

## Oxytocin level in pregnancy

**Aayush Bahl<sup>1</sup>, Nipanshi Tyagi<sup>2</sup>, Pinki Rani<sup>3</sup>,  
Sanhita Banik<sup>4</sup>, Soumya Sharma<sup>5</sup>**

1 Amity Institute of Biotechnology, Noida, India

2 Amity Institute of Biotechnology, Noida, India

3 Amity Institute of Biotechnology, Noida, India

4 Amity Institute of Biotechnology, Noida, India

5 Amity Institute of Biotechnology, Noida, India

### **Abstract**

Oxytocin is a hormone secreted by pituitary glands. It has several effects related to pregnancy. It is proved to delay or somehow control the post parturition symptoms and even the process like lactation. It is very important for the acclimatization towards the new motherhood and new care to be developed towards the new born infant. The stressors include both physical and psychological factors. It also plays a major role in the lactation which is released upon the suckling of the infant. If there is absence of oxytocin level during pregnancy the connection between mother and the infant is not felt. It is basically a connection.

**Keywords-** *Acclimatization, Hormone, Oxytocin, Parturition, Pregnancy*

### **1. Introduction and background history**

#### 1.1 Oxytocin

One particular hormone – oxytocin – has attracted attention among researchers for its multiple roles in reproduction, social interaction, stress management and parental caregiving. Also known as “Cuddle hormone” “Love hormone” and “Trust hormone”. It is hormone released by the pituitary gland and is a nonapeptide produced by hypothalamic neurons, that causes higher contraction of the uterus during labor and stimulates ejection of milk into ducts of breasts. Pleasant touch (via massage or gentle strokes) has also been found to increase the level of oxytocin. Being very precise, we do not yet have any scientific trials documenting what happens to the oxytocin level in the person who gives the massage or provides the pleasant touch, in this case the mother or the father. However, the typical oxytocin effects (lower blood pressure and reduction in stress hormones) have been found in the person giving the massage, suggesting that the level of oxytocin does increase.

As early as 1906, Sir Henry Dale discovered this hormone in the brain and gave it the name oxytocin, from the Greek (oksos: quick and tokos: birth = swift birth). He later learned that oxytocin was also involved in breastfeeding, so for many years, oxytocin was tied to women and to reproduction. Oxytocin also improves the nutrient absorption and digestion in the breastfeeding mothers. Wounds were found to heal faster when oxytocin was administered. Its secretion is important in parturition and essential for lactation. Pitocin, a synthetic form

of oxytocin that is intravenously delivered to pregnant women, is meant to induce labor when they are overdue. It can also augment difficult labor by strengthening and speeding up uterine contractions, and reduce excessive blood loss after vaginal birth. It has several side effects also and the major side effect is fluctuation in the heartbeat.

#### 1.1.1 Oxytocin a energy storing hormone-

At the beginning of pregnancy oxytocin level increases. This increase alters metabolism and women puts up weight. This provides energy store which can be used later when the foetus is growing faster and needs more calories. This process is highest during the first trimester.

#### 1.1.2 Oxytocin as a caution promoting hormone-

The sudden increase and storage of these hormones encourage a mother to be more cautious from any bad or harmful environment. They have sudden reflexes and can keep be womb safe from outside environment.

#### 1.1.3 Oxytocin decreases stress-

When it comes to stress, oxytocin works in a curious way. The first and short term effect of a supplement of oxytocin is an increase in blood pressure, heart rate and stress hormones. The initial stress of social situations in our early evolution was best served by being instantly on the alert, until we had decoded the situation. An interesting illustration is in tango dancing. It is customary to dance at least four dances together, because the stress associated with touching a new dance partner will usually disturb the first few dances. It is linked to the reward system in brain of human body . This area of the brain is primarily concerned with basic survival. Within the mesolimbic pathway is an area called the ventral tegmental area (VTA). The VTA projects to the nucleus accumbens (thought to be the reward center).

#### 1.1.4 Oxytocin creates a comfort zone for baby

The sucking, skin-on-skin activity of breastfeeding triggers an oxytocin release in both baby and mother. It's a natural pacifier. Touching and interacting with your baby, having your baby physically close to you, by either carrying her/him in your arms or in a baby carrier, seems to create a virtual circle where the level of oxytocin is gradually increased in both of you. The frequency of hugs between mother and father has also been found to be related to their oxytocin levels as well.

## 2.STRUCTURE OF OXYTOCIN:

Oxytocin is a nonapeptide , peptide having nine amino acids-tyrosine - isoleucine - glutamine - asparagine - cysteine - proline - leucine - glycine (CYIQNCPLG). It's chemical formula is  $C_{43}H_{66}N_{12}O_{12}S_2$

It has a molecular mass of 1007daltons. Sulphur Bridge is formed by the cysteine residues at position 1 and 6. Structurally it is very similar to vasopressin only that it differs by two amino acids

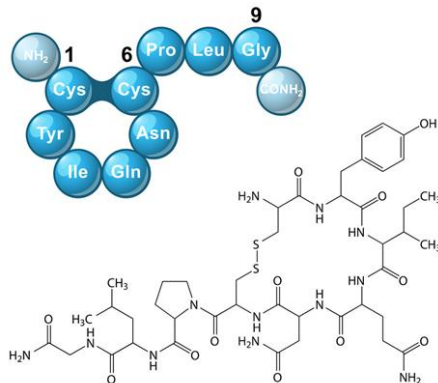


FIGURE: Molecular Structure of Oxytocin. (VectorStock)

### 3.1Metabolism of Oxytocin during pregnancy

The maternal hypothalamic-pituitary-adrenal (HPA) axis undergoes some kind of adaptations during pregnancy and lactation to prevent adverse effects. The (HPA) axis consists of the corticotropin-releasing factor (CRF) neurones in the parvocellular paraventricular nucleus (pPVN) also produces vasopressin that gets imbibed in the hypophyseal portal system. These set of neurosecretory neurons stimulate the portal system by stimulating the CRF1 and V1B receptor to release ACTH by anterior pituitary gland to release excessive quantities of glucocorticoids by the adrenal system which affects the immune system and metabolic functions of the body. Stressors (Psychological or physical), the signals that actually affect the bodily functions override these mechanisms. Extensive glucocorticoid feedback mechanisms help in lowering stress levels.

#### ➤ Early pregnancy-

The early salivary cortisol level is lower when compared to later stages of pregnancy because of the fact that the increased glucocorticoid levels may cause miscarriage which is again increased in between 1-3 weeks. But there is found to be a little response of the HPA axis during early pregnancy because it might jeopardize pregnancy.

#### Late pregnancy-

In late pregnancy it was difficult to assess the results of the maternal HPA axis because the placenta also secretes the peptides.

➤ Parturition-

The circulating HPA axis hormone levels are increased during expulsion and dilation stages but this is not necessarily maternal response as human placenta and endometrium system also performs the same functions.

Central oxytocin is the inhibitor of HPA axis but during parturition although there is increased secretion of the oxytocin in the brain there is HPA activity still persisting.

➤ Lactation-

It is also a HPA axis hypoactivity state but in pregnancy it is maintained by the suckling of the infant which excites the oxytocin and prolactin secretion. Suckling also increases the ACTH and the corticosterone secretion which stimulate the cells for milk production. In lactating women the reduced ACTH and corticosteroid secretion on the suckling is the indication of increased oxytocin production. But it was proved that centrally released oxytocin may act to reduce the stress conditions but not during lactation.

### 3.2 Plasma Oxytocin Concentration during Pregnancy is associated with Development of Postpartum Depression

Postpartum depression (PPD) affects a significant percentage of the pregnant women in the society but non-peptide oxytocin (OXT) has some relation with the symptoms of PPD and the acclimatization of the new set of condition for the maternal connections. PPD has significant effects on the new born child as they are believed to develop mental disorders in later stages of life.

### 4. Effects of Oxytocin during Pregnancy-

#### Effects of oxytocin

1. On fetal and placental growth
2. On maternal weight gain
3. Accumulation of body fat
4. Role of IGF (INSULIN LIKE GROWTH FACTOR) which is mediated by inducing oxytocin. Pregnant rat were injected with oxytocin once a days subcutaneously during gestational period. During pregnancy there had higher circulating levels of IGF-I, fetuses, larger placentas, and newborn pups and also contained less body fat at last of pregnancy. Food - restricted pregnant rat which is treated with oxytocin had no effect on fetal and placental growth.
5. Food restriction attenuates the normal increase in **Insulin like growth factor** binding with protein-3 protease proteolysis during pregnancy. This shows oxytocin may affect maternal adaptations to pregnancy and also stimulate fetal growth.

### 5. Deficiency of Oxytocin and its Side Effects-

If there is Deficiency of oxytocin inside us then we would not feel any connections with others. If there is the deficiency of oxytocin in the amygdale of the brain in which social memory is stored, it will produce

- Anxiety
- fear

### 5.1 Oxytocin is a hormone which is normally injected in pregnancy

1. For labor induction
2. To control bleeding after delivery.
3. Helps in milk secretion during breastfeeding.

#### 5.1.1. Oxytocin for labor induction

It is the stimulation of uterine contractions during pregnancy before labor begins on its own to achieve a vaginal birth.

Labour induction is done

- Postterm pregnancy: when anyone is approaching two weeks beyond their delivery date and natural labor is not started.
- When there is an early rupture of the membrane and water has broken but labor is not started.
- During uterine infection
- When the weight of the baby is less than the expected weight
- Oligohydramnios:- when surrounded amniotic fluid is very less
- Placental abruption. When the placenta peels away either partially or completely from the inner wall of the uterus before delivery.

#### 5.1.2. Oxytocin to control bleeding during pregnancy

Oxytocin tightens the blood vessels of the uterus that controls the bleeding after delivery. It is used to contract the uterus, which helps to close uterine blood vessels. From the tightened blood vessels, less blood is released.

#### 5.1.3. Oxytocin in breastfeeding

Sufficient amount of oxytocin causes contraction of cells around the alveoli and milk ducts, in preparation for the suckling. Insufficient amount of oxytocin may result in failure of lactation.

#### 5.1.4. Side effects

High dose intervention with oxytocin may cause many harmful effects on the health of mother and fetus.

Such as

- Uterine tachysystole: - it is a condition when uterine contracts excessively than the normal rate, during pregnancy. It is defined as 6 contractions in a 10-minute period.
- impairment of fetal heart rates
- This occurs due to the reduction or interruption of the blood flow to the intervillous space during contractions
- fetal hypoxemia (It is a condition when the fetus is deprived of an adequate supply of oxygen).
- Fetal acidemia
- Allergic reaction: itching or hives
- Swelling in your face and hands
- Mouth and throat swelling
- Tightness of the chest

- Respiratory problem
- Unusual bleeding
- oversensitivity to the emotions of others.

## 6.Diagnosis of Oxytocin Level-

### 6.1Oxytocin ELISA methodology

#### 6.1.1Method of detection

Colorimetric is the method of detection of oxytocin level and presence

#### 6.1.2Precision-

Sample	n	Mean	CV%
Low	20	39.9pg/ml	12.6%
High	20	363.7pg/ml	13.3%

#### 6.1.3Type of sample used

Cell culture supernatant, Serum, Plasma, Milk, Urine

#### 6.1.4Type of assay

Competitive

#### 6.1.5Sensitivity

15 pg/ml

#### 6.1.6Range

15.7 pg/ml - 1000 pg/ml

Sample	Average
Serum	104
Saliva	90
Urine	111

#### 6.1.7Assay time

25hr

#### 6.1.8Duration

Multiple steps standard assay

### 6.1.9 Reactivity of species

**Reacts with:** Human

- Oxytocin *in vitro* competitive ELISA (Enzyme-Linked Immunosorbent Assay) kit is designed for the quantitative measurement of Oxytocin in Human Serum, Saliva, Tissue Culture media, Urine, Cerebrospinal Fluid.
- A goat anti-rabbit IgG antibody has been precoated onto 96-well plates.
- Standards are added to the wells, along with an alkaline phosphatase (AP) conjugated-Oxytocin antigen and a polyclonal rabbit antibody specific to Oxytocin.
- After incubation the excess of reagents are washed away.
- pNpp substrate is added and after a short incubation the enzyme reaction is stopped and the yellow color generated is read at 405 nm.
- The intensity of the yellow coloration is inversely proportional to the amount of Oxytocin captured in the plate.
- Oxytocin is a neuro-hypophysial peptide which is produced in the paraventricular nuclei of the hypothalamus. This is stored in the posterior pituitary.
- The molecule consists of 9 amino acids which are linked with a [1-6] disulfide bond and by a partially flexible carboxyamidated tail. Oxytocin is also functions as a neurotransmitter, social/sexual behavior and is important in male reproductive physiology and may be involved in neuropsychiatric disorders.

### 6.1.10 Cross Reactivity

Compound name	% Cross Reactivity
Mesotocin	7.0
Oxytocin	100
TRH	<0.2
Somatostatin	<0.2
Met-Enkephalin	<0.2
VIP	<0.2
Lys8-Vasopressin	<0.2
Arg8-Vasopressin	<0.2
Arg8-Vasotocin	7.5
Ser4,Ile8-Oxytocin	<0.2
Tocinoic acid	<0.2
Melanostatin	<0.2
Growth Hormone	<0.2

COMPONENTS OF THE KIT

Components	1 x 96 tests
Oxytocin standard	1 x 0.5ml
Assay Buffer	1 x 27ml
Goat anti-rabbit IgG Microplate (12 x 8 wells)	1 unit
Oxytocin Alkaline Phosphatase Conjugate	1 x 5ml
Oxytocin Antibody	1 x 5ml
20X Wash Buffer Concentrate	1 x 27ml
Plate Sealer	1 unit
pNpp Substrate	1 x 20ml
Stop Solution	1 x 5ml

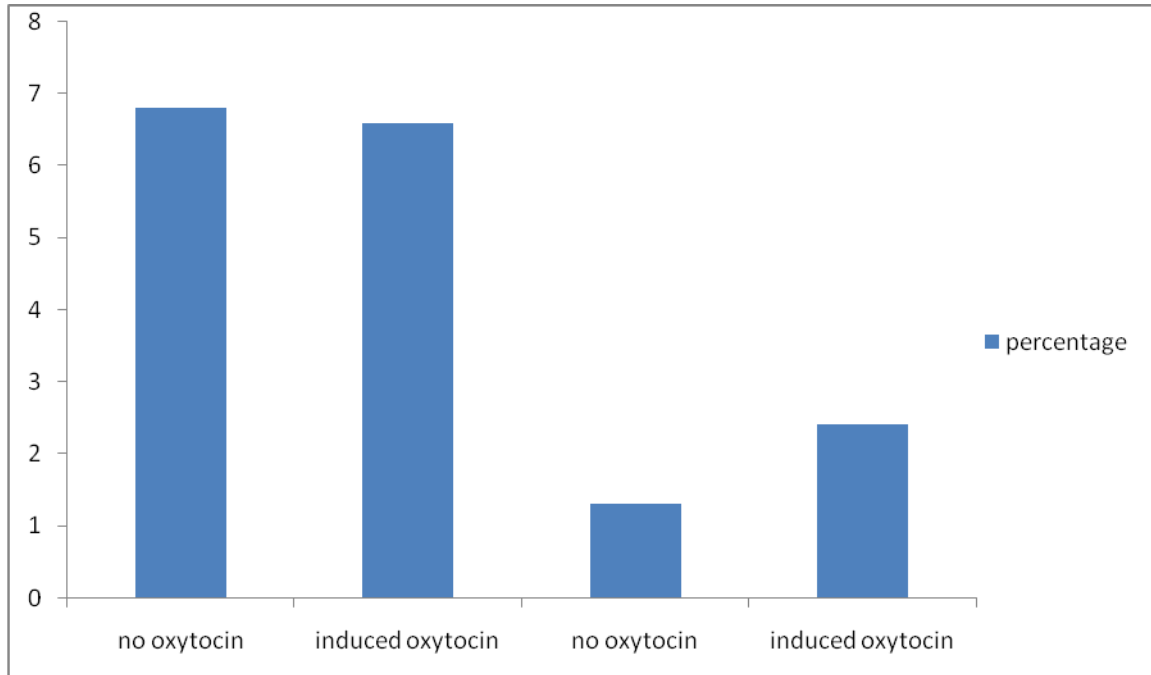
- The high levels of oxytocin which is reported by immunoassays which is not extracted form of plasma probably arise from plasma protein interfere with antibody binding that produces a high and wholly baseline.
- No more than a random number generator which return arbitrary values with a high variance.

**EXAMPLE: Survey**

This study shows the variation in oxytocin endogenous levels in postpartum and pregnancy state. We also explored the associations between oxytocin levels and delivery variables. Study includes 272 mothers in their 1<sup>st</sup> trimester of pregnancy. The blood samples were examined during 1<sup>st</sup> and 3<sup>rd</sup> trimester of pregnancy and at 8 weeks of postpartum. As a result, the survey shows in most women, levels of circulating oxytocin increased from the first to third trimester of pregnancy followed by a decrease in the postpartum period. Oxytocin levels varied considerably between individuals, ranging from 50 pg/mL to over 2000 pg/mL. The oxytocin level changes from the 1<sup>st</sup> trimester to 3<sup>rd</sup> trimester. Oxytocin levels in the third trimester of pregnancy predicted a self-reported negative labor experience and increased the chances of having an epidural. Intrapartum exogenous oxytocin was positively associated with levels of oxytocin during the postpartum period. Our exploratory results suggest that circulating oxytocin levels during the third trimester of pregnancy may predict the type of labor a woman will experience. The quantity of intrapartum exogenous oxytocin administered during labor predicted plasma oxytocin levels 2 months



postpartum, suggesting a possible long-term effect of this routine intervention, the consequences of which are



Almost two thirds of the pregnant women received oxytocin during the early stages of labor (induction or augmentation of labor) (N=6,991). In a total of 1,221 vaginal deliveries (10.8%), blood loss was  $\geq 500$  ml (moderate PPH) and in 209 (1.86%) vaginal deliveries the amount of blood loss was  $\geq 1,000$  ml (severe PPH). Among all 11,323 vaginal deliveries, only 40 (0.35%) received blood transfusion. However, when we analyzed only the subpopulation that received AMTSL, we found that moderate PPH was 6.7% (275/4,084) and severe PPH was 1.2% (50/4,084). Only 12 patients out of the 4,084 that received AMTSL required blood transfusion (0.29%).

**Graph:** Use of oxytocin on 1<sup>st</sup> and 2<sup>nd</sup> laborst Moderate PPH

SeverePPH

**7.CaseStudies**

**Case 1: Identification**

The 19-year-old G1 P0 female, admitted in 39 weeks during active labor with 3 cm dilatation after uncomplicated pregnancy. Patient has normal progress in cervical dilatation with a prolonged 2<sup>nd</sup> stage which requires oxytocin increasing and ultimately vacuum extraction (VE) delivery of a 4600-gram neonate. Placenta delivered within 5 minutes. Oxytocin was started by diluting 20 U in D5RL and running at 125 cc/hr.

Patient passed large clots in 20 minutes after delivery. Normal BP 120/80, pulse 90. Uterus should be soft and up to the umbilicus.

Patient received: 1 ampoule of carboprost in every 15 minutes IM. Patient was not examined. Oxytocin mixture was opened widely. Bleeding doesn't stop. BP 90/60, pulse 130.

1. Stepwise identification of bleeding source by OB exam

2. Dosing carboprost
3. What blood products to order and in what amount
4. What other lab studies other than hematocrit

Response time:

- i. Anesthesia
- ii. Blood bank
- iii. Surgeon

Pelvic examination reveals bleeding from cervical OS with no tears in vagina and “boggy” uterus. Clots expressed, patient “shocky.” BP 70/40, pulse 158

- Oxytocin algorithm
- Treatment of shock

In spite of 6 ampoules of IM methylergonovine and carboprost, bleeding continues and also there is “oozing” from the IV site.

- a) Consumption coagulopathy
- b) Rapid fluid and blood
- c) Timetable
- d) Surgical therapy

### Case 2: Prevention

40-year-old G7P6 female, which was admit in active labor at 39 weeks gestation. History of postpartum hemorrhage during the last delivery is requiring blood transfusions. Contractions in every 2-3 minutes. Vaginal exam: Cervix 8 cm, vertex –1 station bulging bag. Prenatal Hct 27.9%. Within 4 minutes vertex crowning SROM.

- I. Risk for PPH
- II. IV access 3
- III. 10 U IM oxytocin postpartum if no IV
- IV. Active management third stage
- V. Availability of carboprost (Hemabate)
- VI. If patient presented at 3 cm, type and screen

### 8. Conclusion

Hence, we conclude that Oxytocin is a necessary hormone present in the human body. And most of us are not aware about the presence of the hormone. It’s a short review paper summarizing all the informations of Oxytocin.

### 9.References-

- ✓ Neuropsychopharmacology volume36.  
<https://psychcentral.com/lib/about-oxytocin/>
- ✓ Prevost Marie, Phyllis Zelkowitz, et al. “ Oxytocin in pregnancy and the postpartum: relations to labor and its management”. Front. Public Health, 27 January 2014 | <https://doi.org/10.3389/fpubh.2014.00001>
- ✓ Akerlund M. “Vasopressin and oxytocin in normal reproduction and in the patophysiology of preterm labour and primary dysmenorrhoea.Development of receptor antagonists for therapeutic use in these conditions”.*AnnalesAcademiaeMedicaeBialostocensis. · Vol. 49, 2004*
- ✓ MorisMariana, Stevens Susan. W et. al. “Plasma oxytocin during pregnancy and lactation in the Cynomolgus monkey”. Biology of Reproduction, 23, 782-787 (1980)
- ✓ Husslein P, Fuchs AR, Fuchs F.“Oxytocin- and prostaglandin plasma concentrations before and after spontaneous labor: evidence of involvement of prostaglandins in the mechanism of placental separation”. Pub Med.gov.1983 May 27;95(11):367-71.
- ✓ Wathes D C, Borwick S C, et. al.“Oxytocin receptor expression in human term and preterm gestational tissues prior to and following the onset of labour”. Journal of Endocrinology (1999) 161, 143–151. Received 29 July 1998 Accepted 18 November 1998
- ✓ Principles of Medicinal Chemistry.byFoye, W.O., T.L. Lemke and D.A. Williams. Williams & Wilkins.Fourth Edition, 1995.
- ✓ BellAleeca F, Erickson Elise N, and Carter C. Sue,“BEYOND LABOR: THE ROLE OF NATURAL AND SYNTHETIC OXYTOCIN IN THE TRANSITION TO MOTHERHOOD”. J Midwifery Womens Health. 2014 January ; 59(1): 35–42.
- ✓ Adaptive Responses of the Maternal Hypothalamic-Pituitary-Adrenal Axis during Pregnancy and Lactation. P. J. Brunton