiboon et al., 2011, Da fonseca et al., 2007, Meis et al., 2003, and Da fonseca et al., 2003.**

As regard success rate our study agrees with the study of "***Flenady et al., 2014***" which Compare CCBs (mainly nifedipine) with other tocolytics (including betamimetics, glyceryltrinitrate (GTN) patch, non-steroidal anti inflammatories (NSAID), magnesium sulphateand ORAs), which show that Calcium channel blockers are effective as first line for tocolysisin the management of preterm labor ***(Flenady et al., 2014).***

On the other hand our study agrees with the result of ***Areeruk and Phupong*** study that compare oral dydrogesterone with placebo in the management of preterm labor there were no difference between dydrogesterone and placebo group ***(Areeruk & Phupong, 2016).***

On the contrary with the results of ***Chawanpaiboon et al.,*** study that shows the success rate of inhibition of contraction was 66% (33/50) with progesterone and 80% (40/50) with nifedipine. There is no statistically significant difference between both groups ***(Chawanpaiboon et al., 2011)***.

The difference in success rate between the current study and the others may be attributed to the demographic factors and number of the patients of each study and the other studies used vaginal and injectable progesterone but in our study we used oral progesterone.

As regardsmaternal complications in our study were in agreement with the study done by ***(Oei S, 2006)*** and ***(Flenady et al., 2014)***; Which Compare CCBs with betamimetics, there were fewer maternal adverse effects requiring discontinuation of therapy (average RR 0.36, 95% CI 0.24 to 0.53).

The studies showed that progesterone was associated with a reduction in the risk of preterm birth of less than 37 weeks' gestation, and infant birth weight of less than2500 grams in the patients who had previous history of the preterm birth ***(Dodd et al., 2013).*** Nifedipine was studied and was strongly recommended to inhibit contractions. The side effects and complication of nifedipine to mother and fetus are fewer than beta-agonist and magnesium sulfate ***(Flenady et al., 2014)***.

Therefore, progesterone and nifedipine were still the promising medication to use with minimal side effects.

There was no study of both drugs in threatened preterm Labor. Therefore; synthetic progesterone and nifedipine to inhibit threatened preterm Labor are studied.

Conclusion

Calcium channel blockers (mainly nifedipine) have benefits over oral progesterone (dydrogesterone) for women in threatened preterm labor with respect to prolongation of pregnancy, and maternal adverse effects allowing time for administration of antenatal corticosteroids and transfer to higher level care.

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