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A Comparative Study of Oxytocin with Calcium Gluconate Versus Oxytocin Alone for Induction of Labour

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Abstract: Induction of labour often requires increasing doses of oxytocin, which may increase the risk of postpartum hemorrhage. Calcium is essential for myometrial contractility and may enhance uterine responsiveness to oxytocin. Objective to compare the effectiveness of intravenous calcium gluconate combined with oxytocin versus oxytocin alone for labour induction, with respect to induction-to-delivery interval, oxytocin dose, and postpartum hemorrhage. This prospective comparative study included 200 term pregnant women undergoing labour induction with a favorable cervix. Participants were allocated into two groups: oxytocin plus intravenous calcium gluconate or oxytocin alone. Maternal outcomes included induction-todelivery interval, total oxytocin dose, and postpartum hemorrhage, while the neonatal outcome was neonatal intensive care unit admission. Baseline characteristics were comparable between groups. The calcium group required a lower mean oxytocin dose (6.08 ± 1.9 vs. 7.02 ± 1.9 units, $p < 0.001$) and had a shorter induction-to-delivery interval (8.01 ± 1.9 vs. 8.82 ± 2.0 hours, $p = 0.004$). Postpartum hemorrhage was less frequent in the calcium group (19.0% vs. 30.0%), without statistical significance ($p = 0.071$). Mode of delivery and neonatal outcomes were similar. Inductionto delivery time showed modest predictive value for successful induction (AUC = 0.605, $p = 0.037$). Intravenous calcium gluconate as an adjunct to oxytocin was associated with improved induction efficiency without increasing maternal or neonatal complications.

Keywords: Labour Induction, Oxytocin, Calcium Gluconate, Uterine Contractions, Induction-to-Delivery Interval, Maternal and Neonatal Outcomes

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1. Introduction

The induction of labour (IOL) is a commonly used obstetric procedure that is performed to induce uterine contractions prior to the onset of labour if it is believed that the baby will be better off born before the end of the pregnancy [1]. Common signs are: post-term pregnancy, premature rupture of membranes,

hypertensive disorders, fetal growth restriction and oligohydramnios [2]. There are several methods of labour induction such as mechanical or pharmacological, one of the most frequently used agents is oxytocin [3].

It is known that oxytocin stimulates uterine contractions by binding to specific receptors on myometrial cells that increases intracellular calcium levels and activates co-ordinated uterine contractions [4]. However, its efficacy has been shown to be inconsistent in women and overdosage can lead to the development of uterine tachysystole, fetal distress and postpartum haemorrhage [5]. Thus, there is a clinical need for determining interventions that can make oxytocin more effective with lower dosages.

In uterine cells, calcium helps to regulate actin–myosin interactions, which are crucial for uterine contractility. Upon activation of the OT receptor, there is increased intracellular calcium release and extracellular calcium influx, causing tight uterine contractions [6]. Experimental studies indicated that calcium deficiency reduces the strength and coordination of myometrial contraction, while calcium sufficiency increases myometrial responsiveness to oxytocin [7,8].

Intravenous calcium gluconate has thus been suggested to be used as an adjunct during labour induction when oxytocin is used. Previously, clinical trials had shown a possible shortening of the labour period and increased uterine efficiency when calcium gluconate was used together with oxytocin [9,10]. However, the results obtained were mainly from aged studies with methodological flaws, making the need for more clinical assessment.

The purpose of this study was to make a comparison between intravenous calcium gluconate along with oxytocin in comparison to oxytocin alone for induction of labour and to compare induction to delivery time, oxytocin requirements, maternal outcomes and neonatal outcomes. The results could provide information on the possible clinical use and safety of calcium supplementation in combination with oxytocin for inducing a labour.

2. Method

A prospective comparative interventional study was carried out at Obstetrics and Gynecology Department of Bint Al-huda Hospital, Thi-Qar, Iraq during 12 months from January 1st 2024 to January 1st 2025. The purpose of this study was to compare the efficacy of oxytocin + calcium gluconate vs oxytocin alone in the induction of labor.

Two hundred pregnant women who were admitted to the hospital for the induction of labour with favourable cervix (Bishop score ≥6) were included in the study. The participants were divided into two groups of 100 women per group. The women in Group A were given iv calcium gluconate plus continued oxytocin infusion, while the women in Group B were given only oxytocin infusion.

While the inclusion criteria were: term pregnancy (>37 weeks gestation), cephalic presentation, favourable cervix (Bishop score ≥6), and an indication for induction of labour that was documented in the mother's case record, such as post-term pregnancy, gestational hypertension or premature rupture of membranes (PROM).

Women who had a previous uterine scar, including former cesarean section or myomectomy, had known hypersensitivity to oxytocin or calcium gluconate, suspected fetal macrosomia (EFCW>4.5 kg) or any contraindication to vaginal delivery (placenta previa, previous classical cesarean section) were excluded. Also, women who had contraindications to calcium gluconate use such as hypercalcemia, severe renal impairment, cardiac arrhythmia, or history of calcium containing renal stones were not included.

Before induction of labour all the participants were subjected to a complete clinical evaluation. Medical and obstetric histories were detailed including personal history, previous pregnancies and deliveries, first

trimester ultrasonography confirmation of gestational age, indication for labour induction, previous medical and surgical history and relevant family history.

A thorough physical exam was carried out, including a general evaluation for systemic diseases and vital signs including blood pressure, body temperature, heart rate and respiratory rate. Pallor, cyanosis and jaundice were also evaluated in the participants. Vaginal examination was done digitally to assess the favourability of the cervix (Bishop scoring system).

Complete blood count (CBC) and urinalysis were performed routinely. Fetal presentation, placental position, amniotic fluid index, fetal viability and estimated fetal weight were evaluated using obstetric ultrasonography.

Based on the induction regimen, participants were randomized to two groups. Group A (oxytocin + calcium gluconate): 100 pregnant women (10% glucose solution + calcium gluconate) received 10 mL of calcium gluconate diluted in 10 mL of 10% glucose solution and infused over 10 minutes intravenously. Right after the infusion of oxytocin was started at the hospital protocol (2 IU/500 mL 0.9% normal saline). A dose of oxytocin was slowly introduced until there were sufficient contractions.

In group B (oxytocin alone), 100 pregnant females were given oxytocin alone intravenously without calcium gluconate. All of the dose adjustments and administration of oxytocin were conducted as in the hospital procedure for Group A. In both groups, doses were adjusted at 30-minute intervals, to ensure good uterine activity, which was defined as 3–4 uterine contractions in 10 minutes, each lasting about 40–60 seconds. All the contractions and fetal condition were monitored by continuous cardiotocography (CTG) during induction.

The two induction regimens were compared in terms of maternal and neonatal outcome. The main outcomes were: induction to delivery interval and total oxytocin used. Other outcomes were postpartum hemorrhage (PPH) and neonatal intensive care unit (NICU) admission. Post-partum haemorrhage was reported in a categorical manner (yes/no) with no quantitative assessment of blood loss.

The analysis of the data was done with the aid of the Statistical Package for the Social Sciences (SPSS). Values for continuous variables were reported as mean ± standard deviation (SD) and frequencies and percentages for categorical variables. Independent-samples t-test was used for continuous variables and a Chi-square test / Fisher's exact test as appropriate for categorical variables in comparison between groups of oxytocin + calcium gluconate vs. oxytocin alone. A p value of < 0.05 was regarded as significant.

The study was conducted after getting the Ethics Committee from the Iraqi Board of Medical Specialization.Ethical approval was given from the Ethics Committee of the Iraqi Board of Medical Specialization before conducting the study. All participants gave informed written consent prior to signing up. Confidentiality and privacy of the participants' personal and medical information were respected during the study.

3. Results

Table 1 shows that, there were no statistically significant differences between groups as regard maternal age (27.9 ± 6.4 vs. 28.4 ± 6.3 years, $P = 0.578$), gestational age (39.07 ± 1.2 vs. 39.02 ± 1.1 weeks, $P = 0.759$), or parity distribution ($P = 0.843$).

Table 1. Comparison of Baseline Maternal and Obstetric Characteristics between the studied groups.

Variables	Oxytocin + Calcium (n=100)	Oxytocin Alone (n=100)	Test	P value
Maternal age (years) Mean ± SD	27.9 ± 6.4	28.4 ± 6.3	t = 0.5568	0.578
Gestational age (weeks) Mean ± SD	39.07 ± 1.2	39.02 ± 1.1	t = 0.3071	0.759
Parity				
Nulliparous (P0)	21 (21.0%)	19 (19.0%)		
Primiparous (P1)	19 (19.0%)	17 (17.0%)	$\chi^2 = 0.34$	0.843
Multiparous (P2+)	60 (60.0%)	64 (64.0%)		

Table 2 shows that the most common indication in both groups was postdate pregnancy (34%), followed by PROM (21%) and gestational diabetes (11%). Less frequent indications included oligohydramnios, preeclampsia, polyhydramnios, elective induction, chronic hypertension, decreased fetal movement, chorioamnionitis, and fetal death. There was no significant difference between the two groups for any of the indications.

Table 2. Comparison of Indications for Labor Induction Between the Studied Groups

Variables	Oxytocin + Calcium (n=100)	Oxytocin Alone (n=100)	Test	P value
Postdate	34 (34.0%)	34 (34.0%)		
PROM	21 (21.0%)	21 (21.0%)		
Gestational diabetes	11 (11.0%)	11 (11.0%)		
Oligohydramnios	9 (9.0%)	8 (8.0%)		
Preeclampsia	9 (9.0%)	9 (9.0%)		
Polyhydramnios	3 (3.0%)	3 (3.0%)	$\chi^2 = 0.054$	1.000
Elective	5 (5.0%)	5 (5.0%)		
Chronic hypertension	5 (5.0%)	5 (5.0%)		
Decreased fetal movement	2 (2.0%)	2 (2.0%)		
Chorioamnionitis	1 (1.0%)	1 (1.0%)		
Fetal death	0 (0.0%)	1 (1.0%)		

The comparison of labor induction details between the two groups in Table 3 showed that the mean dose of Oxytocin was significantly lower in the Oxytocin + Calcium group (6.08 ± 1.9 units) compared to the Oxytocin alone group (7.02 ± 1.9 units) with a highly significant p-value (<0.001). Additionally, the induction-to-delivery interval was significantly shorter in the Oxytocin + Calcium group (8.01 ± 1.9 hours) than in the Oxytocin alone group (8.82 ± 2.0 hours), with a p-value of 0.004.

Table 3. Comparison of Labor Induction Details Between the Studied Groups

Variables	Oxytocin + Calcium (n=100)	Oxytocin Alone (n=100)	Test	P value
Dose of Oxytocin (unit) Mean ± SD	6.08 ± 1.9	7.02 ± 1.9	t = 3.4983	**<0.001**
Induction-to-delivery interval (hours) Mean ± SD	8.01 ± 1.9	8.82 ± 2.0	t = 2.936	**0.004**

Table 4 shows the comparison of maternal and neonatal outcomes between the two groups showed no statistically significant differences. The incidence of primary postpartum hemorrhage was lower in the Oxytocin + Calcium group (19.0%) compared to the Oxytocin alone group (30.0%), but this difference did not reach statistical significance (p = 0.071). Similarly, rates of vaginal delivery (80.0% vs. 78.0%, p = 0.727) and cesarean section (20.0% vs. 22.0%) were comparable between groups. Regarding fetal outcomes, the proportion of healthy neonates (85.0% vs. 80.0%, p = 0.352) and admissions to the neonatal care unit (15.0% vs. 20.0%) did not differ significantly.

Table 4. Comparison of Maternal and Neonatal Outcomes Between the Studied Groups

Variables	Oxytocin + Calcium (n=100)	Oxytocin Alone (n=100)	Test	P value
Primary PPH	19 (19.0%)	30 (30.0%)	$\chi^2 = 3.271$	0.071
Outcome of Labour				
Vaginal delivery	80 (80.0%)	78 (78.0%)	$\chi^2 = 0.121$	0.727
Cesarean section	20 (20.0%)	22 (22.0%)		
Fetal Outcome				
Healthy	85 (85.0%)	80 (80.0%)	$\chi^2 = 0.866$	0.352
Admitted to the neonatal care unit	15 (15.0%)	20 (20.0%)		

Table 5 shows at a cut-off value of 9.0 hours, induction-to-delivery time showed a sensitivity of 62.7% and specificity of 59.5%, demonstrating a statistically significant ability to predict successful labor induction (AUC = 0.605, p = 0.037).

Table 5. ROC Analysis of Induction-to-Delivery Time for Predicting Successful Induction of Labor

Variable	Area (AUC)	Cutoff Value	Sensitivity	Specificity	Std. Error	Asymptotic Sig. (P value)	95% CI Lower Bound	95% CI Upper Bound
Induction-to-delivery time (hours)	0.605	9.00	62.7%	59.5%	0.048	**0.037***	0.511	0.699

4. Discussion

Labour induction is a common obstetric procedure that includes initiating uterine contractions through medical or mechanical methods before the spontaneous onset of labour [11] It is generally indicated when the expected benefits of delivery outweigh the risks associated with continuation of pregnancy for either the mother or the fetus. Common indications include premature rupture of membranes without labour, gestational hypertension, oligohydramnios, non-reassuring fetal status, post-term pregnancy, and maternal medical conditions such as chronic hypertension and diabetes mellitus [12]. Oxytocin remains the main and most commonly used pharmacological agent for both induction and augmentation of labour. It acts by binding to oxytocin receptors, leading to increased frequency and strength of uterine contractions.

Various oxytocin infusion regimens and dosing protocols have been consider in an attempt to optimize labor outcomes while minimizing adverse effects [13]. Effective uterine contraction depends largely on calcium. In myometrial smooth muscle, rising intracellular calcium levels enable actin–myosin interaction, resulting in organized and efficient contractions [14]. For this reason, this study was designed

to evaluate the efficacy of oxytocin combined with intravenous calcium gluconate compared with oxytocin alone for induction of labor.

The present study demonstrated no statistically significant differences between the two groups regarding maternal characteristics, including maternal age (27.9 ± 6.4 vs. 28.4 ± 6.3 years, p = 0.578), gestational age at delivery (39.07 ± 1.2 vs. 39.02 ± 1.1 weeks, p = 0.759), or parity distribution (p = 0.843). These findings indicate appropriate comparability between groups and are consistent with those reported by Farber et al., Yaqub et al., and Cai et al. [15,16] who similarly found no significant baseline differences between women receiving oxytocin with calcium and those receiving oxytocin alone.

In our study, post-term pregnancy was the most common indication for labour induction in both groups (34%), followed by premature rupture of membranes (21%) and gestational diabetes mellitus (11%). Less frequent indications included oligohydramnios, preeclampsia, polyhydramnios, elective induction, chronic hypertension, decreased fetal movement, chorioamnionitis, and fetal death, with no statistically significant differences between groups. A similar pattern has been reported by Rayamajhi et al., Yadav et al. [17,18] who identified post-term pregnancy and PROM as the leading indications for labour induction in their study.

Regarding labour induction outcomes, the present study demonstrated that the mean total dose of oxytocin required was significantly lower in the oxytocin plus calcium group compared with the oxytocin-only group (6.08 ± 1.9 vs. 7.02 ± 1.9 units, p < 0.001). In addition, the induction-to-delivery interval was significantly shorter among women who received calcium supplementation (8.01 ± 1.9 vs. 8.82 ± 2.0 hours, p = 0.004). In this study, calcium supplementation was associated with a stronger uterine response to oxytocin, likely through enhanced myometrial contractility. Similar findings were reported by Cai et al [19]. who observed a shorter induction-to-delivery interval in women receiving oxytocin combined with calcium; however, it should be noted that this study was later retracted, and its findings should therefore be interpreted with caution.

The incidence of primary postpartum hemorrhage was found to be lower in the oxytocin plus calcium group (19.0%) than in the oxytocin-only group (30.0%) but these differences were not statistically significant (p = 0.071). Physiologically, this finding seems to be consistent with known mechanisms, such as increased uterine tone, which could decrease uterine atony and postpartum bleeding. This would support this explanation, a randomized controlled trial by Ansari found a potential decrease in blood loss due to uterine atony.

with calcium supplementation [20]. The results for maternal and neonatal outcomes (such as mode of delivery, neonatal health, and neonatal unit admission) were similar for the two groups, suggesting that the use of calcium did not have a negative impact on maternal or neonatal safety. Moreover, in this study, induction to delivery time was found to have moderate predictive value for successful induction with an area under the curve of 0.605 (p = 0.037) as determined by ROC analysis. Overall, the findings suggest that the use of IV calcium alongside oxytocin during labor induction could have a modest yet statistically significant impact on labor efficiency, by decreasing the amount of oxytocin needed and the length of labor, without any associated risks to the mother or infant.

5. Conclusions

The use of calcium gluconate for labour induction together with oxytocin was found to be significantly associated with reduced oxytocin administration and a shorter induction-to-delivery interval compared to oxytocin alone in the current study. Women taking calcium did not have a statistically significant difference from women who were not taking calcium in terms of PPH incidence. Moreover, there were

no significant difference between the two groups in terms of mode of delivery or neonatal outcomes. The results indicate that calcium gluconate may enhance the efficiency of labour induction by decreasing the doses of oxytocin required, the length of labour, and without increasing the incidence of maternal or neonatal complications in the population studied. There is need for further large scale clinical trials to confirm these results and make a decision on the effectiveness and safety of calcium gluconate as an adjunct during labour induction in the future.

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