A Comparison between the Effect of Oxytocin Only and Oxytocin plus Propranolol on Induction of Labor in Term Pregnancy (A Randomized Controlled Trial)

Thesis

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Mohamed Ashraf Mahmoud Bayomy Okba

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LIST OF ABBREVIATIONS

Abb.	Full term
ACOG	*American college of obstetrics and gynecology*
APGAR	*Appearance, Pulse, Grimace, Activity, and Respiration*
ARR	*Absolute risk reduction*
ARR	*Absolute risk reduction*
AV	*Atrioventricular*
BMI	*Body mass index*
CBC	*Complete blood count*
CS	*Cesarean section*
FFN	*Fetal fibronectin*
FHR	*Fetal heart rate*
HELLP	*Hemolysis elevated liver enzymes low platelets*
LMP	*Last menstrual period*
MAOI	*Monoamine oxidase inhibitor*
Max	*Maximum*
Min	*Minimum*
NICU	*Neonatal intensive care unit*
NNT	*Number needed to treat*
NSAID	*Non steroidal antiinflamatory drugs*
PV	*Pervaginal*
RR	*Relative risk*
SA	*Sinoatrial*
SD	*Standard deviation*
SLE	*Systemic lupus erthymatosis*
U/S	*Ultrasound*
VD	*Vaginal delivery*

ABSTRACT

Objective: To compare the effect of Oral Propranolol and Oxytocin, versus Oxytocin only on induction of labor in nulliparas having term pregnancy.

Materials and Methods: A double blind randomized controlled trial performed in labor ward of Ain Shams maternity Hospital in Cairo, Egypt from August 2016 to August 2018 on 211 nulliparas with uncomplicated term pregnancies who had Gestational age of 38–41 weeks, Bishop Score 5 or more. Participants were divided in two groups. In the group A (Propranolol plus Oxytocin group = 106) before the use of Oxytocin, 20 mg Propranolol was administrated orally and then the Oxytocin was initiated. In group B (placebo plus Oxytocin group =105) Oxytocin was used for the induction of labor.

Results: Induction-Contraction interval, duration of latent phase and induction-active phase interval were measured in minutes. All were significantly lower than in group A (Propranolol plus Oxytocin group) (p value=0.001). Duration of active phase measured in minutes was significantly lower than in group A (Propranolol plus Oxytocin group) (p value=0.008). Duration of 2nd stage measured in minutes was significantly lower in group A (Propranolol plus Oxytocin group) (p value=0.002). Propranolol intake reduced need for operative intervention. On average, 20.8 patients would have to receive Propranolol (instead of placebo) for one additional patient to NOT have (Forceps/CS). On average, 12.05 patients would have to receive Propranolol (instead of placebo) for one additional patient to have a maternal side effect. Propranolol had no statistically significant adverse effects on neonates according to APGAR scores at “1 minute” and “5 minutes”. None of neonates delivered in this study needed NICU admission.

Conclusion: According to the data in the current study the use of Propranolol with Oxytocin in induction of labor at term pregnancy may be beneficial in reducing duration of both first and second stages of labor compared to Oxytocin alone without causing any ominous maternal or fetal harm.

Keywords: Propranolol, Beta Blocker, Bishop Score, Induction of Labor, Active Phase, Latent Phase, Cesarean Section.

INTRODUCTION

"Induction of labor is defined as the process of artificially stimulating the uterus to start labor before its spontaneous onset" ***(Grobman, 2018)***. Over the past years, the rate of labor induction has increased to cut down the duration of pregnancy. In developed countries, the number of infants delivered vaginally at term after induction of labor might be as high as one in four deliveries ***(Declercq et al., 2007; Martin et al., 2007; Caughey et al., 2009)***.

Although an increase in medically and obstetrically indicated inductions contributed to the rise, marginally indicated and elective inductions accounted for a greater proportion of the increase ***(Moore & Rayburn, 2006)***. Reasons for the latter include more relaxed attitudes toward marginal indications for induction, patient and provider desire to arrange a convenient time of delivery, and the availability of better cervical ripening agents ***(Rayburn & Zhang, 2002)***. Patient and provider concerns about the risk of fetal demise with expectant management near term or postterm have also contributed to the increased rate of induction.

Administration of Oxytocin is probably the most common method of labor induction ***(Alfirevic et al., 2009)***. Exogenous Oxytocin administration produces periodic uterine contractions first demonstrable at approximately 20 weeks of gestation. Myometrial responsiveness increases with advancing gestational age until 34 weeks, at which time it levels off until

spontaneous labor begins, when it increases rapidly ***(Caldeyro-Barcia & Poseiro, 1959)***.

The optimum regimen for Oxytocin administration is controversial and no protocol has been subjected to the scientific scrutiny necessary to demonstrate its superiority in both efficacy and safety over another ***(Hayes & Weinstein, 2008)***.

Oxytocin can be used alone or in combination with other agents for labor induction. Propranolol is well established as a β adrenergic receptor–blocking drug that increases the uterine activity in pregnant and non-pregnant women by reversing the suppressive effect of the β agonist Isoproterenol on human uterine motility ***(Kashanian et al., 2008)***.

In many studies Propranolol was found to shorten the duration of labor induction, without any significant adverse effects on neonates ***(Palomäki et al., 2006).*** The first uncontrolled study on the use of Propranolol in dysfunctional labor was conducted about four decades ago. The results showed that administration of Propranolol causes normal uterine activity and delivery without any significant maternal or fetal complications ***(Mitrani et al., 1975).***

The purpose of the present study is to evaluate the effect of Oral Propranolol plus Oxytocin in comparison with Oxytocin alone on induction of labor.

AIM OF THE WORK

To compare the effect of Oral Propranolol and Oxytocin, versus Oxytocin only on induction of labor in term pregnancy.

Research question

Is Oral Propranolol effective for labor induction if added to Oxytocin compared to Oxytocin alone?

Research Hypothesis

Oral Propranolol may be effective for labor induction if added to Oxytocin compared to Oxytocin alone.

INDUCTION OF LABOR

"Induction of labor is defined as the process of artificially stimulating the uterus to start labor before its spontaneous onset" ***(Grobman, 2018)***.

Whereas augmentation of labor is defined as increasing the rate and the strength of previously existing contractions of the uterus in a pregnant woman already in labor but inefficiently progressing, so that vaginal delivery is achieved ***(Goel et al., 2014)***.

During the past years, the rate of labor induction has increased to shorten the duration of pregnancy. In developed countries, the number of infants delivered vaginally at term following induction of labor might be as high as one in four deliveries ***(Declercq et al., 2007; Martin et al., 2007; Caughey et al., 2009)***.

Several professional communities have supported induction of labor in situations where the risks of waiting for the start of spontaneous labor are greater than the risks of induction to shorten the duration of pregnancy.

Such situations may include:

- Post-term pregnancy: gestational age of > 41 weeks.
- Prelabor (premature) rupture of membranes
- Chorioamnionitis

- Preeclampsia, eclampsia, HELLP syndrome, gestational hypertension, chronic hypertension
- Diabetes mellitus
- Placental abruption
- Fetal growth restriction
- Fetal demise
- Oligohydramnios
- Cholestasis of pregnancy
- Alloimmunization with fetal anemia
- Twin pregnancy

(ACOG Committee on Practice Bulletins -- Obstetrics, 2009)

Labor also may be induced for other non-medical reasons, for example; risk of precipitate labor, remoteness from hospital, or psychosocial indications. In such conditions, one of the following criteria should be present or documentation of fetal lung maturity. A mature fetal lung earlier than 39 weeks of gestation, in the absence of proper clinical condition, is not an indication for induction:

- Confirmation of gestational age of ≥ 39 weeks by an Ultrasound measurement at ≤ 20 weeks of gestation.
- Fetal heart activity has been recognized as present for 30 weeks by Doppler ultrasonography.

- 36 weeks have passed since a positive pregnancy test result (serum or urine beta human chorionic gonadotropin).

(ACOG Committee on Practice Bulletins -- Obstetrics, 2009)

American College of Obstetricians and Gynecologists has declared that maternal anxiety or distress related to normal pregnancy; or other non-medical reasons –as mentioned above- are not proper indications for elective early term induction ***(ACOG Committee on Practice Bulletins -- Obstetrics, 2009)***.

It was found that early term neonates (37+0 to 38+6weeks) have larger risk of neonatal morbidity than those born at 39 to 40 weeks, and throughout their first year of life ***(Wang et al., 2004; Escobar et al., 2005; Zhang & Kramer, 2009; Dietz et al., 2012; Wetta & Tita, 2012; Parikh et al., 2014)***.

Contraindications:

Contraindications to induction of labor are usually similar to those of spontaneous vaginal delivery. In such conditions, there is universal agreement that the maternal and/or fetal risks related to labor and vaginal delivery, and consequently induction of labor, are more than the risks related to cesarean delivery; therefore, induction of labor is better avoided, and they include:

- Previous classical or other high risk cesarean incision (e.g. second stage cesarean section)