

Maternal and Neonatal Oxytocin Levels During Cesarean Section With or Without Labor Pain and Puerperal Complications

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The role of Oxytocin (OXT), found in the cerebrospinal fluid (CSF), circulation and umbilical cord blood, in regulation the timing and initiation of labor and puerperal complications is controversial. This study was designed to clarify the possible role of maternal and fetal OXT in the onset of labor and puerperal complications by comparing the parameters in two groups of pregnant women undergoing cesarean section (CS) after the onset of labor, or elective CS.

Material and Methods: In this study, OXT levels were measured in plasma, CSF and umbilical cord in two groups of pregnant women who underwent CS, one group with the onset of labor and the other without it. Puerperal complications were detected and the results of both groups were compared.

Results: No significant differences were noticed between the two groups in the plasma, CSF, and umbilical cord levels of OXT ($p > 0.05$). The amount of postoperative hemorrhage and intensity of after pain in the group with the onset of labor were less than those without labor ($p < 0.05$). In the group with contractions the uterine involution time and lochia were less than in the other group ($p < 0.05$).

Conclusion: The results of this study showed

that there were no differences in maternal and neonatal OXT concentrations among the groups. It was also concluded that onset of labor reduced puerperal and neonatal complications.

Key Words: Oxytocin, Puerperal complications, Labour

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Introduction

Physiological processes in human pregnancy that result in the initiation of parturition and the onset of labor, are poorly defined.¹ Most investigators have suggested a role for uterotonins,² while other researchers have speculated that the mature human fetus is the source of the initial signal for the commencement of the parturition process.³ It is clear, however, that the onset of labor represents the culmination of a series of biochemical changes in the uterus that result from endocrine and paracrine signals coming from both the mother and the fetus.⁴ The relative role of their contribution in regulating parturition, pregnancy outcome and postpartum complications are not yet fully understood.⁵ On the other hand, some pregnancies

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need elective cesarean section without the onset of labor and some of the neuroendocrine changes that occur during parturition and active phase of labor do not take place in these patients.^{4,5} Studies have shown that oxytocin at high levels is found at the time of labor in maternal plasma, CSF, and cord plasma.^{6,7} In one study, Leake et al showed that maternal plasma OXT levels remain low during pregnancy until late in the second stage of labor.⁸ In addition to its classical effects on uterus contraction, during parturition and milk ejection during lactation, oxytocin has several other effects may help to maintain the health of pregnant women and to ensure the optimal well being of the newborn.⁹⁻¹⁴

Oxytocin concentration in CSF is higher than the basal OXT concentration in plasma.¹⁵ Plasma OXT does not readily cross the blood-brain barrier. Animal studies show that there is no relationship between the variations in blood OXT levels and CSF OXT concentrations.¹⁶ During parturition, an increase in the concentration of OXT in CSF may play a major role in establishing maternal behavior.^{2,17}

Human fetuses are known to synthesize OXT in late pregnancy.¹⁸ Several investigators have considered a role for fetal OXT in the initiation of parturition. The human fetal pituitary contains OXT in increasing concentrations 14 weeks of gestation onwards. Concentrations of OXT are higher in the umbilical serum than in maternal serum and are higher in umbilical arterial than in the venous circulation. The role of cord blood OXT has not been established yet. The consensus among investigators is that fetal OXT is unlikely to play a role in regulating the timing of human parturition.³ The role of OXT in parturition is also controversial. Results of several studies suggest that OXT has little involvement in the initiation of labour. Recently it is reported that in mice, OXT is essential for nursing but is not required for parturition or reproductive behavior in this species.^{19,20} It has become apparent that the con-

ceptus is a dynamic unit and the maternal organism responds passively to signals emanating from embryonic-fetal tissues.²¹ The contributions of the conceptus to maternal adaptation to pregnancy and parturition are enormous, but the role of umbilical OT in parturition is not quite clear.²²

The aim of this study was to compare the alternation of maternal plasma, CSF and umbilical cord levels of OXT in pregnant women at term with or without the beginning of contractions and to detect the effect of labor onset on puerperal complications.

Materials and Methods

Patients included in the present study were selected from a cohort scheduled to undergo cesarean section between August 2003 and April 2004. Mothers with term infants (38 weeks gestation or more) were eligible for recruitment into the study. Samples of mothers were matched according to the parity of the mothers. The study was conducted at Al-zahra Teaching Hospital affiliated to the Tabriz University of Medical Sciences, Tabriz, Iran. All patients gave informed consent. The study protocol was approved by the local Ethical Committee.

Two groups of thirty pregnant women each were included in the study. The first group included those without contraction scheduled for elective cesarean section under spinal anesthesia. The second group consisted of those with three 45-second contractions per 10 minutes, and 4 cm or more cervical dilatation, who were also scheduled for the cesarean section under spinal anesthesia. Patients who received OXT for induction of labour had preterm delivery twins, and premature rupture of membranes, and in the phase 2 of parturition, were excluded. In each group, the blood (2ml) was sampled from a maternal peripheral vein at the time of the setting an intravenous line and 0.5 ml CSF was collected through the spinal needle following insertion and prior to injection of the intrathecal anesthetic agent and also 1 ml of

umbilical artery blood was collected just after delivery. In order to prevent OXT degradation, each sample was taken and collected in a chilled tube containing 40 µl of the OXT inhibitors 1, 10 phenanthroline (125 mmol/l) and ethylene diamine tetra acetic (1 mol/l). After centrifugation in a pre-cooled centrifuge, the plasma or supernatant was collected and analyzed in the same day. Hormone concentrations were measured by the ELIZA method using a correlate-EIA OXT enzyme immunoassay kit, catalog No. 900-024. Assay Designs, Inc-U.S.A. Exogenous OXT was infused for all mothers after clamping of the cord. The complications after childbirth including postpartum hemorrhage, postoperative pain, and amount of lochia, mastitis and also neonatal Apgar score and involution time of uterus were determined in both groups and the results compared.

Descriptive statistics were done for the related variables of interest. Categorical variables were compared using chi-square or Fisher exact tests when appropriate. The measured values are given as mean±SD. ANOVA test was used for intra group com-

parison. To compare means, a t-test was carried out. For all statistical analyses, the differences were considered statistically significant at $p < 0.05$. Statistical analysis was performed using SPSS software (Spss 13.0; SPSS, version for windows).

Results

Some characteristics of the pregnant women who underwent cesarean section with and without contraction are shown in Table 1. No significant differences between mean age, mean pregnancy age and mean number of pregnancies were observed between the two groups ($p > 0.05$).

As summarized in Table 2, the OXT concentration was similar in both groups, and did not change with labor. No marked differences were noticed in OXT levels of maternal plasma and CFS and that of umbilical artery blood in either of the 2 groups studied ($p > 0.05$). There was no correlation between maternal CSF and plasma OXT concentration, within groups or between groups.

Table 1. Some characteristics of the contraction positive (+) and negative (–) pregnant women.

Characteristics	contraction(+) (N=30)	contraction(–) (N=30)	P value
Age* (years)	27.2±4.8	29.5±5.5	NS
Age of pregnancy (weeks)	38.1±2.9	38.8±0.75	NS
Number of pregnancies*	3.40±1.7	2.8±1.3	NS

* Data are given as means ± SD

Table 2. Oxytocin level in maternal serum, CFS and umbilical cord serum of the cases with and without labour

Samples	Serum oxytocin level		P value
	Labour (pg/mL)	Non-labour (pg/mL)	
Maternal serum*	62.4±31	70.1±29	NS
Maternal CFS*	53.9±16	59.3±11	NS
Umbilical cord serum*	79.2±13	75.3±17	NS

* Data are given as means ± SD

Table 3. The initiation time of milk secretion, active milk secretion and period of lochia in the groups studied

Parameters	Contraction((+)	contraction(-)	P value
Beginning of milk secretion (days)	1.1±0.34*	1.6±0.71	0.001
Active milk secretion (days)	3.3±84	6.1±0.88	0.001
Lochia rubra (days)	17.3±9.8	23.6±13.8	0.05
Lochia serosa (days)	9.3±5	11.5±5.6	0.11
Lochia alba (days)	8.7±4.7	14.5±7.1	0.01

*Data are given as means ± SD of days

Table 4. Severity of postpartum hemorrhage and intensity of after pain in both groups

Parameters	Contraction(+)			Contraction(-)			P value
	mild	moderate	severe	Mild	moderate	severe	
Hemorrhage	17	6	4	6	18	6	0.03
After pain	9	13	1	4	11	15	0.01

Comparing the mean time of beginning of milk secretion and active milk secretion of both groups, significant differences were noticed (Table 3). Beginning of the milk secretion time and its active secretion in the group with contraction were higher than the group without contraction ($p < 0.05$).

The period of lochia were determined in both groups and compared; as shown in table 3, significant differences were found in duration of rubra and alba discharges but no differences were observed in lochia serousa.

The involution time in both groups were also compared. In both cases with and without contraction, complete involution occurred in 40.6 ± 5.8 and 43.6 ± 3 days, respectively ($p > 0.24$).

The number of patients suffering from postpartum hemorrhage and after pain and the severity of the hemorrhage and intensity of the pain in the both groups are compared in table 4.

The frequencies of moderate and severe hemorrhage in non-labor cases were significantly higher than contraction positive cases.

The frequency of severe after pain after elective cesarean section was significantly higher.

Other variables such as Apgar score, neonatal hyperbilirubinemia, thrombophlebitis, wound infection, breast engorgement and sexual desire were evaluated in both groups studied, but no significant differences were observed between the groups ($p < 0.05$).

Discussion

The physiological mechanisms underlying the onset and progress of spontaneous labor remain obscure.²¹ Since exogenous administration of OXT results in uterine contractions that are clinically indistinguishable from those of spontaneous labor it is considered important. The role of oxytocin administration after delivery for reduction of blood loss and prevention of uterine atony is well known.²³ During labor, an elevation in plasma level of OXT has been reported.⁷ The hormone is the first uterotonic implicated in the initiation of parturition, but recently it has been reported that the hormone does not ap-

pear to play a role in initiation of parturition.²⁴ Once phase 1 of parturition is in place, however, OXT may be one of several participants in ensuring the effectiveness of active labor. Oxytocin seems to be very important in the active phase of parturition.⁷

Late in pregnancy, at some time during phase 1 of parturition, there is a striking 50 fold or more increase in the number of OXT receptors in myometrium.²⁴ This coincides with the increase in uterine contractile responsiveness to OXT.⁷ In addition, prolonged human gestation is associated with delay in this increase in receptors.²⁴ Failure of the uterus to contract properly following delivery is a common cause of obstetrical hemorrhage and is prevalent in patients with the overdistended uterus and inadequate contractions; this may show the role of adequate contractions before delivery in good involution of uterus after delivery. Blanks and Thornton reported that during the first stage of labor determination of plasma OXT has produced widely differing results, usually attributed to the pulsatile release of the hormone.¹ Many studies in human subjects neglected to measure OXT serially throughout labor and most studies failed to document OXT fluctuation.^{2,24,25}

During the second stage of labor, uterine contractions often increase in frequency and intensity. Determination of plasma OXT in the second stage of labor has also produced conflicting results. Some authors reported an increase,²⁶ whereas others have failed to document a change.²⁷

In this study detectable, but not significantly different, levels of OXT were observed in pregnant women at term with and without contractions. Our results are in agreement with those of reported by Thornton et al⁷ and may suggest a role for the hormone at term with or without labor. No differences in the plasma levels of OXT between the two groups studied may raise questions about the function of OXT during labor.

The amount of OXT entering from the posterior pituitary to the maternal circulation is

small.²⁶ The hormone is released from the pituitary in two situations, during the final stages of labor in response to stretching of lower genital tract (Fergusson's reflex) and in the puerperium in response to suckling.

Bergan et al, obtaining serial samples from women during labor showed that basal OXT levels are unmeasurable initially but the number of samples with detectable levels increase as labor progress.²⁵

In the present study, no meaningful differences between the levels of plasma, CFS and umbilical OXT in women before and after the onset of labor were found.

Oxytocin is also released by the fetus during the expulsive stage of labor but its significance is not clear.³ The differences between OXT levels of umbilical OXT in the two groups were not marked. We have no data about the level of OXT during the expulsive stage because all cases underwent cesarean section. The role of OXT in the fetus-infant is not clear and must be elucidated. Fetal OXT may be responsible for the immediate secretion of ACTH in response to some kinds of stress in fetal sheep^{31,32} while in humans, under certain physiological conditions, OXT might control ACTH release.^{28,29}

Studies showed that transient tachypnea of the newborn (TTN) was higher in infants delivered by elective CS without preceding labor.³⁰

Treatment with increasing doses of OXT provoked sedative effects and antipyretic effects. In humans, intrathecal injection of OXT was effective in treating low back pain. Oxytocin levels were elevated in the CSF of patients with chronic low back pain, perhaps a compensatory response to the painful condition.^{34,35} This may suggest a role for OXT in CFS in pregnant women who are in labor, but the results of this study showed no significant differences in CFS levels of OXT between the two groups. Perhaps the role of OXT in CFS is not dependent on the manner of delivery or beginning of contractions. The hormone may control the pain and surveil-

lance under physiological condition in a specific manner.⁸

Oxytocin is released during suckling and causes contraction of myoepithelial cells in the alveoli and ducts of the breast and hence aids in milk ejection. The association of breast feeding with the pain of uterine contraction is a familiar reminder of this suckling-induced of OXT.³³ We observed significant differences between the beginning time and active milk secretion in the mothers with and without contractions. In earlier reports it has been documented in humans, breast-feeding within 1 hour of birth, when OXT levels are high, supports a long-lasting mother-infant bond and has a beneficial effect on the development of the child.²⁶

The exact mechanisms involved in uterine involution are a subject of debate. They may be hormonal and relate to withdrawal of placental hormones. The results of this study showed that the effect of labor on the involution time is significant and it may be related to the paracrine effect of OXT.²⁵ The duration of lochia and hemorrhage after parturition were different in the two groups and shorter in the group with contraction. The results confirmed the importance of contrac-

tions and onset of spontaneous labor prior to cesarean section.

In conclusion, the findings of the present study indicate that the onset of labor may have an important role in reducing puerperal complications. Events connected with mode of parturition do not affect the OXT levels of maternal and neonatal plasma, and maternal CSF, but do affect the puerperal complications. There is a possible role for mother's and newborn's OXT and further comprehensive studies are needed to compare the levels of maternal and neonatal plasma OXT at different stages of pregnancy termination. It is necessary to consider an effect for fetal OXT on the regulation and time of parturition in term and preterm pregnancies with and without labor.

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