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Systematic Review (Pages: 6541-6553)

The Effect of the Use of Oxytocin in Labor on Neonatal Jaundice: A Systematic Review and Meta-Analysis

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Abstract

Background: Neonatal Jaundice is a common problem that occurs in most preterm and term neonates. This systematic review aimed to examine the evidence for the effects of oxytocin in labor on neonatal jaundice.

Materials and Methods: In this systematic review study, English databases including PubMed, Google Scholar, Embase, Cochrane Library, Scopus, Web of Sciences, and Persian databases including SID, Magiran, and Barakat Knowledge Network System Were searched from Jan 1980 to Dec 2017. Persian and English human clinical trials were targeted. The review was limited to human clinical trials examining the effect of oxytocin in labor on neonatal jaundice. The searched MESH vocabulary was "neonatal hyperbilirubinemia" OR "jaundice" in combination with "oxytocin in labor" OR "induction of labor". Two authors examined the articles separately and the disagreements were resolved through discussion.

Results: Out of 583 articles searched in the databases, 440 title, 83 abstracts, and 60 full texts were reviewed, of which 5 English language articles entered the study and 4 articles entered the meta-analysis. Meta-analysis results showed that oxytocin did not affect the serum bilirubin level of the umbilical cord (Mean difference: 1.60; 95% confidence interval [CI]:-2.50 to 5.69; P=0.44; I^2=78%). Furthermore, administering oxytocin in labor did not significantly affect serum bilirubin level on days 1 (-0.32; -1.36 to 0.71; P=0.54; I^2=72%), and day 3 (3.75; -11.76 to 18.90; P=0.65; I^2=63%), while it significantly affected serum bilirubin level on day 2 (-1.63; -2.81 to -0.45; P=0.007; I^2=0%).

Conclusion: The result of meta-analysis showed that the administration of oxytocin during labor does not affect serum bilirubin level on days 1 and 3, while induction of labor with oxytocin causes serum bilirubin to increase on the second postnatal day. However, due to the high heterogeneity of the studies, better designed clinical trials are recommended to achieve better results.

Key Words: Hyperbilirubinemia, Induction, Labor, Neonatal, Oxytocin, Systematic review.

*Please cite this article as: Seyedi R, Mirghafourvand M, Osouli Tabrizi Sh. The Effect of the Use of Oxytocin in Labor on Neonatal Jaundice: A Systematic Review and Meta-Analysis. Int J Pediatr 2017; 5(12): 6541-53. DOI: **10.22038/ijp.2017.26526.2277**

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Received date: Sep.17, 2017; Accepted date: Nov.12, 2017

1- INTRODUCTION

Neonatal jaundice is a common and benign problem that occurs in 60% of term and near term neonates and 80% of preterm neonates (1). Neonatal jaundice presents as yellow color in skin, sclera, and mucous membranes due to bilirubin accumulation, which is also associated with increased bilirubinemia (2). The severity of jaundice varies among different neonates and may be related to factors such as race, feeding method, delivery method, gestational age, preeclampsia, gender, maternal diabetes and labor induction with oxytocin (3, 4).

Nowadays, in modern obstetrics, oxytocin is widely used to stimulate and accelerate labor and prevent prolonged labor (5). The use of oxytocin has reduced the interval between induction and delivery. The risks of induction of labor with oxytocin are fetal distress and low Apgar score (6). Oxytocin is also associated with side effects such as an increased incidence of neonatal jaundice, possible causes including immature activity of glucuronyl-transferase, hepatic damage due to hypoxia, increased fetal placental transportation, increased erythrocyte fragility and mechanical trauma to erythrocytes (7).

Oxytocin is an antidiuretic hormone, and causes hyponatremia and hyposmolarity in the mother and subsequently in the fetus with water retention. Hyposmolarity causes swelling of the red blood cells and makes them fragile and susceptible to hemolysis (8). Various studies have approved the effects of oxytocin on jaundice. Some studies have suggested that the extensive use of oxytocin in labor induction is one of the factors leading to neonatal jaundice (9-11). Since the induction of labor with oxytocin will possibly increase neonatal jaundice, so that jaundice can be prevented by reducing the oxytocin dose in labor (11). Clinical trials provide the best results to show if oxytocin leads to jaundice. The present systematic review was performed to examine the clinical trial evidence of the effects of oxytocin on jaundice. This study aimed to determine the effect of administering oxytocin in labor on neonatal jaundice compared with spontaneous vaginal delivery.

2- MATERIALS AND METHODS

2-1. Search strategy

First, the search in Cochrane started with keywords: "neonatal jaundice", "hyperbilirubinemia", and "oxytocin in labor". According to the search, there was no review study based on clinical trials on the effect of oxytocin in labor on neonatal jaundice. Then English databases including PubMed, Google Scholar, Embase, Cochrane Library, Scopus, Web of Sciences, and Persian databases including SID, Magiran, and Barakat Knowledge Network System were searched from Jan 1980 to Dec 2017. Persian and English human clinical trials were targeted. The searched MESH vocabulary was "neonatal hyperbilirubinemia" OR "jaundice" in combination with "oxytocin in labor" OR "induction of labor".

2-2. Study selection

This systematic review collected and evaluated clinical trials on the effect of oxytocin administration in labor on neonatal jaundice. Persian and English human clinical trials were targeted. PICO was used as a guide for searching articles: the participants in this study were term pregnant women with singleton pregnancy, with oxytocin intervention for labor induction, along with the control group including women with spontaneous vaginal delivery. The study outcome was neonatal jaundice. The exclusion criteria were absence of a comparison group and the comparison of oxytocin with other therapeutic groups, such as amniotomy,

prostaglandin, and misoprostol without a spontaneous vaginal delivery group.

2-3. Assessment quality of articles

The researcher collected and evaluated clinical trials on the effect of oxytocin administration in labor on neonatal jaundice. Persian and English human clinical trials were targeted. These studies were evaluated in terms of inclusion criteria and relevance to the subject of the review study. Out of 583 articles searched in the databases, 440 title, 83 abstracts and 60 full texts were reviewed, of which 5 articles entered the study and 4 articles entered the meta-analysis. The collected articles were then carefully studied and the two authors separately evaluated the title and abstract of all the articles in terms of inclusion criteria. Meanwhile, articles that were not consistent with the inclusion criteria were completely eliminated. Based on the search, 583 articles were found, 578 of which were not included in this study for the following reasons: descriptive studies, not related to the title, not examining the desired outcome (neonatal jaundice), comparing the effects of oxytocin on jaundice with a Prostaglandin F2α or amniotomy group, and absence of spontaneous vaginal delivery control group. Of the five articles entering this review study, the article by D'Souza et al. (14) did not enter the meta-analysis because its results were based on frequency (percentage), and its results were reported separately (**Figure.1**).

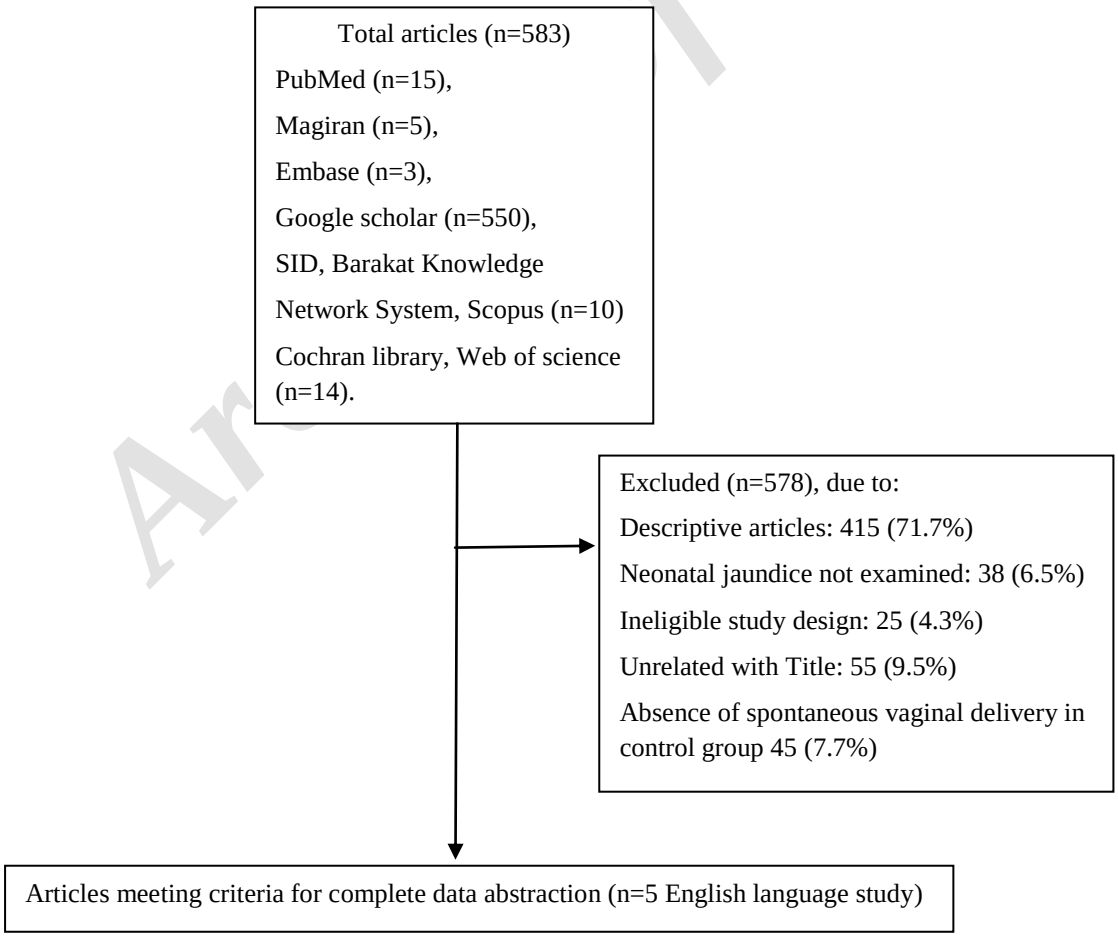

Fig1: Flowchart of study.

2-4. Assessment of risk of bias in included studies

Risk bias was determined for each of the five included articles according to the following criteria by the two Author of this Article (RS and SO) separately and the disagreements were resolved by referring to the third researcher (MM) and through discussion. The types of bias studied in this study according to the Cochrane Handbook (12) were as follows:

2-4-1. Random sequence generation (checking for possible selection bias):

- Low risk of bias: Use of any random process like random numbers table, computer random number generator, coin, and dice.
- High risk of bias: Use of any non-random process like date of birth, day or date of admission, file number.
- Unclear risk of bias: Insufficient information.

2-4-2. Allocation concealment (checking for possible selection bias):

- Low risk of bias: A central assignment such as random with phone or web-based, opaque and sealed envelopes.
- High risk of bias: Alternate allocation, based on birth date or hospital file number.
- Unclear risk of bias: Insufficient information.

2-4-3. Blinding of participants and personnel (checking for possible performance bias):

- Low risk of bias: Blinding is not complete but the outcome is not affected by the lack of blinding. Complete blinding of the participants and personnel.
- High risk of bias: Blinding is not complete but the outcome is affected by the lack of blinding.
- Unclear risk of bias: Insufficient information.

2-4-4. Blinding of outcome assessment (checking for possible detection bias):

- Low risk of bias: Complete blinding of the outcome evaluator.
- High risk of bias: No complete blinding of the outcome evaluator.
- Unclear risk of bias: Insufficient information.

2-4-5. Incomplete outcome data (checking for possible attrition bias):

- Low risk of bias: When there are no or little missing data, or the reasons for the sample loss are the same in the two groups.
- High risk of bias: When the amount of missing data is high or the loss in the two groups is unbalanced.
- Unclear risk of bias: Insufficient information.

2-4-6. Selective reporting (checking for reporting bias):

- Low risk of bias: All predicted results of the study are reviewed and reported.
- High risk of bias: When all of the preset results are not reported or are incomplete and useless.
- Unclear risk of bias: Insufficient information.

The studies of Patil et al. (13), Omigbodun et al. (16), and Leijon et al. (17) are at high risk of selection bias because random allocation sequences and concealing the allocation haven't been used. These three studies provide no information regarding blinding. There is no sample loss in them and the main outcome is reported in all three studies. In the study by D'Souza et al. (14), women were randomly divided into two groups: labor induction with oxytocin and spontaneous labor, but no concealing of the allocation was done. It provides no information regarding blinding. There is no sample loss and the main outcome was reported. The study by Oral et al. (15) is at a high risk of selection bias because

random allocation and allocation concealment were not done. It provided no information regarding blinding. The study appears to be subject to sample loss. All main outcomes were reported in this study (**Table.1, Figure.2**).

2-5. Statistical Analysis

Five English language articles entered this study. Their data were extracted by two authors separately and combined using the RevMan software-version 5.3 for analysis. Data from four studies entered the meta-analysis and the results of a study did not enter the meta-analysis, because they were reported as frequency (percentage). In three meta-analyses (**Figure 3-5**), random effect was used instead of fixed effect as I^2 was above 25 (12).

Table-1: Characteristics of included studies and their risk of bias

Patil et al. (2015) (13)		
Methods	RCT	
Participants	Participants included 100 full terms parturient. The subjects were divided into two groups including oxytocin induced labor (n=50) and normal vaginal delivery following spontaneous onset of labor (n = 50). Inclusion criteria: All the gestation were 38 weeks duration or more, uncomplicated pregnancies. None of the newborn infants had any signs of respiratory distress syndrome. New born infant born with APGAR score of less than 6 were excluded from the study.	
Interventions	Intervention group: Oxytocin induced labor in 5% dextrose, control group: Normal vaginal delivery following spontaneous onset of labor.	
Outcomes	Neonatal serum bilirubin on day 1, 3 and 5 after delivery.	
Results	There was significant increase in bilirubin level in oxytocin induced group compared to control group on day 1 and 3. There was insignificant increase in bilirubin level in oxytocin induced group on day 5.	
Risk of bias		
Bias	Authors' judgment	Support for judgment.
Random sequence generation (selection bias)	High risk	100 full term parturient were divided two groups including oxytocin induced labor (n=50) and normal vaginal delivery following spontaneous onset of labor (n = 50).
Allocation concealment (selection bias)	High risk	This study is non randomized trial.
Blinding of participants and personnel (performance bias)	Unclear	No specific information regarding blinding of personnel and participants was given.
Blinding of outcome assessor (detection bias)	Unclear	No specific information regarding blinding of outcome assessor was given.
Incomplete outcome data (attrition bias)	Low risk	There were no exclusions after entering the study.
Selective reporting (reporting bias)	Low risk	Main outcomes have been reported.
D'Souza et al. (1986) (14)		
Methods	RCT	
Participants	Participants included 193 mothers with normal singleton pregnancy and prospects of a normal vaginal delivery. The control group (n = 29) consisted of mothers who had a spontaneous onset of labor at term. The remaining mother (n=164) in the study groups had oxytocin induction of labor. Inclusion criteria: The gestational age of all women was 39-40 weeks.	

Interventions	Intervention group consisted of 164 mothers who had oxytocin induction of labor. Oxytocin (10 units) in 5% dextrose solution (500ml) was used. After satisfactory uterine activity was induced either the oxytocin infusion was managed according to routine delivery unit practice (n = 36), or infusion rates were halved (n = 45), or quartered (n = 43), or discontinued (n = 40). Control group (n = 29) consisted of mothers who had a spontaneous onset of labor at term.	
Outcomes	Hyponatraemia and jaundice.	
Results	In the induction group, six (46%) of 13 hyponatremic infants had neonatal jaundice as compared with 22 (13%) of 151 normonatremic infants. No hyponatremia with jaundice was observed in the control group and 2 of 27 normonatraemic infant had neonatal jaundice.	
Risk of bias		
Bias	Authors' judgment	Support for judgment.
Random sequence generation (selection Bias).	Low risk	Women were randomized to oxytocin group and spontaneous onset of labor.
Allocation concealment (selection bias)	High risk	This study is non randomized trial.
Blinding of participants and personnel (performance bias)	Unclear	No information provided.
Blinding of outcome assessment (detection Bias).	Unclear	No information provided.
Incomplete outcome data (attrition bias).	Low risk	All participants completed the study.
Selective reporting (reporting bias).	Low risk	Main outcomes have been reported.
Oral et al. (2002) (15)		
Methods	RCT	
Participants	n=80 patients managed with oxytocin during labor and n=40 multiparous patients delivering without oxytocin infusion. Inclusion criteria: Singleton term pregnancy (37–42 weeks) with no Rhesus negative blood group and no known medical disease or fetal problem.	
Interventions	Intervention group: A total of 80 patients managed with oxytocin during labor were randomly divided into isotonic % 0.9 saline (Group 1) and 5% glucose solutions (Group 2). Control group: Forty multiparous patients delivering without. Oxytocin infusion formed the control group (Group 3).	
Outcomes	Neonatal bilirubin levels on day 1 and 2.	
Results	Cord plasma bilirubin levels and day 1 and 2 hematocrit and plasma bilirubin levels were not statistically different between the groups.	
Risk of bias		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection Bias).	High risk	A total of 80 patients managed with oxytocin during labor were randomly divided into isotonic % 0.9 saline (Group.1) and 5% glucose solutions (Group 2). Forty multiparous patients delivering without Oxytocin infusion formed the control group (Group.3).
Allocation concealment (selection bias).	High risk	This study is non randomized trial.
Blinding of participants and personnel (performance bias).	Unclear	No information provided.

Blinding of outcome assessment (detection Bias).	Unclear	No information provided.
Incomplete outcome data (attrition bias).	High risk	The patients delivering with forceps or vacuum extraction and cesarean section were discarded from the study (10 cesarean deliveries and 1 vacuum extraction in group 1 and 4 cesarean deliveries in group 2) and further evaluations were not carried out on these patient.
Selective reporting (reporting bias).	Low risk	Main outcomes have been reported.
Omigbodun et al. (1992) (16)		
Methods	RCT	
Participants	82 parturient women requiring oxytocin infusion in labor were randomized into two groups receiving 0.9% saline or 5% glucose, respectively. A group of 82 women not requiring oxytocin were recruited for comparison. Inclusion criteria: Singleton pregnancies with a minimum gestational age of 37 **weeks** did not have a Rhesus negative blood group and had no obvious medical complications of pregnancy such as hypertension, diabetes mellitus, pyrexia, jaundice or anemia.	
Interventions	Intervention group: 82 parturient women requiring oxytocin infusion in labor were randomized into two groups: n=40 receiving 5% glucose (group1) and n=40 receiving 0.9% sodium chloride (group2) as diluent for oxytocin. Control group: 82 of parturient women who were not received any intravenous fluids or oxytocin (group3).	
Outcomes	Neonatal bilirubin levels on day 3.	
Results	The cord plasma bilirubin and the neonatal bilirubin levels at the age of 3 days were significantly higher in the glucose group than in each of the other two groups.	
Risk of bias		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection Bias).	High risk	Eighty-two parturient Nigerian women requiring oxytocin infusion in labor were randomized into two groups receiving 0.9% saline or 5% Glucose, respectively. A group of 82 women not requiring oxytocin were recruited for comparison.
Allocation concealment (selection bias).	High risk	This study is non randomized trial.
Blinding of participants and personnel (performance bias)	Unclear	No information provided.
Blinding of outcome assessment (detection Bias).	Unclear	No information provided.
Incomplete outcome data (attrition bias).	Low risk	All participants completed the study.
Selective reporting (reporting bias).	Low risk	Main outcomes have been reported
Leijon et al. (1980) (17)		
Methods	RCT	
Participants	84 infants, 43 born after induced labor and 41 after spontaneous labor were originally included. (To compare the bilirubin levels in newborn infants in a randomized prospective study in spontaneous and induced labor at full term).	
Interventions	Intervention group: Forty-three infants born after elective induction with oxytocin using the Cardiff infusion system.	

	Control group: 38 infants born after spontaneous delivery.	
Outcomes	Neonatal bilirubin levels on days 1, 2, 3 and maximal bilirubin.	
Results	There were no differences in bilirubin levels on days1, 2, and 3 or in the maximal bilirubin levels during the neonatal period.	
Risk of bias		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection Bias).	High risk	To compare the bilirubin levels in newborn infants in a randomized prospective study in spontaneous and induced labor at full term.
Allocation concealment (selection bias).	High risk	This study is non randomized trial.
Blinding of participants and personnel (performance bias).	Unclear	No information provided.
Blinding of outcome assessment (detection Bias).	Unclear	No information provided.
Incomplete outcome data (attrition bias).	Low risk	All participants completed the study.
Selective reporting (reporting bias).	Low risk	Main outcomes have been reported.

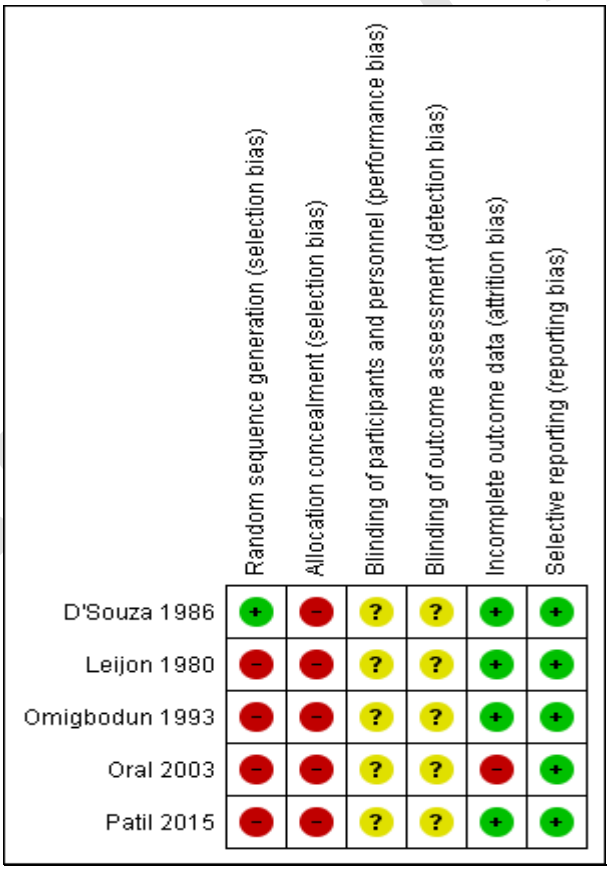

Fig.2: Diagram of Bias in the Included Studies.

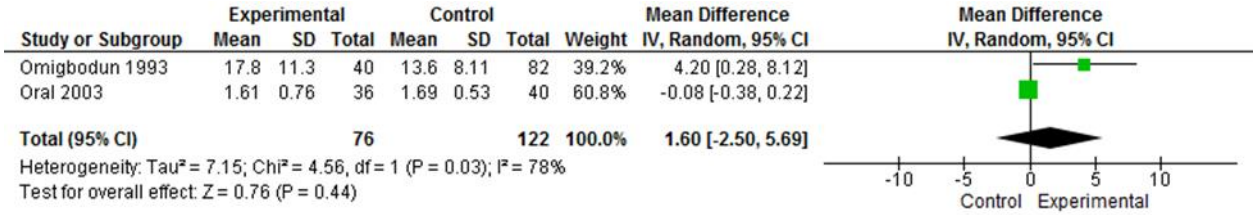

Fig.3: The effect of oxytocin on bilirubin level of the umbilical cord blood.

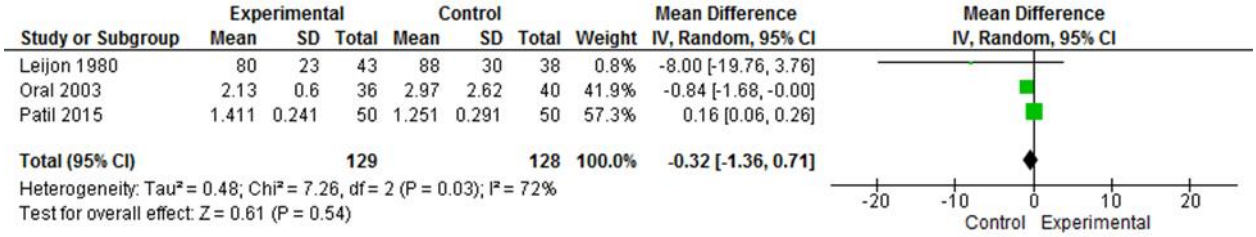

Fig.4: The effect of oxytocin on serum bilirubin level on days 1.

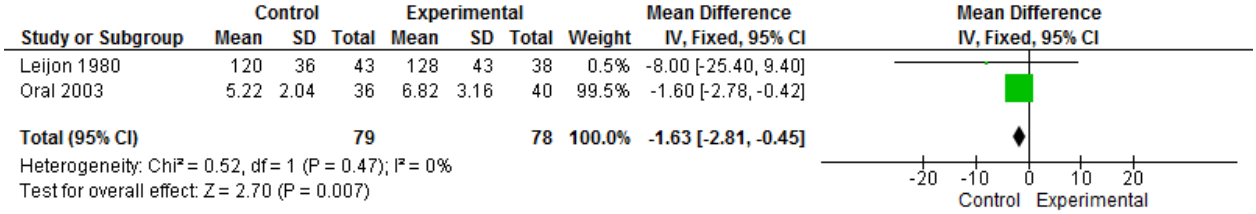

Fig.5: The effect of oxytocin on serum bilirubin level on days 2.

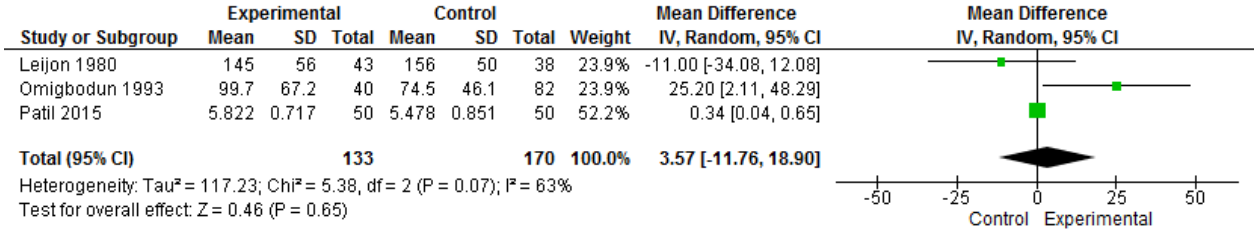

Fig.6: The effect of oxytocin on serum bilirubin level on days 3.

3- RESULTS

The study by Patil et al. (2015) was conducted on 100 term pregnant women in two groups (13). The first group consisted of 50 neonates from women who had oxytocin-induced labor, and the second group had 50 women with spontaneous vaginal delivery. All women had a gestational age of 38 weeks or more without any pregnancy complications. None of the neonates had symptoms of

respiratory distress syndrome, and the neonates with an Apgar score less than 6 were excluded. Neonatal bilirubin was measured on days 1, 3 and 5 using blood samples. The result of the study showed that there was a significant increase in bilirubin levels on days 1 and 3 in labor induction group (mean day 1= 1.411 and mean day 3= 5.822) compared to the control group (mean day 1= 1.251 and mean day 3= 5.478). However, there was no significant difference in bilirubin levels on day 5 in the two groups (mean for induction group= 4.912 and mean for control group=4.789). In the study by D'Souza et al. (1986), 193 pregnant mothers with singleton pregnancy waiting for vaginal delivery were selected (14).

The mothers with spontaneous labor formed the control group (n=29), and the rest of the mothers formed the induction group (n=164). In the labor induction group, 10 units of oxytocin was infused into 500 mL of dextrose 10% serum. When uterine contraction reached an acceptable level, mothers were randomly divided into 4 groups: In group one (n=36), infusion rate was different according to personnel opinions. In group two (n=45), infusion rate decreased by half. In group three (n=43), the infusion rate was reduced to a quarter.

In group four (n=40), the infusion stopped. Umbilical cord blood was collected after birth. The results showed that the comparison of hyponatremic and normonatremic cord blood showed no significant differences in plasma bilirubin levels, while in subsequent follow-up, hyponatremic neonates tended to have jaundiced more. In the labor induction group, 6 of 13 hyponatremic neonates (46%) had jaundice, and 22 of 151 neonatremic neonates (13%) were jaundiced after induced labor, while in the control group, no jaundice was reported with hyponatremic neonates and only 2 of 27 normonatremic neonates were jaundiced. The study by Oral et al. (2003) was conducted with the aim to determine the relationship between neonatal bilirubin levels, and oxytocin infusion in 5% glucose solutions and isotonic 0.9% saline (15). Criteria for entering the study were singleton pregnancy and gestational age of 37-42 weeks without any known diseases or disorders. Eighty pregnant women who had labor induction entered the study and were randomly divided into two groups. Group one (n=40), received dextrose 5%, and group two (n=40) normal saline 9%. Forty multipara pregnant mothers with no oxytocin infusion formed the control group. In the labor induction group, 10 units of oxytocin was injected into the serum of dextrose 5% or normal saline 9% to induce labor. After birth, the umbilical cord blood was first taken and the levels of bilirubin and sodium were measured. Then, serum bilirubin and hematocrit levels were measured on days 1 and 2. Data from 29 neonates from group one, 36 neonates from group two, and 40 neonates from group three were analyzed. Results showed that the levels of umbilical cord blood bilirubin, as well as bilirubin and hematocrit levels on days 1 and 2, were not significantly different among the groups.

The study by Omigbodun et al. (1993) was conducted on 82 pregnant women who needed oxytocin induction (16). The inclusion criteria were singleton pregnancy and a minimum gestational age of 37 weeks without pregnancy complications. Women were randomly divided into two groups. Group one (n=40), had labor induction with intravenous oxytocin in dextrose 5%, while group two (n=42) had labor induction with saline serum. A group of 82 patients who did not receive any serum or oxytocin formed the control group. The results of the study indicated that the level of umbilical cord blood and neonatal bilirubin on day 3 was significantly higher in dextrose 5% group

than in other groups. The study by Leijon et al. (1980) was a randomized prospective study with the aim of investigating the relationship of labor induction with oxytocin and plasma bilirubin levels compared with spontaneous vaginal delivery on 84 term neonates (17). Forty-three neonates after labor induction and 41 neonates after spontaneous labor entered the study. The results of the study showed that there was no significant difference between the two groups in terms of hemoglobin and hematocrit in the umbilical cord and on day 2, the levels of bilirubin on days 1 and 3, and maximum bilirubin. Information on the serum bilirubin of neonates was collected from all five articles and combined using the RevMan software. The article by D'Souza et al. (14) did not enter meta-analysis because of not reporting mean and standard deviation. The remaining four articles entered the meta-analysis. Due to the high level of heterogeneity in evaluating bilirubin of umbilical cord (I^2=78%), day 1 (I^2=72%), and day 3 (I^2=63%), random effect was used instead of the fixed effect. The fixed effect was only used for evaluation of bilirubin on day 2 (I^2=0). The I^2 statistic shows that the percentage of variation across studies is due to heterogeneity (12).

Meta-analysis results showed that oxytocin did not affect the bilirubin level of the umbilical cord blood (Mean difference: 1.60; 95% confidence interval [CI]:-2.50 to 5.69; P=0.44; I^2=78%) (**Figure.3**). Furthermore, administering oxytocin in labor did not significantly affect serum bilirubin level on days 1 (Mean difference: -0.32; 95% CI:-1.36 to 0.71; p=0.54; I^2=72%) (**Figure.4**), and 3 (mean difference: 3.75; 95% CI:-11.76 to 18.90; p=0.65; I^2=63%) (**Figure.6**), while it significantly affected serum bilirubin level on day 2 (Mean difference: -1.63; 95% CI:-2.81 to -0.45; p=0.007; I^2=0%) (**Figure.5**).

4- DISCUSSION

This systematic review examined the evidence for the effects of oxytocin in labor on neonatal jaundice Out of 583 articles searched in the databases, 440 title, 83 abstracts, and 60 full texts were reviewed, of which 5 articles entered the study and 4 articles entered the meta-analysis. The findings of this study showed that administration of oxytocin to mothers in labor versus spontaneous vaginal delivery did not affect serum umbilical cord blood bilirubin level on days 1 and 3, but induction of labor with oxytocin increased serum bilirubin on day 2 compared to the spontaneously vaginal delivery. Chalmers et al. (1975) conducted a retrospective study on the administration of oxytocin in labor and the incidence of neonatal jaundice on 10,591 neonates. Participants were divided into three groups: Group one those who received oxytocin to induce labor, Group two those who had a spontaneous vaginal delivery without labor induction, and Group three those who were induced only with amniotomy. The results of the study showed that in group one, 412 out of 3,326 neonates (12.4%) were jaundiced after the administration of oxytocin. In group two, 476 out of 5,896 neonates (8.1%) were jaundiced after spontaneous labor.

In group three, 82 out of 1369 neonates (6%) were jaundiced after induction with amniotomy. Therefore, the incidence of jaundice in infants born after induction of labor with oxytocin was higher than that of other groups (18). The prospective study by Chew et al. (1977) was conducted on 181 neonates divided into three groups. Group A had 54 neonates with spontaneous labor and without oxytocin administration. Group B had 28 neonates with spontaneous labor onset and using oxytocin to stimulate labor. Group C had 99 neonates with induced labor with amniotomy and oxytocin. The results of the study showed that the mean serum

bilirubin on days 1, 3 and 6 in the group C was significantly higher than in group A. There was no statistically significant difference between groups A and B (6). The study by Abbas et al. (2015) was a prospective cohort study with the aim of evaluating the incidence of neonatal jaundice in neonates exposed to maternal oxytocin for induction of labor in comparison with spontaneous labor. In this study, 308 neonates were enrolled in two groups. Group A was neonates exposed to maternal oxytocin for induction of labor, and group B was neonates born with spontaneous labor with oxytocin used to stimulate labor. The results showed that the incidence of neonatal jaundice in group A and B was 25% and 12%, respectively. Therefore, oxytocin administered for induction of labor was associated with a higher neonatal bilirubin (11). The study by Suvasuriya et al. (1978) was conducted on 114 neonates of (a) spontaneous labor, (b) labor induction with amniotomy, (c) labor induction with amniotomy and oxytocin, and (d) labor induction with amniotomy and Prostaglandin E2 (PGE_2). It showed that there was no significant difference in serum bilirubin levels on days 1 to 5 between the four groups (19). In the study by Ghaemi et al. (2000) conducted in 2000 in a case-control design on 162 neonates, the case group (mothers who received oxytocin for induction of labor), had 89 members that were compared with 73 neonates in the control group (mothers who did not receive oxytocin), and evaluated up to five days after birth for hyperbilirubinemia. Twenty-six of 89 neonates in the case group (26.2%) and 11 of 73 neonates in the control group (15%) had pathological jaundice. Therefore, induction of labor with oxytocin is probably one of the causes of neonatal jaundice, which is due to the hemolytic mechanism of its antidiuretic property along with high fluid intake during delivery and on days 4 and 5 after birth (20).

4-1. The Strengths Limitations of the study

The strengths of the reviewed articles were that all were RCT studies and oxytocin was infused in 5% dextrose in all of them. There was also a control group (spontaneous labor) in all of the studies, and the outcome of neonatal jaundice was evaluated in all of them. One of the limitations of this systematic review was high heterogeneity of included studies. Other limitations of this study were that the number of RCT studies is low.

5- CONCLUSION

This systematic review study limited to human clinical trials examining the effect of oxytocin in labor on neonatal jaundice. Five English language articles entered the study and 4 articles entered the meta-analysis. The results showed that the administration of oxytocin during labor versus spontaneous vaginal delivery does not affect serum bilirubin level on days 1 and 3, while induction of labor with oxytocin causes serum bilirubin to increase on the second postnatal day compared to spontaneous vaginal delivery. However, due to the high heterogeneity of the studies, a better designed clinical trial is recommended to achieve better results.

6- CONFLICT OF INTEREST: None.

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