SydPath
ST VINCENT'S PATHOLOGY

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OSMOLALITY INFORMATION SHEET

GENERAL

Osmolality is a count of the number of particles in a fluid sample. The unit for counting is the mole which is equal to 6.02 x 1023 particles (Avogadro's Number). Molarity is the number of particles of a particular substance in a volume of fluid (eg mmol/L) and molality is the number of particles dissolved in a mass weight of fluid (mmol/kg). Osmolality is a count of the total number of osmotically active particles in a solution and is equal to the sum of the molalities of all the solutes present in that solution. For most biological systems the molarity and the molality of a solution are nearly exactly equal because the density of water is 1 kg/L. There is a slight difference between molality and molarity in plasma because of the non-aqueous components present such as proteins and lipids which make up about 6% of the total volume. Thus serum is only 94% water and the molality of a substance in serum is about 6% higher than its molarity. Except in unusual circumstances this difference is unimportant and the terms molarity and molality are often used interchangeably. Note that the size of the particle is unimportant so that a single small molecule, eg glucose, contributes as much to the serum osmolality as a single large protein molecule, eg albumin.

The osmolality of physiological fluids tends to be dominated by small molecules which are present in high concentrations. For example in serum, sodium, potassium, chloride, bicarbonate, urea and glucose are the only components present in high enough concentrations to individually affect the osmolality. Together these make up over 95% of total osmolality of serum. Large serum components contribute little to the overall osmolality. For example the molar concentration of albumin, the most abundant serum protein, is only about 0.6 mmol/L. Only a few exogenous compounds such as ethanol, methanol, ethylene glycol and mannitol can be present in the blood at high enough quantities to significantly affect the osmolality.

PHYSIOLOGY

Plasma

The osmolality of plasma is closely regulated by anti-diuretic hormone (ADH). In response to even small increases in plasma osmolality (usually rises in plasma sodium), ADH release from the pituitary is increased causing water resorption in the distal tubules and collecting ducts of the kidney and correction of the increased osmolality. The opposite happens in response to a low plasma osmolality with decreased ADH secretion and reduced water loss through the kidneys. Note that ADH is also secreted in response to hypovolaemia and this stimulus will over-ride any response to serum osmolality.

Urine

Urine osmolality may vary between 50 and 1200 mmol/kg in a healthy individual depending on the state of hydration. The urine osmolality is the best measure of urine concentration with high values indicating maximally concentrated urine and low values very dilute urine. The main factor determining urine concentration is the amount of water which is resorbed

in the distal tubules and collecting ducts in response to ADH. In a dehydrated patient with normally functioning pituitary and kidneys, a small volume of highly concentrated urine will be produced. In a patient with fluid overload the opposite will be an appropriate response. Note that there is no reference interval ("normal range") for urine osmolality as the interpretation depends on the clinical condition of the patient to determine an appropriate response.

MEASUREMENT

The osmolality of a solution can be measured using an osmometer. The most commonly used instrument in modern laboratories is a freezing point depression osmometer. This instrument measures the change in freezing point that occurs in a solution with increasing osmolality. Osmolality can be measured in samples of serum (gold top tube) or heparin plasma (lime top tube).
Plasma osmolality can also be calculated from the measured components. While there are many equations, a simple one is as follows:
Osmolality (calc) = 2 x Na + Glucose + urea (all measurements 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 difference between the measured and calculated plasma osmolality is known as the osmolal gap and normally is between 0 and 10 mmol/kg.

INDICATIONS FOR MEASUREMENT

Serum osmolality is used in two main circumstances: investigation of hyponatraemia and identification of an osmolar gap.
Urine osmolality is an important test of renal concentrating ability, for identifying disorders of the ADH mechanism, and causes of hyper-or hyponatraemia.
Faecal osmolality can be used to assist with diagnosis of the cause of diarrhoea.

SERUM OSMOLALITY

Serum osmolality is a useful preliminary investigation for identifying the cause of hyponatraemia. If a patient with significant hyponatraemia (serum sodium < 130 mmol/L) has a normal plasma osmolality, the patient may have pseudohyponatraemia due to excess lipids or proteins, or the sample may have been collected from a drip arm containing dextrose. If the patient has an increased osmolality it is likely the patient has reactive hyponatraemia due to an excess of solute pulling water out of cells. Examples of this include glucose in diabetes mellitus or hyperglycinaemia after trans-urethral resection of the prostate. The finding of a hypo-osmolar hyponatraemia ("true hyponatraemia") then leads to further investigation of the cause. See also: Sodium

SERUM OSMOLAL GAP

The osmolal gap is determined by subtracting the calculated osmolality from the measured osmolality.

Osmolal Gap = Measured osmolality - calculated serum osmolality

While there are many formulae for the calculated osmolality, the most commonly used is:
Calculated osmolality = 2 x serum sodium + serum glucose + serum urea (all in mmol/L).
The normal osmolal gap is 0 - 10 mmol/L.

Values in excess of this usually indicate the presence of an exogenous agent. The most common by far is ethanol, but methanol, ethylene glycol, acetone, mannitol and isopropyl alcohol can occasionally be present in sufficient quantities to produce an increased osmolar gap. The equation to calculate the osmolar gap when ethanol has been measured, as a screen for the presence of other substances, is as follows:

Calculated osmolality = 2 x serum sodium + serum glucose + serum urea + 270 x ethanol
(all in mmol/L except ethanol in mg/dL or %, ie the units in use at SydPath).

Calculated serum osmolality = 2 x sodium + glucose + urea + 1.25 x ethanol
(all in mmol/L including ethanol*).

Clinically significant toxicities, particularly from ethylene glycol, can occur with a normal osmolar gap as the toxic concentrations are quite low. With the passing of time from ingestion of alcohol, methanol or ethylene glycol the osmolar gap falls and the anion gap rises due to conversion to negatively charged substances. In diabetic ketoacidosis an increased osmolar gap may be due to acetone accumulation.

* the factor of 1.25, which is included in the factor of 270 in the preceeding equation, is due to ethanol contributing more to the osmolar gap than would be expected from its molecular weight of 46 (Pursell RA et al Ann Emerg Med 2001;38:653-659).

URINE OSMOLALITY

Urine osmolality is an important test for the concentrating ability of the kidney. Interpretation of urine osmolality must always be made in the light of the appropriate physiological response to the state of hydration of the patient. The test is useful in the following areas:

- For determining the differential diagnosis of hyper- or hyponatraemia.
- For identifying SIADH (urine osmolality > 200 mmol/kg, urine sodium > 20 mmol/L, low serum sodium, patient not dehydrated and no renal, adrenal, thyroid, cardiac or liver disease or interfering drugs).

- For differentiating pre-renal from renal kidney failure (high urine osmolality is consistent with pre-renal impairment, in renal damage the urine osmolality is similar to plasma osmolality).
- For identifying and diagnosing diabetes insipidus (low urine osmolality not responding to water restriction).

FAECAL OSMOLAL GAP

Faecal osmolality is used to determine the faecal osmolal gap.

Faecal osmolal gap = measured faecal osmolality - calculated faecal osmolality

Calculated faecal osmolality = 2 x (faecal Na+K)

If the faecal osmolal gap is greater than 100 mmol/L this is consistent with an osmotic diarrhoea. Causes of osmotic diarrhoea include high faecal carbohydrates due to poor absorption (eg mannitol, sorbitol, lactulose); monosaccharides; short chain fatty acids; or magnesium as used in antacids). A normal faecal osmolar gap indicates a secretory diarrhoea indicating damage or irritation of the gastro-intestinal mucosa. The faecal osmolar gap can only be applied to faecal samples which contain a high fluid content.