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Oxytocin- The Hormone of Love

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Abstract: *"Cuddle Hormone" or the "Love Hormone," (OXT) was discovered in 1835 by the great Italian scientist Nicholas Farraye. Oxytocin is apotent molecule with a unique and unusually broad profile of loving sense with biological and behavioral effects. In this Article we have discussed All about the importance of the hormone oxytocin in a person's experience of love. Oxytocin, also known as the "cuddle chemical", "plays an important role in romantic love, as a hormone that encourages cuddling between lovers and increases pleasure during lovemaking. The hormone stimulates the smoothmuscles and sensitizes the nerves, and snowballs during sexual arousal." Oxytocin is also linked to the feeling of "closeness" Since Oxytocin is released through physical touch, including "stroking, cuddling, hugging, kissing, or having sex", it can be concluded that it is also associated with the release of other distinct hormones in the body. In fact, "oxytocin works in tandem with other neurotransmitters such as testosterone…oxytocin may also influence how the feel-good neurotransmitters dopamine and norepinepherine hit the reward parts of the brain." When this various hormones and neurotransmitters are released, the body can associate this feeling with love. However, hormones are also extremely important in the feeling of addiction, dopamine especially. Perhaps it is this feeling of "addiction" that keeps couples together. Women like to cuddle after intercourse, while men just want to sleep. This is a wellknown "fact" that is commonly shared by society. But, interestingly, there is actually a biological reason for this desire. "Women experience stronger effects of oxytocin than men because women have more estrogen, and estrogen makes oxytocin receptors more sensitive."*
Hence, in this review we have discussed The Love Hormone, The human behaviour, Chemistry of love, Biology of love, Pharmacology of love Hormone, Oxytocin's effects on emotion, potential benefits of oxytocin, Release Profile Of OXT, Oxytocin Signaling Pathway. We all have that one person in our lives in whose absence our existence seems utterly meaningless. This article is dedicated to the love of my life.

Key words: *Oxytocin The Love Hormone, The human behaviour, Oxytocin's effects on emotion, potential benefits of oxytocin, Release Profile Of OXT, Oxytocin Signaling Pathway, Chemistry , Biology & Pharmacology of love Hormone.*

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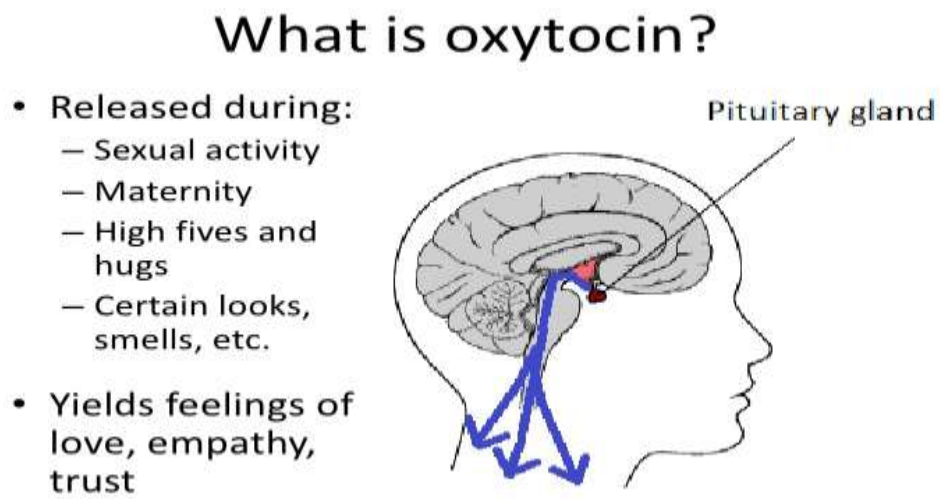
I. Introduction



What is oxytocin, and what does it do?

Oxytocin is a hormone that is made in the brain, in the hypothalamus. It is transported to, and secreted by, the pituitary gland, which is located at the base of the brain.1 In chemistry, oxytocin is classed as a nonapeptide (a peptide containing nine amino acids), while its biological classification is as a neuropeptide. It acts both as a hormone and as a brain neurotransmitter.

The release of oxytocin by the pituitary gland acts to regulate two female reproductive functions:1,2

1. Childbirth
2. Breast-feeding.

The release of the hormone during labor increases uterine motility, making the muscles of the uterus (womb) contract. The release of oxytocin is triggered by the widening of the cervix and vagina during labor, and this effect is in turn increased by the subsequent contractions.3 "It is released in large amounts during labor, and after stimulation of the nipples. It is a facilitator for childbirth and breast-feeding."

Stimulation of the nipples results in oxytocin release and milk let-down.

Other researchers sum up the reproductive importance of oxytocin by saying it "serves the continued propagation of a species," adding that through evolution its "repertoire has expanded to maintain a central role in more complicated aspects of reproductive behavior. For these reasons, we call oxytocin the great facilitator of life."1 Oxytocin, used as a prescription drug, is sold under the brand name Pitocin (and Syntocinon, although this is no longer on the market).4 Doctors prescribe oxytocin to start birth contractions or strengthen them during labor. It is also used to reduce bleeding after child delivery.4,5 The drug also has a role in the medical termination of pregnancy or during miscarriage.5

Actual facts on oxytocin:-

- Oxytocin is a neuropeptide produced in the hypothalamus and secreted by the pituitary gland.
- Oxytocin is released during sex, childbirth and lactation to aid reproductive functions.
- This neuropeptide exerts multiple psychological effects, influencing social behavior and emotion.
- Oxytocin is prescribed for a variety of obstetric and gynecological reasons, including to aid in childbirth.
- High levels of the "love hormone" have been observed in couples in the first six months of a relationship.
- Oxytocin has an anti-anxiety (anxiolytic) effect and may increase romantic attachment and empathy.

- Research shows that oxytocin may have beneficial effects for people with autistic spectrum disorders.
- Oxytocin appears to play a role in protecting the intestine from damage, with potential for use in treatment of irritable bowel disease.

Oxytocin's Effects on Emotion:- Oxytocin released into the bloodstream affects the uterus and lactation, but its release into defined regions of the brain also affects emotional, cognitive, and social behaviors.One review of the evidence says oxytocin "has attracted intense attention" after the discovery of its "amazing variety of behavioral functions." The review, by Inga Neumann, states that oxytocin's impact on "pro-social behaviors" and emotional responses contributes to:6

- Relaxation
- Trust
- Psychological stability.

However, another review notes that the hormone does not act alone in the chemistry of love, but is "just one important component of a complex neurochemical system that allows the body to adapt to highly emotive situations."7

Oxytocin has been the focus of research into the biology of love.

Scientific research has nonetheless uncovered brain oxytocin's specific ability to modulate social behavior, including effects on motherly care and aggression, bonding between couples, sexual behavior, social memory, and trust.6 Brain oxytocin also reduces stress responses, including anxiety - and these anxiolytic effects have been demonstrated in a number of species.6,8 'Love hormone' studies was published in 2012, and it examined oxytocin levels in new lovers versus those in single people. It found that there were high levels of the hormone in the first stages of romantic attachment, and that these were sustained for six months.[9]

Oxytocin released during sex :- In all genders, sexual activity stimulates the release of oxytocin, which has a role in erection and orgasm. The reason for this is not fully understood, although in women, it has been proposed that the increased uterine motility may help sperm to reach their destination.3 Some researchers believe oxytocin may play a part in the experience of sexual orgasm, proposing a correlation between the concentration of oxytocin and the intensity of orgasm.10

Behavioral effects of oxytocin

Recent developments on oxytocin's emotional effects:- "Oxytocin" the monogamy hormone? This study, published in the journal PNAS in November 2013, examined brain scans of men who had received oxytocin or placebo via a nasal spray. The oxytocin was associated with activation of the men's reward centres in their brains, and with greater feelings of attraction to their partners versus other women in photographs. This followed a very similar study in The Journal of Neuroscience in November 2012: A hormone can help keep men faithful. High oxytocin levels "trigger oversensitivity to emotions of others."Released in January 2014, this study in Emotion found that people receiving oxytocin nasal spray saw facial expression of emotions in others more intensely. Oxytocin makes you feel more extroverted. This 2011 research paper in Psychopharmacology

gave results from intranasal oxytocin improving self-perception in social situations, amplifying personality traits such as warmth, trust, altruism and openness.The hormone that allows us to love may also encourage us to lie. This 2014 study found participants given oxytocin were more likely to lie for the benefit of the group.

Oxytocin as potential psychiatric therapy

How oxytocin could help people with disorders such as autism to better understand other people's emotions: The research to uncover oxytocin's "anxiolytic and pro-social influences, beneficial to relief, reproduction, and love" is what has led scientists to describe it as a one of the "most promising neuromodulator/neurotransmitter systems of the brain for psychotherapeutic intervention and treatment of numerous psychiatric illnesses, for example social phobia, autism, and postpartum depression."6 "Oxytocin is of potential use in enhancing interpersonal and individual wellbeing, and might have more applications in neuropsychiatric disorders, especially those characterized by persistent fear, repetitive behavior, reduced trust and avoidance of social interactions." 11

Recent development on oxytocin in psychotherapy

Oxytocin activates "social" brain regions in children with autism. A research study involving 17 children with autism spectrum disorders, published in December 2013, used functional magnetic resonance imaging (fMRI) to see differences created by oxytocin in brain responses to social and non-social pictures. Although this was a small study, the researchers found "oxytocin temporarily normalized brain regions responsible for the social deficits seen in children with autism." Oxytocin may also have a role to play in anger management, with research finding that certain polymorphisms of the oxytocin receptor (OXTR) gene are associated with an increased tendency to react more angrily to situations. Specifically, differences in OXTR gene expression appears to affect the regulation of the relationship between alcohol and aggressive behaviour.13

Other potential benefits of oxytocin:-

Recent research has shown that oxytocin increases the release of prostaglandin E2 in cells lining the intestines, which helps encourage repair of intestinal injury and to protect against such injury. This may make oxytocin a useful therapy for preventing chemo-radiotherapy induced intestine injury, as well as a novel and safe treatment for irritable bowel disease (IBD). 12

How it works ?

Oxytocin suppresses the activity of the brain region known as the amygdala, the area that processes fear and communicates it to the rest of the brain. A small sample group of 15 men inhaled either oxytocin or a placebo before performing a task in which they sorted pictures of angry or fearful faces and threatening scenes. During the test the researchers monitored the subjects' brain activity with functional magnetic resonance imaging and found that the oxytocin group indeed had reduced activity in the amygdala.

Oxytocin reduces fear:-

Animal and human studies indicate the major role of the amygdala in controlling fear and anxiety. The amygdala is involved in detecting threat stimuli and linking them to defensive behaviors. This is accomplished by projections connecting the central nucleus of the amygdala to the brain stem and to hypothalamic structures, which organize fear responses. Oxytocin tempers the excitatory inputs into the amygdala.

Smiles, social skills, interactions with others:- Oxytocin may increase one's ability to remember happy smiling faces but I have not seen studies yet that smiling itself increases one's oxytocin levels. This "love hormone" has a tremendous effect on kids' ability to function socially. Children blessed with naturally high levels of oxytocin are more savvy at communicating with others and interpreting social signals or situations.

Weight loss hormone? A 2016 small study found in spray form, the "love hormone" oxytocin might aid weight loss. A single dose of oxytocin nasal spray decreased impulsive behavior in overweight and obese men. However, the benefits and risks of long term use of this spray are not well understood and it is possible tolerance could develop.

Availability of oxytocin drug by prescription:- Oxytocin is sold as nasal spray (Syntocinon). A nasal spray containing the hormone oxytocin, which is essential to the production and flow of breast milk, does not improve milk output in mothers expressing milk for preterm infants.

Intranasal administration of oxytocin causes a substantial increase in trusting behavior and the perception of the person a person is intimate with as appearing more appealing than a stranger, 2013, Proceedings of the National Academy of Sciences. 14

II. Oxytocin Signaling Pathway

Figure 1: Metabolic effects of oxytocin: OT is secreted from the posterior lobe of the pituitary gland and binds to its receptor in peripheral tissues. In adipose tissue, it induces fatty acid oxidation and lipolysis, and formation of small adipocytes. Small adipocytes increase secretion of adiponectin and decrease leptin secretion, which improve insulin sensitivity in adipose tissue, liver, and muscles. In pancreas, it induces insulin secretion via phosphoinositide (PI) turnover and activation of protein kinase C, and regeneration of pancreatic β-cells. In liver and muscles, it enhances glucose uptake by stimulation of intracellular release of calcium, and activation of phosphoinositid-3-kinase (PI3K), calcium-calmodulin kinase kinase (Ca-CAMKK), and AMP-activated protein kinase (AMPK). 15

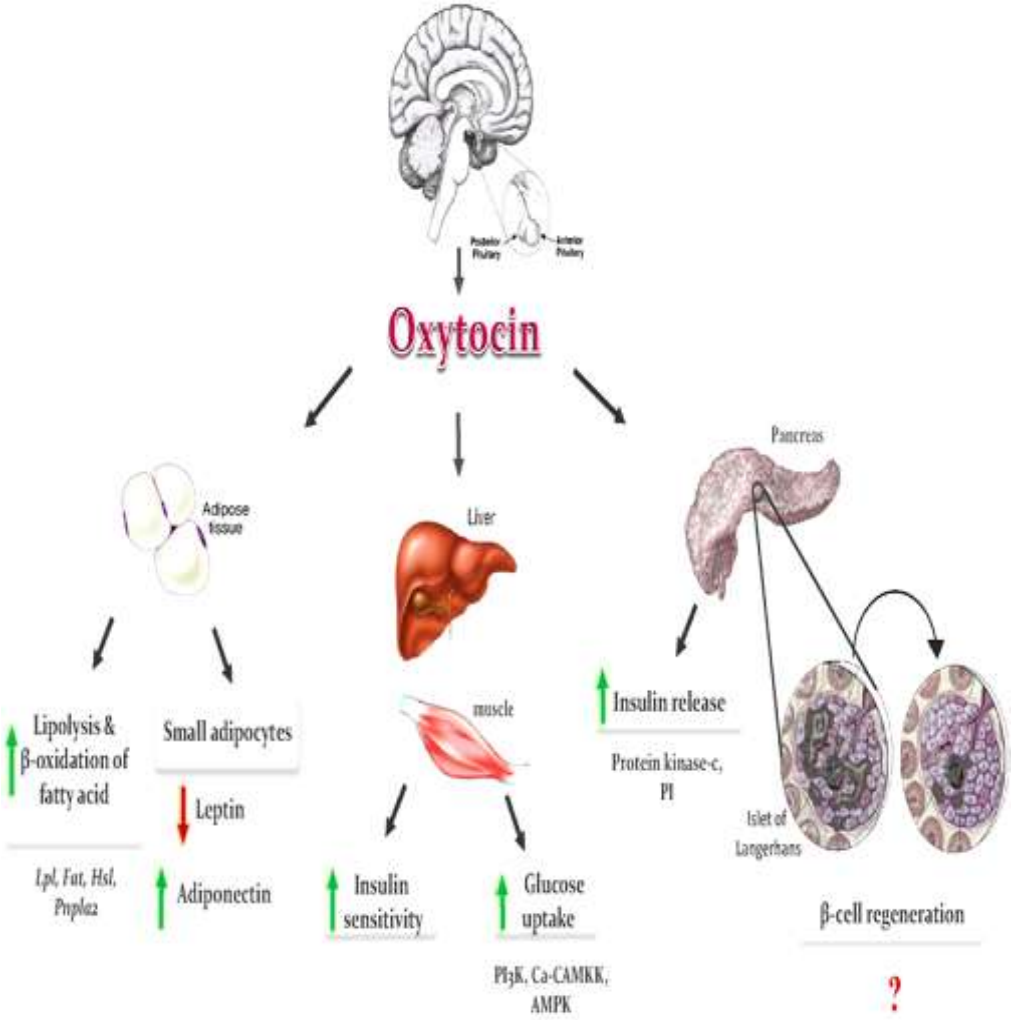


Figure 2: Oxytocin signaling in bone cells: OT binds to its receptor in osteoclast (OC) and osteoblast (OB), and initiates several cellular cascades. It induces OB differentiation by inducing c-fos expression and MAP-kinase phosphorylation. OT induces release of Ca2+ from intracellular stores. In OB, the increase in Ca2+ provokes several cellular cascades (JNK, P38, ERK, PKA, and PI3K), which lead to an increase in prostaglandin E2 synthesis, with positive effects on OB. In OC, OT increases OC formation directly, by activating MAPK signaling, and indirectly through the up-regulation of RANK-L from OB. The increase in Ca2+ induces NF-kb and IP3 which inhibit bone resorption of mature OC. 16

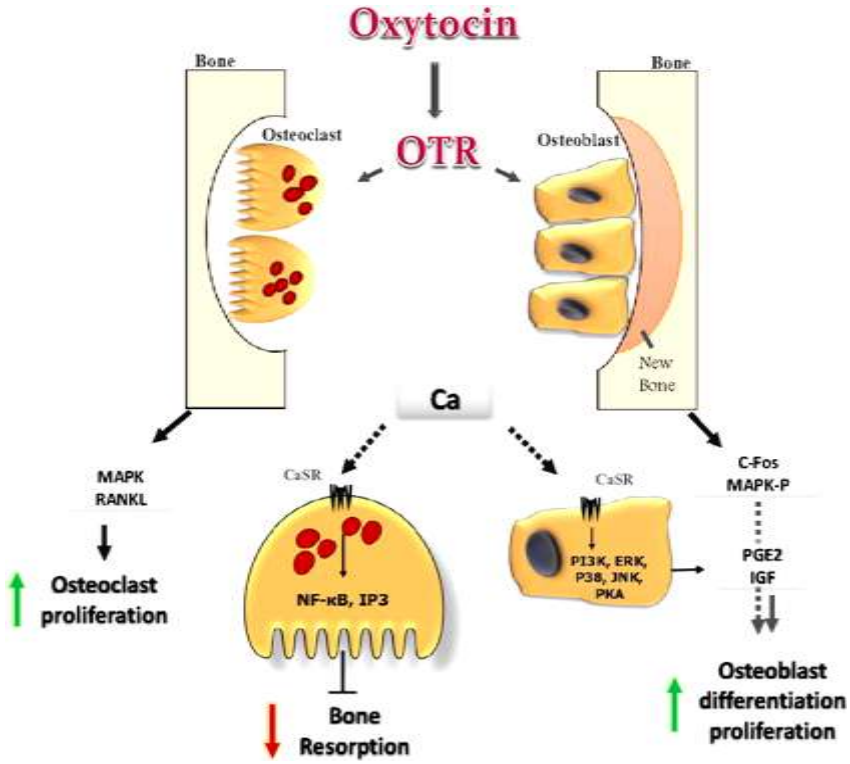
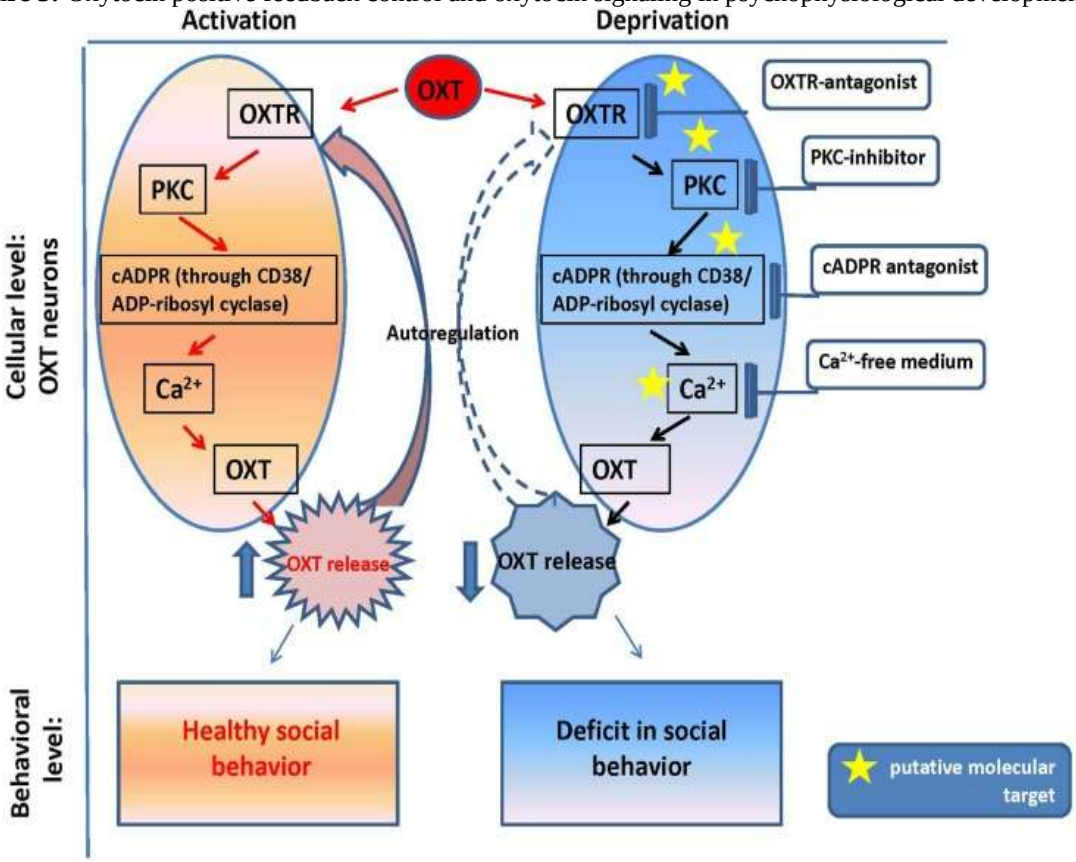


Figure 3: Oxytocin positive feedback control and oxytocin signaling in psychophysiological development.17



III. Chemistry Of Love Hormone

The most important ingredients in love chemistry are hormones. They are behind all emotions and also regulate our feelings of love and attachment. Oxytocin and vasopressin are the most prominent hormones implicated in pair bonding and love, not just between partners, but also between friends, or mother and child18.

Production of oxytocin, nicknamed the "cuddle and trust" hormone, is initiated by caressing and cuddling and is responsible for the pleasant feeling and comfort this gives us19. Principally, oxytocin triggers the muscular contractions required for birth and milk release during lactation, thereby also creating unconditional maternal love. Mothers who have had a caesarian section have, especially in the beginning, a weaker instinct for the cry of their child compared to mums who gave birth the natural way, initiated by oxytocin.20

BIOLOGY OF LOVE

"Love is nature's way of tricking people into reproducing" 21.why didn't we just continue to be self copying RNA as described in "The Selfish Gene", or simply procreate by cell division22?

IV. Pharmacology Of Oxytocin

Oxytocin is a nonapeptide secreted by the posterior pituitary along with vasopressin (ADH). Pituitary extract was first used in labour in 1909. Controversy as to whether the antidiuretic and uterine stimulating activities were due to one substance or two separate principles was finally resolved by du Vigneaud in 1953 when he separated Oxytocin and Vasopressin, determined their chemical structure and synthesized them. Both are nonapeptides which differ at positions 3 and 8. Both oxytocin and ADH are synthesized within the nerve cell bodies in supraoptic and paraventricular nuclei of hypothalamus; are transported down the axon and stored in the nerve endings within the neurohypophysis. They are stored in separate neurones as complexes with their specific binding proteins (neurophysins). Both are released by stimuli appropriate for oxytocin—coitus, parturition, suckling; or for ADH—hypertonic saline infusion, water deprivation, haemorrhage, etc., or nonspecific—pain and apprehension. However, the proportion of oxytocin to ADH can vary depending upon the nature of the stimulus.

V. Mechanism Of Actions

1. Uterus Oxytocin increases the force and frequency of uterine contractions. With low doses, full relaxation occurs inbetween contractions; basal tone increases only with high doses. Increased contractility is due to hightened electrical activity of the myometrial cell membrane— burst discharges are initiated and accentuated. Estrogens sensitize the uterus to oxytocin; increase oxytocin receptors. Nonpregnant uterus and that during early pregnancy is rather resistant to oxytocin; sensitivity increases progressively in the third trimester; there is a sharp increase near term and quick fall during puerperium. Progestins decrease the sensitivity, but this effect is not marked in vivo. The increased contractility is restricted to the fundus and body; lower segment is not contracted, may even be relaxed at term. Mechanism of action Action of oxytocin on myometrium is independent of innervation. There are specific G-protein coupled oxytocin receptors which mediate the response mainly by depolarization of muscle fibres and influx of Ca^{2+} ions as well as through phosphoinositide hydrolysis and IP3 mediated intracellular release of Ca^{2+} ions.

The number of oxytocin receptors increases markedly during later part of pregnancy.

Oxytocin increases PG synthesis and release by the endometrium which may contribute to the contractile response. Distinct subtypes of oxytocin receptors have been shown on the myometrium and the endometrium.

2. Breast Oxytocin contracts myoepithelium of mammary alveoli and forces milk into the bigger milk sinusoids—'milk ejection reflex' (milk letdown in cattle) is initiated by suckling so that it may be easily sucked by the infant. It has been used in milch cattle to facilitate milking.

3. CVS Conventional doses used in obstetrics have no effect on BP but higher doses cause vasodilatation → brief fall in BP, reflex tachycardia and flushing. This action is most marked in chicken—used for bioassay. The umbilical vessels are markedly constricted; oxytocin may help in their closure at birth.

4. Kidney Oxytocin in high doses exerts an ADH-like action—urine output is decreased: pulmonary edema can occur if large amounts of i.v. fluids and oxytocin are infused together. Conventional doses are without any effect.

1. Labour Oxytocin is released during labour and the uterus is highly sensitive to it at this time. However, it does not appear to be obligatory for initiating parturition—delivery occurs in hypophysectomized animals and humans, though labour may be prolonged in its absence. A facilitatory role is more plausible. PGs and PAF are complementary to oxytocin.

2. Milk ejection reflex It is mediated by oxytocin. The myoepithelial cells in breast are more sensitive than myometrium to oxytocin; milk ejection reflex is absent in the hypophysectomized.

3. Neurotransmission Oxytocin appears to function as a peptide neurotransmitter in the hypothalamus and brainstem to regulate autonomic neurones.

VI. Pharmacokinetics

Being a peptide, oxytocin is inactive orally and is generally administered by i.m. or i.v. routes, rarely by intranasal spray. It is rapidly degraded in liver and kidney; plasma t½ ~6 min, and is still shortened at term. Pregnant uterus and placenta elaborate a specific aminopeptidase called oxytocinase—which can be detected in maternal plasma.

Unitage and preparations 1 IU of oxytocin = 2 μg of pure hormone. Commercially available oxytocin is produced synthetically.

OXYTOCIN, SYNTOCINON 2 IU/2 ml and 5 IU/ml inj., PITOCIN 5 IU/0.5 ml inj.

USE

1. Induction of labour Labour needs to be induced in case of postmaturity or prematurely in toxaemia of pregnancy, diabetic mother, erythroblastosis, ruptured membranes or placental insufficiency. For this purpose oxytocin is given by slow i.v. infusion: 5 IU is diluted in 500 ml of glucose or saline solution (10 milli IU/ ml)—infusion is started at a low rate and progressively accelerated according to response (0.2–2.0 ml/min). Before starting infusion, confirm that presentation is correct, foetal lungs are adequately mature, there is no cephalopelvic disproportion, no placenta previa, no foetal distress and no uterine scar (due to previous surgery). Uterine contractions are then closely monitored: the drug is discontinued when they are strong enough. Usually a total of 2–4 IU is needed.

2. Uterine inertia When uterine contractions are feeble and labour is not progressing satisfactorily— oxytocin can be infused i.v. (as described above) to augment contractions. It should not be used to hasten normally progressing labour. Too strong contraction can be catestrophic: use should only be made in selected cases and by experienced people.

Oxytocin is the drug of choice and is preferred over ergometrine/PGs for the above two purposes:

(a) Because of its short t½ and slow i.v. infusion, intensity of action can be controlled and action can be quickly terminated.

(b) Low concentrations allow normal relaxation inbetween contractions—foetal oxygenation does not suffer.

(c) Lower segment is not contracted: foetal descent is not compromised.

(d) Uterine contractions are consistently augmented.

3. Postpartum haemorrhage, Cesarean section Oxytocin 5 IU may be injected i.m. or by i.v. infusion for an immediate response, especially in hypertensive women in whom ergometrine is contraindicated. It acts by forcefully contracting the uterine muscle which compresses the blood vessels passing through it to arrest haemorrhage from the inner surface exposed by placental separation.

4. Breast engorgement It may occur due to inefficient milk ejection reflex—oxytocin is effective only in such cases: an intranasal spray may be given few minutes before suckling. It does not increase milk production.

5. Oxytocin challenge test It is performed to determine utero-placental adequacy in high risk pregnancies. Oxytocin is infused i.v. at very low concentrations till uterine contractions are elicited every 3–4 mins. A marked increase in foetal heart rate indicates utero-placental inadequacy. The test is risky.

Adverse effects

(i) Injudicious use of oxytocin during labour can produce too strong uterine contractions forcing the presenting part through incompletely dilated birth canal, causing maternal and foetal soft tissue injury, rupture of uterus, foetal asphyxia and death.

(ii) Water intoxication: because of ADH like action of large doses given along with i.v. fluids, especially in toxaemia of pregnancy and renal insufficiency. It is a serious (may be fatal) complication. 23

VII. Conclusion

The Article on The Love Hormon has concluded that the disciplines of biology, chemistry and pharmacology, are all important in analyzing love. oxytocin exposure early in life not only regulates our ability to love and form social bonds, it also has an impact on our health and well-being. OXT facilitates both intercourse and conception then helps bring the woman into labour. As the fetus descends the birth canal, the resultant vaginal distension by the presenting part causes an even greater outpouring of the same hormone which in turn produces: expulsive contractions and the actual birth, immediate maternal bonding behaviour towards her baby, milk ejection. The same hormone is probably also produced by the fetus for purposes so far unknown, but in any case the baby receives high levels of the hormone in its mother's milk to probably help it bond towards its mother whilst receiving warmth by causing breast skin vasodilatation, and nourishment.

OXT is demonstrated as hormone of love Because of It's effects on male and female sexuality, male and female reproduction, male and female mood, childbirth, breastfeeding and nurturing, creating much interpersonal love within the family as a result, OXT is a hormone of love.

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