Osmotic Pressure in Biological Fluids

Application to Patients in General Practice

PROF. J. GATT MD. MSc,
FRCP, FRC Path, DTM +H
DEPT. DIRECTOR. DEPARTMENT OF PATHOLOGY

Dr. V. HOLECEK, MD, BSc
CONSULTANT BIOCHEMIST. DEPARTMENT OF PATHOLOGY

Osmotic pressure in biological fluids is one of the most important physical values. Different solutions at the same temperature and the same concentration (activity) of ions have the same osmotic pressure. This means that a big molecule of protein for instance has the same osmotic effect as the small ion of sodium. Osmolality expresses the number of dissolved particles in a given weight of solvent. The solution of one mole of each fully dissociated compound has the osmotic pressure of 22.412 atm. The formula for checking the osmotic pressure is:

$$P = R \times T \times c$$

Where P = osmotic pressure, R = universal gas constant (0.08204), T = temperature in the Kelvin's scale, c = concentration in moles.
If we want to imagine the force which the osmotic pressure can produce, the following experiment could be done: (Fig. 1)

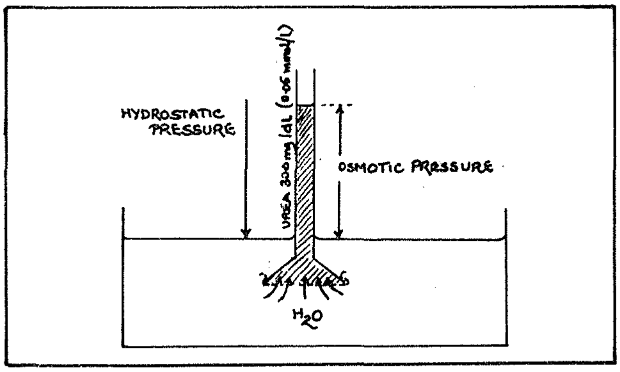

Figure 1

In the vessel there is distilled water, in the funnel there is a 300 mg% solution of urea (0.05 mol/ℓ). Both fluids are separated by a semipermeable membrane, which enables the passage of water into the compartment with the urea solution. According to the law of isoosmolality, when two solutions are separated by a semipermeable membrane and on both sides of the membrane there are different osmotic pressures, the water and the ions will pass through the membrane until the osmotic pressures on both sides are equal; the water from the vessel will dilute the solution in the funnel. The equilibrium occurs when the hydrostatic pressure will be in balance by the osmotic pressure (shown by the column of fluid in the funnel.)

We can calculate the absolute osmotic pressure (at 20° C and the barometric pressure of 760 mm Hg):

$$P = 0.08204 \times 293 \times 0.05 = 1.2 \text{ atm}$$

This pressure corresponds to: 760 x 1.2 = 912 mm Hg (=14.2 m of water). If we realise that the patients with renal insufficiency often have such a urea concentration in the blood and that there are many other ions in high concentrations (Na^+, K^+, HCO_3^-, glucose etc.) we can easily imagine how changes in osmotic pressure of body fluids can be fatal.

We have to distinguish the terms osmolarity (osmotic pressure in 1 litre of the solution) and osmolality (osmotic pressure in 1 kg of the solution). Both these values in the serum are not much different. Usually we use osmolality due to the methods of estimation. Mostly we use the cryoscopic method (by dissolving of a solute (compound) the properties of the solvent change, e.g. 1 mole of a substance dissolved in 1 kg lowers the freezing point of water by 1.86° C.) The boiling point of the solution also increases; the vapour tension decreases; osmotic pressure and conductivity increase. The estimation of other physical parameters as conductometry, densitometry of the solution etc. are complicated and inaccurate and therefore not in use.

In biochemistry in the past we used a unit the osmol (Osm), equal to 10^{-3} x a smaller unit, the milliosmol (mOsm). In the new SI units convention we use mmol as a unit. There is no change in the numerical value. 1 mmol/kg = 2.58 kPa at 37° C.

The osmotic pressure (osmolality) can be calculated according to the formula:

$$\text{mmol/kg} = \frac{\text{mg of the compound in 1 kg x the number of active compounds (ions)}}{\text{relative molecular mass}}$$

For example the osmotic pressure of the saline isotonic solution (0.9%) is:

$$\text{mmol/kg} = \frac{9000\ \text{mg/kg} \times 2\ (\text{number of ions, i.e. } Na^{+} + Cl^{-})}{58.5\ (\text{relative molecular mass of NaCl})} = \mathbf{308\ mmol/kg}$$

But we know that the normal osmolality of the blood is 285 ± 10 mmol/kg. (Higher values = hyperosmolality, lower values = hypoosmolality).

Blood is not an ideal water solution and therefore NaCl is dissociated by 93% only = 308 x 0.93 = **286 mmol/kg** and this osmolality already corresponds with the osmolality of the blood. This so called "physiological solution" is not really "physiological" due to the lack of Na^+ in correlation to Cl^-, yet this solution is isotonic.

The osmolality of the blood is lower than the calculated amount of the osmotic active compounds. (Fig 2). Collectively there is, in the serum, 150 mmol/kg of cations, the same amount of anions + 10 mmol/kg (urea & glucose) = 310 mmol/kg. The osmolality of 285 mmol/kg is lower due to the incomplete dissociation rate of the solute; i.e. 25 mmol/kg lower. It is well known that the erythrocytes in hypertonic solutions lose water and reduce volume, in hypotonic solution the erythrocytes absorb water, their volume increases and this can lead to haemolysis due to the rupture of the membrane.

There are several formulas available which help us calculate the osmolality of the serum. A very simple formula is the following:

mmol/kg = 1.86 (Na^+ + K^+ mmol/kg) + urea mmol/l + blood glucose mmol/l + 10 (for simplification we use osmolality and osmolarity together).

But no calculation can substitute the actually measured osmolality. It is well known that in healthy people the calculated osmolality is very near to the real (i.e. measured) osmolality. But that in patients where catabolism predominates, the difference between the calculated and measured osmolality is greater. Some authors (e.g. in toxicology) consider the high difference between these values to be the indications for dialysis. Other possibilities of higher measured osmolalities compared with calculated osmolalities are: decrease of serum water or the presence of uncalculated substances if present (e.g. mannitol, sorbitol, acetone, ethanol, glycerol, trichlorethane etc.)

The osmotic pressure in nature is sometimes very high, but it can act only in those cases where there is a difference between two or more systems. Slight differences of osmolality enable the transport of ions and compounds across the semipermeable membranes. It sometimes happens that the osmotic pressure suddenly increases. For example: after dislocation of a joint, at one point of the anatomy at a specific point in time, haemorrhage occurs. The extravasated blood proteins in the tissues are haemolysed and degraded to smaller compounds at a geometrical rate and the osmotic pressure locally increases quickly. From the surrounding tissues with lower osmolality the water flows (according to the law of isoosmolality) and the joint becomes swollen. Similar changes can occur in the brain when e.g. in diabetic coma and injection of insulin, the blood glucose and blood osmolality rapidly decrease. These changes in the central nervous system are delayed, the glucose level in cerebrospinal fluid decreases slowly and the water is attracted into the brain spaces and this leads to oedema of the brain sometimes with lethal consequence. Therefore, the therapeutic decrease of the hyperosmolality must be slow (2-4 mmol/hour). Another example: Alcohol produces hyperosmolality due to dehydration as the urine volume increases. After alcohol intoxication and loss of water osmolality increases and the osmotic receptors of the body provoke the sense of thirst. After drinking of water the osmolality decreases, but again the delayed response (slower decrease of osmolality) in the central nervous system and in cerebrospinal fluid leads to severe headache. Administration of salts will help with water by reducing the differential values. In the therapy of brain oedema we can use the administration of urea to the patient. Urea is distributed very quickly in the body with the exception of cerebrospinal fluid. The penetration of urea into the CSF is delayed and this fact can turn the water-flow from the brain compartment back to the body fluid compartment. Similar changes can occur after a rapid haemodialysis in cases of renal insufficiency.

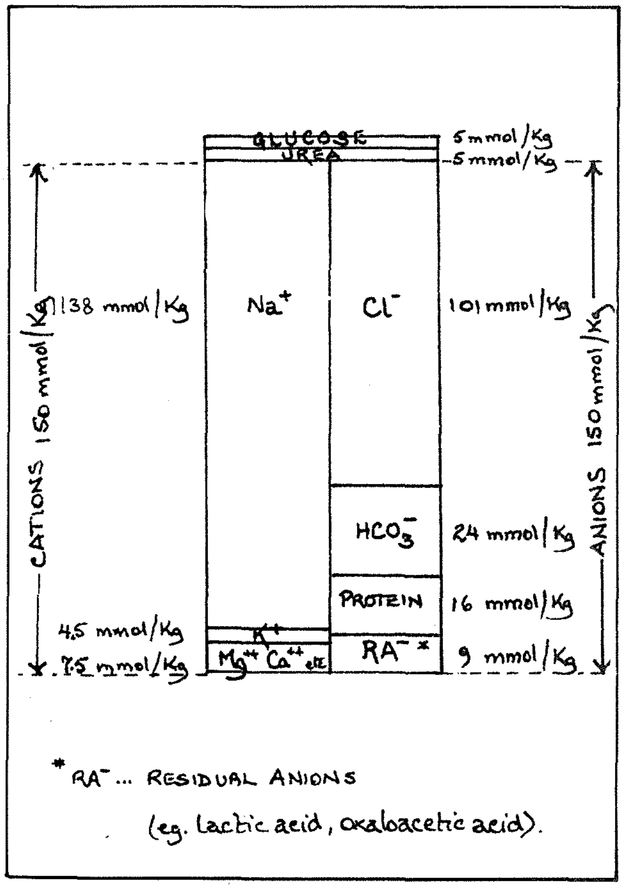

Figure 2.

From these examples we can see the importance of changes in osmolality in clinical medicine.

Increased serum osmolality occurs in water depletion, infantile gastroenteritis (high milk osmolality), in hyperosmolar non-ketonic diabetic acidosis and in diabetic ketoacidosis. Low blood pH values also lead to high dissociation rate of some compounds and leading to the increase of osmolality. Increased breakdown of proteins leads to hyperosmolality, e.g. after burns cases (alas often treated with high protein intake). Cerebral lesions, diabetes insipidus, alcohol intoxication (increased elimination of water) lead to hyperosmolality as well. Inability to drink (e.g. unconsciousness), loss of sense of thirst (old age), lack of water of low electrolyte concentration (shipwrecked person, wrong parenteral nutrition) and hypostenuria are other causes of hyperosmolality.

Decreased serum osmolality occurs in adrenocortical insufficiency, untreated severe panhypopituitarism; salt loss, water intoxication, wrong parenteral nutrition and inappropriate ADH secretion. Catabolic states lead to decrease of protein (albumin), lower oncotic pressure (osmotic pressure of proteins) and therefore to the flow of water from the blood vessels into the tissues (hypoproteinamicoedemas). Similar changes occur in renal diseases with albuminuria. In catabolic conditions the body weight and osmolality are decreasing in a parallel fashion. However when the tissue mass only decreases and not osmolality we expect oedema to appear; (the patient begins to retain water and ions) therefore the loss of body weight is masked by the oedema. If the osmolality is decreasing, but not the body weight there is a danger of water intoxication.

Under physiological conditions the osmotic pressure is controlled by osmoreceptors. Hypo-osmolality leads to stimulation of osmoreceptors and causes decreased secretion of antidiuretic hormone. The water resorption in the kidneys is diminished and the kidneys excrete the excess of water during 2-3 hours. A close correlation is seen between osmolality and viscosity of the body fluids. The increase of osmolality leads to the decrease of blood flow (especially in arteriosclerosis). Hyperosmolality leads to the highly concentrated urine excretion (and/or bile excretion) and increases the danger of lithiasis and infection.

Acute disorders of osmolality. Rapid injury of the cells, due to toxic agents or hypoxia, leads to catabolism in the cells; the amount of degradation products increases and even osmolality increases. The cells absorb water by imbibition, necrotic cells increase the amount of catabolites and the kidneys are unable to eliminate all these osmotically active compounds with sufficient speed; as a result, osmolality increases.

Chronic disorders of osmolality. Severely ill persons are not able to restore all the cell structures and plasma protein levels, especially, fail to return to normal levels. The ability of retaining cations and anions in the body fluids is diminished and the osmolality decreases.

Practical Problems

Example A

1. The patient weighs 60 kg, his blood osmolality is 285 mmol/kg. What happens if he receives an infusion of 3 litres of isotonic NaCl solution?

   Usually the total amount of water is 60% of body weight = 60× 0.6 = 36 l(kg)
   Intracellular fluid is usually 40% = 60 × 0.4 = 24 l(kg)
   Extracellular fluid is usually 20% = 60 × 0.2 = 12 l(kg)

   Na^+ and Cl^- are extracellular ions and therefore the 3 litres are retained in the extracellular fluid = 12l + 3l = 15l. Due to isotonicity, the osmotic pressure will not change but the extracellular volume will increase. (Fig. 3)

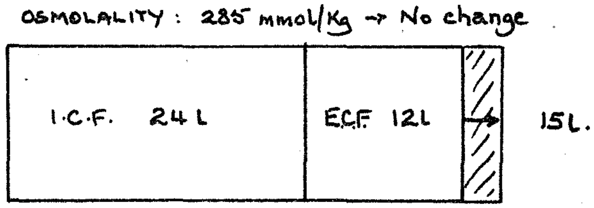

Figure 3

Example B

2. What happens if the same patient receives an infusion of 3l 5% glucose?

   Glucose is metabolised to water and CO_2. 3 litres of water will dilute intracellular and extracellular fluid according to the law of isosmolality, i.e. 2 litres go to intracellular fluid and 1 litre goes to extracellular fluid. The osmolality of the blood of the patient was 285 mmol/kg. Total amount in both body fluids of osmotic active compounds was 36 (kg) x 285 = 10260 mmol. The new volume (weight) of body water is 36 + 3 kg = 39 kg. The new osmolality is 10260 ÷ 39 = 263 mmol/kg, i.e. decrease of 22 mmol/kg. Therefore there has been a drop in the osmolality of intra and extracellular fluid. (Fig. 4).

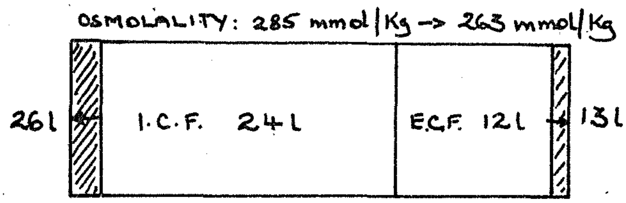

Figure 4

Example C

3. What happens if the same patient receives an infusion of 1 litre of isotonic NaCl solution and 2 litres of 5% solution of glucose?

   1 litre of isotonic saline solution increases the amount of the extra-cellular fluid. 2 litres of 5% glucose after its oxidation to water increase the amount of both fluids in relation 2:1. Intracellular fluid therefore increases from 24 l to 24 + (2:2/3) = 25.33 l. Extra-cellular fluid increases from 12 l to 12 + 1 + 2:1/3 = 13.66 l. The osmolality will change (for simplification we consider litre = kg) : total amount of osmotic active compounds is 10260 + 285 = 10545 mmol. The amount of water is 39 l. The new osmolality is 10545 : 39 = 270.4 mmol/kg. Therefore there has been a drop of osmolality in the extracellular and intracellular fluid from 285 to 270.4 mmol/Kg. (Fig. 5)

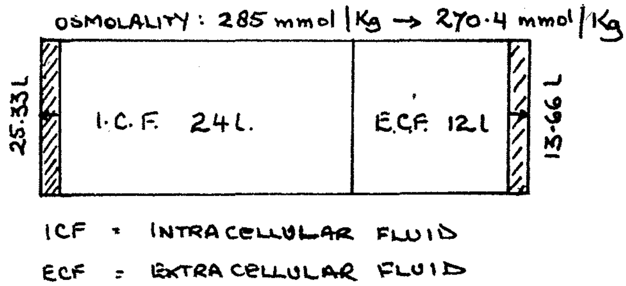

Figure 5

The checking of the osmolality of any solutions is a quick quality control.

Example D

4. We need to give 1 litre of infusion solution 0.3g KCl and 0.33g $CaCl_2$. How many g of NaCl we must add to the solution, if final osmolality should be 295 mmol/kg?

   Molecular weight of KCl: 74.6, $CaCl_2$: 111.1 and NaCl : 58.5

   The amount of g K in 0.3 g KCl:

$$\frac{\text{at. wt. of K} \times 0.3}{\text{mol. wt. of KCl}} = \frac{39.1 \times 0.3}{74.6} = 0.157 \text{ g } (= 157 \text{ mg})$$

   The amount of mmol K in 0.3 g KCl:

$$\frac{157}{39.1} = \mathbf{4\ mmol/l}$$

   The amount of Cl in 0.3g KCl:

$$\frac{35.5 \times 0.3}{74.6} \times \frac{1000}{35.5} = 4.0 \text{ mmol/1}$$

The amount of mmol Ca in 0.33 g $CaCl_2$:

$$\frac{40.1 \times 0.33}{111.1} \times \frac{1000}{40.1} = \mathbf{3.0\ mmol/l}$$

The amount of mmol Cl in 0.33 g $CaCl_2$ must be 2 times higher than Ca = **6.0 mmol/l**

Total osmolality of 0.3 g KCl and 0.33 g $CaCl_2$ is 4 + 4 + 4 + 3 + 6 = 17 mmol/l

295 (wanted osmolality) - 17 mmol/l = 278 mmol/l = we must add 278:2 = 139 mmol of Na and 139 mmol Cl: 139 x 58.5 = 7131.5 mg NaCl = **7.1315g NaCl**

Example E

5. A patient weighs 60.0 kg and ingests 29.25g of NaCl. What happens to his osmolality (previous was 285 mmol/kg) and to his extra - and intracellular fluids?

   29.25g NaCl corresponds 29.25: 58.5 = 0.5 mol of NaCl — 500 mmol NaCl = 1000 mmol of osmotically active compounds.

   Before the intake of NaCl the body fluid osmotic active compounds divided into:
   total body fliuds = 36 x 285 + 10260 mmol

   extracellular fluid 12 x 285 = 3420 mmol
   intracellular fluid 24 x 285 = 6840 mmol

   New amount of mmol = 10260 + 1000 + 11260 mmol (in total body fluid) NaCl increased only the amount of osmotic active compounds in the extracellular fluid: 3420 + 1000 = 4420 mmol

   The new osmolality in the body will be 11260: 36 =312.777 mmol/kg. The volume of the extracellular fluid will be = 4420 ÷ 312.777 = 14.13l.

   After ingestion of 19.25g NaCl increases the osmolality to 312.777 mmol/kg and the extracellular fluid volume increased to 14.13ℓ (2.13ℓ more) the intracellular fluid volume decreased to 21.87ℓ

   These calculations show the importance of deionisation of drinking water. Increase of extracellular volume puts a greater load on the heart, but healthy kidneys can regulate the electrolyte balance and correct for extra load.

Urine Osmolality

Under physiological conditions the water and the ion uptake is very variable. The smallest quantity of water which is needed for the elimination of all the catabolites in urine (resting adult people, maximal concentration rate of the kidneys) is 500-600 ml/24 hours. The urine osmolality increases to 800-1100 mmol/kg. The concentration index of osmolality (I_{OSM}) can reach the value:

$$I_{OSM} = \frac{U_{OSM}}{P_{OSM}} = \frac{1100}{285} = 3.86$$

(U_{OSM}= osmolality of the urine in mmol/kg, P_{OSM} = osmolality of the plasma in mmol/kg).

I_{OSM} expresses the objective concentration ability of the kidneys. The higher values are reached by 15-19 years old individuals. The concentration rate of kidneys is age dependent and at the age of 60-69 years has its highest values of 796 mmol/kg. In young healthy people 1 mmol of osmotic active compounds can be eliminated by 0.8 - 10.0 ml of water. The amount of osmotically active catabolite during 24 hours during fasting and at rest is 200-500 mmol. People under normal conditions and normal nutrition produce 600-1200 mmol/24 hours. Heavy catabolism in patients produces 1200-1400 mmol/24 hours and more. The daily amount of osmotically active compounds which should be eliminated by urine is increased by: physical load, uptake of electrolytes and food, increased (body) temperature, pathological conditions, operation, infection, intoxication, x-rays, necrosis, increased proteolysis, metabolic disturbancies (diabetes, hypoxia, fasting). As a result the urine shows very high level of urea. Again glucose in diabetics needs much more water to be excreted (45g of glucose need 250-1000 ml of water).

When the kidneys of a patient lose their concentrating and diluting ability, I_{OSM} is near to 1.00. In such cases the kidneys will need 1200-1700 ml of water (sometimes more) for elimination of the catabolites under resting conditions. For elimination of 1 mmol/kg of osmotic active compounds such patients need 3.5 ml of water.

Clearance of osmotic active compounds (C_{OSM})

C_{OSM} is the amount of plasma in ml which is cleared of osmotic active compounds during 1 minute. It is calculated as follows:

$$C_{OSM} = \frac{U_{OSM} \times V}{P_{OSM}}$$

(U_{OSM} urine osmolality in mmol/kg, V.. 1-minute volume of urine, P_{OSM}•• average plasma osmolality in mmol/kg). In healthy people the osmotic clearance is 2.0-3.0 ml/min.

In renal insufficiency the kidneys are unable to excrete enough of the osmotically active compounds. This leads to an increase of plasma osmolality, C_{OSM} decreases. Increase of osmotic clearance (osmotic diuresis) is an important datum for the physician since it reflects upon the metabolism of drugs which have been administrated to the patient. These are eliminated in urine at a higher rate i.e. proportional to C_{OSM}• Other values are often caluclated, i.e.: EF_{OSM} (Excretion fraction of osmotically active compounds in % shows us what part of filtrated amount of osmotic active compounds is actually eliminated into the urine (C_{Cr}•• clearance of creatinine)

$$EF_{OSM} = \frac{C_{OSM}}{C_{Cr}} \times 100\ (\%)$$

Normal values: up to 3.5%. Resorption fraction is 100 - EF_{OSM}•

When hypertonic urine is formed (U_{OSM} is higher than P_{OSM}) the so called non-solute water (T_{H_2O}) in the collecting tubules is resorbed. The intensity of the resorption of the non-solute water is calculated:

$$T^c_{H_2O} = C_{OSM} - V\ \text{(ml/min)} \qquad (V = \text{minute volume of urine})$$

related to C_{Cr}: $$\frac{T^c_{H_2O}}{C_{Cr}} \times 100\ (\%)$$

Normal values: maximum by osmotic diuresis: 5%.

When hypotonic urine is formed (U_{OSM} is lower than P_{OSM}) the cells in such urine are quickly destroyed; relatively higher resorption of osmotically active compounds takes place in the distal part of nephron than that of water. The intensity of resorption of osmotically active compounds without water is the renal clearance of non-solute water (C_{H_2O}):

$$C_{H_2O} = V - C_{OSM}\ \text{(ml/min)}$$

related to C_{Cr}:

$$\frac{C_{H_2O}}{C_{Cr}} \times 100\ (\%)$$

Normal values: average 10.38%

All these biochemical parameters enable us to evaluate even the slight disturbances of kidney function. There are many other important estimations of osmolality in practice, but in this paper we wanted to give the reader only the rudimentary informations

Conclusions:

A summary of osmotic relationships in the human body fluids has been given. The importance of the osmolality is great, the application of it saves lives. The osmolality of urine cannot be substituted by urine density estimation or other examinations. Monitoring of urine osmolality is another important parameter in the diagnosis of kidney insufficiency. Intravenous infusion of electrolytes, hypervolaemia or hypovolaemic states, parenteral feeding and electrolyte imbalance cannot be managed efficiently without the knowledge of plasma and urine osmotic parameters.

Reference: NEJEDLY B (1980): *Internal Environment*, AVICENUM, PRAGUE.