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Osmolality, osmolarity, and fluid homeostasis

What is fluid homeostasis?

In the steady state, our total body water content and salt content remain constant. An increase or decrease in water and salt intake is paralleled by an equivalent change in renal water and salt excretion[1]. Fluid homeostasis is achieved through the process of glomerular filtration of plasma to produce an ultrafiltrate. The tubules then process this ultrafiltrate so that the final urine flow rate and solute excretion meet the homeostatic needs of the body.

Osmolality and osmolarity are measurements of the solute concentration of a solution. In practice, there is negligible difference between the absolute values of the different measurements. For this reason, both terms are often used interchangeably, even though they refer to different units of measurement[2].

Alterations in water homeostasis can disturb cell size and function. Although most cells can regulate cell volume in response to osmolar stress, neurons are particularly at risk. Therefore, regulating water balance is fundamental to survival[3].

What is osmolality?

Osmolality is an estimation of the osmolar concentration of plasma and is proportional to the number of particles **per kilogram of solvent**; it is expressed as mOsmol/kg (the SI unit is mmol/kg but mOsmol/kg is still widely used). This is what is used when values are measured by a laboratory. Osmolality is measured by clinical laboratories using an osmometer - either a freezing point depression osmometer or a vapour pressure depression osmometer. The normal osmolality of extracellular fluid is 280-295 mOsmol/kg.

What is osmolarity?

Osmolarity is an estimation of the osmolar concentration of plasma and is proportional to the number of particles **per litre of solution**; it is expressed as mmol/L. This is what is used when a calculated value is derived.

It is derived from the measured Na+, K+, urea and glucose concentrations. The osmolarity is unreliable in various conditions - eg, pseudohyponatraemia such as hyperlipidaemia in nephrotic syndrome, or hyperproteinaemia.

Osmolality calculation

The following equations can be used to calculate osmolarity:

Calculated osmolarity = 2 (Na+) + 2 (K+) + Glucose + Urea (all in mmol/L); OR **Calculated osmolarity = 2 (Na+) + Glucose + Urea (all in mmol/L)**.

The doubling of sodium accounts for the negative ions associated with sodium and the exclusion of potassium approximately allows for the incomplete dissociation of sodium chloride.

The term osmolarity has largely been superseded by osmolality, even when discussing calculated values. Osmolality is used for the rest of this article.

Osmotic gap

The osmotic gap (also called osmolal gap) is an arbitrary measure of the difference between the actual osmolality (measured by the laboratory) and the calculated osmolality. It is normally less than 10-15 mOsmol/kg (see local laboratory for range). Where the osmotic gap is increased, it indicates the presence of other osmotically active solutes which are not taken into account in the calculated osmolality - eg, in methanol or ethylene glycol ingestion.

Clinical relevance of osmolality

As cell membranes in general are freely permeable to water, the osmolality of the extracellular fluid (ECF) is approximately equal to that of the intracellular fluid (ICF). Therefore, plasma osmolality is a guide to intracellular osmolality.

This is important, as it shows that changes in ECF osmolality have a great affect on ICF osmolality - changes that can cause problems with normal cell functioning and volume (may even induce cytolysis).

- In normal people, increased osmolality in the blood will stimulate secretion of antidiuretic hormone (ADH). This will result in increased water reabsorption, more concentrated urine and less concentrated blood plasma. Diabetes insipidus is a condition caused by hyposecretion of, or insensitivity to, the effects of ADH. Elevation may be associated with stroke mortality.
- A low serum osmolality will suppress the release of ADH, resulting in decreased water reabsorption and more concentrated plasma.
- An increase of only 2% to 3% in plasma osmolality will produce a strong desire to drink. A change of 10% to 15% in blood volume and arterial pressure is required to produce the same response.

ADH

The kidney controls water excretion largely through ADH - a polypeptide secreted by the supraoptic and paraventricular hypothalamic cells with axons ending in the posterior pituitary gland. Its half life is 5-20 minutes; this allows for rapid adaptation to fluctuations in plasma osmolality. Secretion of ADH is controlled by osmoreceptors and baroreceptors. Though the body will try to control osmolality more than volume, if the volume drops dangerously low, the kidney will conserve water at the expense of osmolality, ie even though water conservation will reduce the osmolality of body fluids.

Osmolality measurements[4]

- Plasma osmolality - this is usually ordered to investigate hyponatraemia. Osmotic gap may also be requested if presence of osmotically active agents such as mannitol, and glycine (a chemical used in surgical irrigation fluids), is suspected[2] .
- Urine osmolality - this is frequently ordered along with plasma osmolality to help with diagnosis - see table below.

- Stool osmolality - this may help evaluate chronic diarrhoea that does not appear to be due to a bacterial or parasitical infection, ie stool may contain osmotically active substance (eg, laxative). Stool osmotic gap may also be calculated[2] .

Serum osmolality	**Urine osmolality**	**Causes**
Normal or increased	Increased	Dehydration Renal disease and uraemia Congestive heart failure Addison's disease Hypercalcaemia Diabetes mellitus/hyperglycaemia Hypernatraemia Alcohol ingestion Mannitol therapy
Normal or increased	Decreased	Diabetes insipidus
Decreased	Increased	Syndrome of inappropriate ADH secretion (SIADH)
Decreased	Decreased (with no increase in fluid intake)	Overhydration Hyponatraemia Adrenocortical insufficiency Sodium loss (diuretic or a low-salt diet)

This table is a guide. The effect on serum and urine osmolality can vary depending on the individual clinical situation - eg, hypernatraemia may cause a decreased urine osmolality and hyponatraemia may cause an inappropriately increased urine osmolality.

There is limited evidence of the diagnostic utility of any individual clinical symptom, sign or test or combination of tests to indicate water-loss dehydration in older people [5] .

Further reading

- Intravenous fluid therapy in adults in hospital; NICE Clinical Guideline (Dec 2013, updated May 2017)

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