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Letter to the Editor – not accepted
Appraisal for a better understanding of osmolarity and osmolality of intravenous fluids
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Dear editor,
In a recent review by Hoorn [1] about intravenous fluids, the values presented as osmolality (mosmol/kg H_2O) of plasma and intravenous fluids (Table 3) are confusing and may result in erroneous consequences:

- Saline 0.9% was evaluated correctly as isotonic, but the osmolality should be 286 and not 308 mosmol/kg H_2O.
- Lactated Ringer's was evaluated correctly as hypotonic, but the osmolality should be 256 and not 279 mosmol/kg H_2O.
- Sterofundin was evaluated correctly as isotonic, but the osmolality should be 287 and not 309 mosmol/kg H_2O.
- PlasmaLyte was inaccurately presented as isotonic: The manufacturer indicates a theoretical osmolarity of 294 mosmol/L, which results in an osmolality of 274 mosmol/kg H_2O (mildly hypotonic).
- Glucose 5% was evaluated correctly as hypotonic, but the presented value of 278 should be the theoretical in-vitro osmolarity (mosmol/L) and not the in-vitro osmolality, which is 290 mosmol/kg H_2O. Of importance, the in-vivo osmolality after glucose metabolization is 0 (=pure water).
- Lactate, acetate, gluconate and maleate are bicarbonate precursors and not buffers.

The theoretical osmolarity of fluids is calculated by adding up all osmotically active ingredients relative to 1 liter (mosmol/L). The actual (real) osmolality (rather than osmolarity) can be measured using freezing point depression (FDP) or calculated using a novel formula based on results of blood gas analysis (POCT; mean difference 0.5 mosmol/kg H_2O compared to FDP [2]). By pure chance, the actual (real) osmolality of plasma (288 mosmol/kg H_2O) is practically identical to the theoretical osmolarity (291 mosmol/L) calculated from its analytical composition [3]. This coincidence is presumably responsible for some of the confusion in the medical literature. In accordance with Hoorn [1], an osmolality of 288 mosmol/kg H_2O should be used as a reference point for an isotonic or iso-osmolal electrolyte solution [2].
Saline 0.9% has a theoretical osmolarity of 308 mosmol/L (=154 mmol/l Na^+ + 154 mmol/L Cl^-) or an actual (real) osmolality of 286 mosmol/kg H_2O (=theoretical osmolarity 308 × osmotic coefficient 0.926/water content 0.997). The difference can be explained by the fact that a part of the electrolytes infused are not osmotically effective because of absorption on proteins and cell membranes [3]. As compared to plasma and extracellular fluid, lactated Ringer's (=Hartmann's) solution is hypotonic (276 instead of 308 mosmol/L or 256 instead of 288 mosmol/kg H_2O) and glucose 5% has an (isotonic) in-vitro osmolality of 290 mosmol/kg H_2O (=theoretical osmolarity 278 × osmotic coefficient 1.013/water content 0.97), but is extremely hypotonic in-vivo after glucose metabolization (0 mosmol/kg H_2O). Therefore, infusion of large volumes may reduce the plasma osmolality and result in hypoosmolality and encephalopathy.

We agree with Hoorn [1] that the use of isotonic rather than hypotonic intravenous fluids is now well established, especially in pediatrics [4], but from our point of view and in accordance with recent warnings by the European Medicines Agency [5], a better understanding of the sometimes confusing items osmolarity (mosmol/L) and osmolality (mosmol/kg H_2O) of plasma and intravenous fluids is urgently needed when evaluating the safety of different electrolyte solutions to avoid iatrogenic hypoosmolality and encephalopathy.

References

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