Hormones of the posterior pituitary

The two hormones synthesized in the hypothalamus and released from the posterior pituitary are oxytocin and vasopressin. Although structurally similar, being composed of nine amino acids, they have markedly different physiological roles.

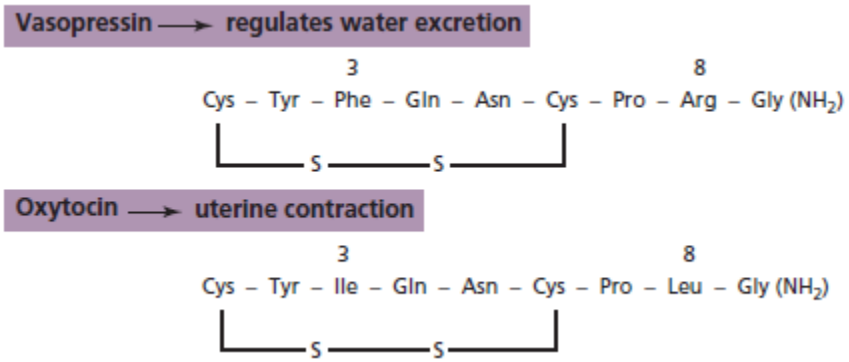

Figure1: The structures of vasopressin and oxytocin are remarkably similar, yet the physiological effects of the two hormones differ profoundly.

1. Vasopressin

Clinically, vasopressin is also known as 'antidiuretic hormone' (ADH) and has also been called 'arginine vasopressin'. The biology of vasopressin is summarized below:

Physiology

• Circulates largely unbound → rapidly metabolized in the liver and filtered by the kidney → t1/2 - 15 min

Function

• Regulates water excretion by the kidney

– its main action at normal circulating vasopressin levels:

° Acts on the distal convoluted tubule → increased permeability to water → water resorption → increased urine concentration

• Potent vasoconstrictor

Cellular mechanism of action

• Distinct cell-surface G-protein–coupled receptor (V) sub-types and second messengers:

° V1 (two further sub-types) → phosphatidylinositol (PI) metabolism and raised intracellular Ca2+ → vascular smooth muscle contraction

° V2 → cAMP → renal water excretion

Effects and mechanism of action

In the kidney, the presence of vasopressin and the high osmolality of the renal interstitium lead to water movement out of the final section of the distal convoluted tubule along the osmotic gradient. The effect can be truly remarkable. For example, a child weighing 30 kg needs to excrete a solute load of ~ 800 mOsm in 24 h: at its most dilute (~50 mOsm/kg), this load requires 16 L of urine; under maximal vasopressin stimulation, it can be achieved with little over 700 mL (~1100 mOsm/kg). Vasopressin is a potent vasoconstrictor and has been utilized either directly or in synthetic analogue form to achieve haemostasis, e.g. in severe gastrointestinal bleeding or post-partum haemorrhage. It also acts on vascular tone at normal physiological levels. During fetal development, vasopressin serves as an additional stimulus for ACTH release from corticotrophs.

Regulation of production

The main physiological regulator of vasopressin release is serum osmolality detected by osmoreceptors in the hypothalamus. Circulating volume is detected by baroreceptors in the carotid sinus and aortic arch, and by plasma volume receptors in the left atrium.

Following are the factors modulating vasopression release:

Serum osmolality (SOSM)

• **High (e.g. dehydration**) → increased vasopressin release → increased water retention → decreased SOSM

• **Low (e.g. water intoxication)** → decreased vasopressin release → decreased water retention → increased SOSM

Volume

• Fall in blood volume ≥8% (e.g. haemorrhage) → increased vasopressin release → vasoconstriction

O_2 and CO_2 tension

• Decreased arterial O_2 partial pressure (PaO_2) → increased vasopressin release

• Increased arterial CO_2 partial pressure ($PaCO_2$) → increased vasopressin release

In addition to above factors the angiotensin II, epinephrine, cortisol and the female

sex steroids, oestrogen and progesterone, can also modulate vasopressin release. The latter may explain the fluid retention that can occur in the latter part of the menstrual cycle. As with other hypothalamic hormones, the CNS plays an important part in the regulation of vasopressin. **Pain and trauma** associated with surgery cause a marked increase in the circulating vasopressin concentration, as do nausea and vomiting. The activity of the neurohypophyseal system is also influenced by environmental temperature; **a rise in temperature stimulates** vasopressin release prior to any change in plasma osmolality.

Clinical disorders

Excess vasopressin/syndrome of inappropriate antidiuretic hormone

The syndrome of inappropriate ADH (SIADH) refers to the release of vasopressin when normal regulatory mechanisms should restrict its secretion into the circulation. This is a difficult and dangerous clinical situation where hyponatraemia and low osmolality can cause irreversible brain damage and death.

Causes

- Tumours (e.g. small cell cancer of the lung)
- Any brain disorders (trauma, infection, tumour)
- Pneumonia
- Cytotoxic therapy (chemotherapy or radiotherapy)
- Narcotics and analgesics
- Hypothyroidism
- Hypoadrenalism

Symptoms and signs

Headache and apathy progress to nausea, vomiting, abnormal neurological signs and impaired consciousness. In very severe cases, there may be coma, convulsions and death. Generalized oedema is not a feature because free water is evenly distributed across all body compartments.

Deficiency of vasopressin/diabetes insipidus

Even when damage to the posterior pituitary occurs, vasopressin or oxytocin deficiency commonly does not arise so long as the hypothalamic neurones that transport the hormones remain intact. When deficiency of vasopressin or its action does occur, it results in diabetes insipidus (DI). Deficiency of vasopressin production by the hypothalamus and posterior pituitary

is termed '**cranial DI'**, whereas deficient action at the V2 receptor causes 'nephrogenic DI'. In the former, the vast majority of vasopressin production needs to be lost (≥90%) before water balance is necessarily affected.

Symptoms and signs

Patients with DI pass extremely large and frequent volumes of low osmolality urine (potentially 20 L in 24 h). This polyuria and passing urine at night (nocturia) demonstrate that in DI the patient is unable to reduce urine flow. Clinically, problems only tend to arise when the patient also lacks sensation of thirst or is deprived of water, when plasma osmolality rises.

2. Oxytocin

The major roles of oxytocin are during birth and breast-feeding. It is also emerging as a brain neurotransmitter with roles in modulating behaviour and overeating.

Effects and mechanism of action

Oxytocin has two main sites of action: the uterus and the mammary gland. It is the hormone of parturition, literally meaning 'quick birth'. It increases the contraction of the myometrium during labour causing expulsion of the fetus and the placenta. In this role progesterone appears to antagonize and oestrogen potentiate the uterine response to oxytocin. Post-partum in the mammary gland, oxytocin causes contraction of the myoepithelial cells surrounding the alveoli and ducts to expel milk from the breast. Like vasopressin, oxytocin circulates largely unbound and so is removed rapidly by the kidney (t1/2 ~5 min). Outside parturition and breastfeeding, it circulates in very low concentrations and is normally undetectable in the blood. Oxytocin binds to its cell-surface G-protein–coupled receptor and signals intracellularly via phosphatidylinositol metabolism and calcium.

Regulation of production

Oxytocin stimulates uterine muscular contraction which moves the fetus into the distending vagina, which in turn sends neural inputs back to the brain to enhance oxytocin secretion. This positive feedback loop is only broken once the fetus is expelled. Other factors, such as the fall in progesterone and the presence of oestrogen, may play a minor part in regulating oxytocin release. Similarly, positive feedback regulates oxytocin release during breast-feeding. Suckling of the nipple causes release of oxytocin and leads to ejection of milk. Even the sight and sound of an infant can stimulate milk ejection. Stimulation of oxytocin secretion ceases once the baby stops suckling.

Clinical disorders

Endocrine syndromes of oxytocin excess and deficiency have not been described. However, increased oxytocin appears to improve behaviour in autism spectrum disorder.