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Pharmacological Role of Oxytocin – A Short Review

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Abstract:
Oxytocin is a hormone, predominately belonging to mammalian family; it is secreted by the posterior pituitary gland. After its release in the blood stream it cannot re-enter the brain due to the presence of blood brain barrier .Oxytocin is a hormone that has both peripheral and central actions (32). They are synthesized in the magnocellular neurons present in the supra–optic and Para –ventricular nucleus present in the hypothalamus. The universally known functions would include its role at the time of labour and ejection of milk. The functions which remain partially unknown are in erectile responses, ejaculation, bonding, and feeling of love and maintaince of eye contact during a conversation. This review is aimed at bringing into nutshell the common functions, defiency states and the commercially available forms of the same.

Key words:
Oxytocin, bonding, pitocin, labour.

INTRODUCTION:

Oxytocin is a mammalian hormone predominantly, in human beings it is synthesized by specialized cells in the supra optic and paraventricular nucleus of the hypothalamus. Oxytocin acts as a neurotransmitter in the brain (15). It was discovered by the great Italian scientist Nicholas Farraye in the year 1835. It has a molecular formula of $C_{43}H_{66}N_{12}O_{12}S_{2}$. The structure of oxytocin is similar to that of vasopressin but with a few differences.

Apart from the well known function of uterine contraction and milk ejection, oxytocin is said to play a major role in creating an effective bond between child and mother, in trusting people, maintain eye to eye contact during a conversation. Most of us regard Oxytocin to be a hormone which is found only in the female counterparts, fortunately this hormone is found in males as well. It is said to help in the maintenance of monogamous relationships. Oxytocin secretion in general was found to increase during sexual intercourse, breast feeding, during parturition. In case of male it helps in erection and ejaculation. Apart from the above mentioned functions Oxytocin helps in creating bonding, trust, social recognition, and calmer attitude and further more. Thereby drugs that induce the feeling of trust and attraction use Oxytocin as their prime component. This hormone commercially available as intravenous and intramuscular injections and as nasal sprays for various purposes.

PHYSIOLOGICAL ROLE OF OXYTOCIN

Oxytocin and emotions:

Oxytocin is secreted from the hypothalamus and stored in the posterior pituitary gland. Secretion of this hormone partially depends on the limbic system .Researchers have found out that this hormone is secreted during pleasurable feeling such as receiving a hug from our soul mate, at the first touch of a male / female who we are attracted to. The release of Oxytocin creates a sense of pleasure and hence prompts us to repeat the act again. The release of Oxytocin tends to alter the brain signals which produce facial expressions, perhaps changing the firing for amygdala, which is very important for the processing of emotional stimuli (28).

Oxytocin, eye to eye contact and trust:

Oxytocin is very essential for establishing eye to eye contact and trust individuals whom we interact with. This hormone was therefore administered to children affected with autism via intranasal sprays; some autism affected children were given a placebo of saline intranasal spray (14). The children who were using Oxytocin sprays were found to establish better eye contact and they began to trust people better than the children who were administered with a placebo. Thereby few researchers are at a thought of administering Oxytocin based drugs to boost their trust (14).

Oxytocin and sexual activity:

The role of Oxytocin to sexual arousal remains ambiguous in both sexes. Oxytocin is said to increase the erectile response in male. When Oxytocin was administered to male rats, spontaneous erectile responses were noted.(26) In females it is said to increase during sexual intercourse and there the women tends to relate a feeling of pleasure or happiness. However in disinterested female i.e. in females who were not willing to have sex with their counterpart it is said to create a sense of irritation (1, 11).

Uterine contraction:

The most common function of Oxytocin which does not remain unknown even to a lay-man is the act of uterine contraction. At the event of labour the levels of progesterone falls, the normal Oxytocin level causes cervix dilation, thereby increasing pain; this reflex increases the release of Oxytocin, increasing cervix dilation leading to parturition.

Lactation:

When the nipples of the mother get sensitized by the stimuli of sucking, impulses are sent to the hypothalamus to release this hormone. Bursts of the hormone are sent. The contractile apparatus of the alveoli cause the ejection of milk. The entire process is known as the “let down reflex” (23, 1, and 15).

Oxytocin and bond:

Oxytocin is said to create a sense of affection among people. The bond between the child and the mother is said to be the strongest due to the reason that there is increased level of Oxytocin in the maternal circulation at the time of

delivery. This hormone is said to induce maternal characters (8). When research was conducted by administering Oxytocin to female rats they were said to exhibit increased maternal characters, even virgin rats when injected with the same tend to show the same results. On the contrary if mother rats were given Oxytocin blockers, they did not show any maternal behaviour with their own off springs. These studies when done in humans also showed the same results (3, 27).

In cases of relationship, Oxytocin surge plays a vital role. When there are increased levels of Oxytocin the blood stream the male / female tends to bond better with their mate. Couples were chosen for studies, they were asked to talk for a while and their Oxytocin levels were noted. Later an injection of Oxytocin was administered to a couple and the other was given a placebo, they were asked to continue their conversation. It was found that the couple who were administered with Oxytocin showed greater intimacy and they were found to argue less on topics that had previously created a conflict between them (8).

Oxytocin and monogamous relationship:

Recent studies have shown that Oxytocin helps men to be in a monogamous relationship. In the research men who were in relationship were administered with Oxytocin intranasal sprays and a few men were given a placebo of saline. After its administration they were asked to interact with attractive women, men who had taken Oxytocin sprays showed increased distance from the women than those who were under the effect of the placebo (7)

Oxytocin and love:

Oxytocin is that hormone that makes people fall in love. When two people of the opposite sex meet, exhibit Oxytocin surge, they are found to mutually like each other therefore falling in love. Due this unique property of Oxytocin it is widely called as the"love hormone" by researchers. Further it is also believed that levels of Oxytocin tend to increase during hugging and kissing (24, 25).

Oxytocin and heart:

At the time of c-section, Oxytocin injection is said to cause tachycardia i.e. increased heart rate and increase in the intra- martial pressure. Here the concentration of Oxytocin injected plays a vital role (13).

Oxytocin and trauma:

Children who had experienced childhood trauma for years, decades were found to have low levels of Oxytocin. This is said to be an adaptive mechanism but the low level of Oxytocin is said to have notable effects on relationships which they establish or willing to establish (11).

Oxytocin deficiency:

An impaired synthesis of Oxytocin would lead to Oxytocin deficiency. Most common manifestation of Oxytocin deficiency would be generalised depression and anxiety, sleep disturbances, isolation and panic attacks (22). Oxytocin defiency is also said to be associated with conditions like autism, uterine inertia and schizophrenia

Autism:

Autism is a mental condition, present from early childhood, characterized by great difficulty in communicating and forming relationships with other people and in using language and abstract concepts. Autism can partly, 10% of autism cases, be attributed to a single gene disorder where there is genomic deletion of Oxytocin receptor gene (30). To identify genes involved in autism, characterization of copy number variants (CNVs), that is, chromosomal deletions and duplications, can be assessed . CNVs show that autism involves almost all chromosomes. Other methods were also used to characterize autism related CNVs which included cytogenetic G-banding metaphase fluorescence *in situ* hybridization (FISH) Southern blotting , loss of heterozygosity (LOH) analysis quantitative polymerase chain reaction (PCR) and, more recently, genotyping and representational oligonucleotide microarray analysis (ROMA) (12,30,31)

Uterine inertia:

Uterine inertia is caused due to some defects in posterior pituitary gland. At the time of labour low levels of oxytocin would weak and uncoordinated contractions of the uteruses a result labour is prolonged and also delays the birth of the baby (12,27).Decreased Oxytocin secretion may eventually lead to postpartum haemorrhage i.e. haemorrhage after delivery . In these cases more than 500 ml of blood is lost during normal delivery and more than 1000 ml is lost during c-section.

Schizophrenia:

Schizophrenia is a wide-reaching mental disorder.

Causes may be as follows:

- Genetic – Increased risk is seen in people whose relatives suffer from the same disorder. This is due to genetic inheritance, though it may involve different genetic contributions.
- Environmental – Adulterant environment plays i.e. the environment in which the early adulthood days were spent plays an evident role.
- Substance abuse – Intake of psychoactive drugs such as amphetamines and cannabis (4,28)

As mentioned above Oxytocin plays a key role in establishing trust , falling in love , parturition , milk ejection, mother – child bond , erection and ejaculatory response in males. Oxytocin insuffiency is leads to increased stress and sleep disturbances.

The solution to the above mentioned problem lies in creating a drug which can mimic the functional properties of Oxytocin, which was achieved. Oxytocin has been widely used in the field of gynaecology to induce labour. It is also administered to patients i.e. mothers who are unable to produce milk after parturition. The invention of Oxytocin nasal sprays is not unknown. Recommended doses when administered to autism patients are proven to increase the sense of trust at the time of communication.

PHARMACOLOGICAL ROLE OF OXYTOCIN

Oxytocin drugs:

Oxytocin is also known as Pitocin, Syntocinon, Ocytocin, Endopituitrina, Oxitocina, Oxytocine, Oxytocinum, Oxytocic hormone and Orasthin. It has a molecular formula of $C_{43}H_{66}N_{12}O_{12}S_2$. They are commercially available as intravenous and intramuscular injections , nasal sprays and sublingual tablets .The commonly used

drug types are pitocin and syntocinon, the chemical resemblance to Oxytocin makes them an ideal drug of choice for various cases for example at time if parturition . Pitocin is composed of oxtocic acid/ml along with chlorobutanol , a chloroform derivative. However medical supervision is mandatory to rule out the onset of complications (20,31).

The general uses of these Oxytocin drugs would include induction of labour .Under appropriate level , at the time delivery, Oxytocin binds to the receptors present in the myometrium , activates the pathway of hydrolysis of phoshotidyl inositol and diacyl glycerol, there by activating the same. This activation causes the release of intracellular Ca^{+} which causes contraction of the uterus .In conditions associated with low level of Oxytocin production this process is carried out by Oxytocin drugs (29, 27) Incase of people suffering from autism, administration of pitocin is said to reduce repetitive behaviour and also enhances speech. Few researches have proved the improvement of trust in people affected by autism when they were given pitocin nasal sprays. It also enhances eye to eye contact in these individuals. Pitcoin helps in social interaction in people who suffer from schizophrenia . So pitocin may not only combat hallucinogens and psychosis, but also make human interaction easier . Being a new field if research there is not enough evidence to prove the role pitocin in both autism and schizophrenia. Further, they are also used to cure problems in erectile responses, ejaculation, depression, anxiety, and stress management (25.20)

Dosage:

10 units by intravenous route or 20-40 mUnit/min by Intramuscular route are injected for post partum haemorrhage. 0.5-1 mUnit/min by intravenous route for the induction of labour.10-20 mUnit/min is administered along with other drugs for termination of pregnancy(32)

Pharmacodynamics

Uterine contractions are seen after 3-5 minutes and approx 1 minute of amistration through intramuscular and intravenous routes respectively. A steady state of the drug is reached after 40 mins of parenteral route of administration. It is distributed throughout extracellular fluid compartment of the mother; small amounts may cross the placental barrier and reach foetus. Metabolism takes place rapidly via the liver and plasma by the enzyme oxytocinase a few steps of metabolism also takes place via mammary gland. It has a half-life of 1-5 minute. Kidney and liver help in the elimination of Oxytocin drugs(9) unchanged form of this drug is rarely excreted in urine (30). Overdose can cause titanic uterine contractions, impaired blood flow to the uterus, uterine ruptures, seizures and amniotic fluid embolism contractions, impaired blood flow to the uterus, uterine ruptures, seizures and amniotic fluid embolism.

Contraindications

Significant cephalopelvic disproportion
Unfavourable foetal positions
Obstetric emergencies which favours surgery
Hyperactive or hypertonic uterus
When vaginal delivery is contraindicated,
Anaphylactic patients
Foetal distress
Polyhydramnios
Partial placenta pervia
Elective labour induction

Side effects

- Nausea or vomiting
- Memory problems or confusion
- Runny nose, sore throat, or coughing
- severe headaches
- hallucinations
- vomiting
- confusion
- Seizures and severe hypertension
- irregular heartbeats,

Storage:

The optimum temperature for storage of Oxytocin drugs is at 20-25 degree Celsius (28)

CONCLUSION:

Oxytocin, a naturally occurring hormone in the human body, is said and proved to produce many important physiological actions. Oxytocin when present in optimum level helps to maintain emotional homeostasis, pleasure, love, orgasm and also improves social memory and cognition. Deficiency of oxytocin in the amygdala causes anxiety and fear which are often found in conditions like autism and Schizophrenia. Deficiency of the same at the time of labour leads to uterine inertia and post partum bleeding. These complications are trespassed by the commercial availability of the hormone in various forms. The synthetically produced, oxytocin replacing hormones, pose certain potential threats to homosapiens.Thus further research is being conducted to coin substances that mimic the property of natural oxytocin and also discards the risk which occurs due to external intake.

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