The concept of hypertonic solutions

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Hypertonic crystalloids (around 2500 mOsm/L), often in combination with colloids, have been studied both experimentally and clinically. They produce increased osmolarity in extracellular fluid which results in movement of water from the intracellular compartment to the interstitial and vascular compartments[1]. A recent study demonstrated that the same plasma volume volume expansion is obtained either with 4 ml/kg of hypertonic solution or 27 ml/kg of Ringer's lactate[2]. Hypertonic solutions have the advantage of limiting or reducing the interstitial edema. In addition to plasma volume expansion, several other effects contribute to explain the efficacy of hypertonic solutions. Their sustained duration of action is due to reflex mechanisms responsible for venous constriction and increased cardiac contractility[3]. The pathways and centers of these reflex mechanisms continue to be discussed. The presence of intact vagus nerves and the orthosympathetic system appears essential. The increase in cardiac contractility could also be a reflex or it could result from a direct action of hyperosmolarity on myocardial fibers[4]. Hyperosmolarity vasodilates the splanchnic and renal tissue beds[5], an effect that is particularly useful in the setting of hemorrhagic and septic shock. As well, the shrinking of erythrocytes and of swollen vascular epithelium could facilitate tissue oxygenation[6]. Furthermore, hypertonic saline solutions have a strong effect on intracranial water volume distribution substantially decreasing intracranial pressure[7]. Antiinflammatory effects of hypertonic solutions are now well documented. These solutions decrease the action of neutrophils and endothelial cells[8]. As a consequence, the increase in capillary permeability which is generally associated with shock is significantly reduced with the treatment with hypertonic solutions. The MAP kinase p38 appears to be the key enzyme whose activity is modify by osmolarity changes[9]. A multicenter study in trauma patients[10] has suggested that treatment with hypertonic solutions may be associated with an improvement in coagulation and a decrease in acute respiratory distress syndrome, and acute renal failure. In all, hypertonic solutions should be considered to be not only volume as volume expanders, but also drugs with anti-inflammatory actions, systemic and regional cardiovascular effects.

Several trials have compared initial resuscitation of trauma patients with hypertonic saline combined with colloid to resuscitation with isotonic crystalloid alone. A study by Molls[11] demonstrated that hypertonic solution combined with hydroxyethyl starch is associated with a significant reduction in the total volume of infused crystalloids and colloids and with a significant improvement in the duration of initial resuscitation. A meta-analysis[12], reported that overall, the use of hypertonic saline alone for resuscitation from hemorrhagic shock was

not associated with improvement in mortality rates. However, as shown by 2 other meta-analyses[13,14], several subgroups of patients, (e.g. patients with hypotension and severe head trauma, patients with penetrating injuries) may significantly benefit from the treatment with of hypertonic saline especially when combined with a colloid.

Hypertonic saline solutions combined with hydroxyethylstarch are now registered and available in several European countries including Italy.

Bibliography

1. Mazzoni MC, Borgstrom P, Arfors KE, Intaglietta M: Dynamic fluid redistribution in hyperosmotic resuscitation of hypovolemic hemorrhage. Am J Physiol 1988; 255: H629-37
2. Tollofsrud S, Elgjo GI, Prough DS, Williams CA, Traber DL, Kramer GC. The dynamics of vascular volume and fluid shifts of lactated Ringer's solution and hypertonic-saline-dextran solutions infused in normovolemic sheep. Anesth Analg. 2001;93:823-31.
3. Lopes OU, Pontieri V, Rocha e Silva M, Jr., Velasco IT: Hyperosmotic NaCl and severe hemorrhagic shock: role of the innervated lung. Am J Physiol 1981; 241: H883-90
4. Mouren S, Delayance S, Mion G, Souktani R, Fellahi JL, Arthaud M, Baron JF, Viars P: Mechanisms of increased myocardial contractility with hypertonic saline solutions in isolated blood-perfused rabbit hearts. Anesth Analg 1995; 81: 777-82
5. Kien ND, Reitan JA, White DA, Wu CH, Eisele JH: Cardiac contractility and blood flow distribution following resuscitation with 7.5% hypertonic saline in anesthetized dogs. Circ Shock 1991; 35: 109-16
6. Boldt J, Zickmann B, Rapin J, Hammermann H, Dapper F, Hempelmann G: Influence of volume replacement with different HES-solutions on microcirculatory blood flow in cardiac surgery. Acta Anaesthesiol Scand 1994; 38: 432-8
7. Prough DS, Whitley JM, Taylor CL, Deal DD, DeWitt DS: Regional cerebral blood flow following resuscitation from hemorrhagic shock with hypertonic saline. Influence of a subdural mass. Anesthesiology 1991; 75: 319-27
8. Pascual JL, Khwaja KA, Ferri LE, Giannias B, Evans DC, Razek T, Michel RP, Christou NV. Hypertonic saline resuscitation attenuates neutrophil lung sequestration and transmigration by diminishing leukocyte-endothelial interactions in a two-hit model of hemorrhagic shock and infection. J Trauma 2003; 54:121-30
9. Loomis WH, Namiki S, Ostrom RS, Insel PA, Junger WG. Hypertonic stress increases T cell interleukin-2 expression through a mechanism that involves ATP release, P2 receptor, and p38 MAPK activation. J Biol Chem. 2003 14;278:4590-6.

10. Mattox KL, Maningas PA, Moore EE, Mateer JR, Marx JA, Aprahamian C, Burch JM, Pepe PE. Prehospital hypertonic saline/dextran infusion for post-traumatic hypotension. The U.S.A. Multicenter Trial. Ann Surg. 1991 ; 213: 482-91.

11. Mols P, Robert P, Henry B, Fox A, Gillet JB, Flamand JP, Bepperling F: Study on the feasibility and hemodynamic efficacy of intravenous administration of small volume 7.2% NaCl hydroxyethyl starch 200/0.5 6% in trauma patients during the prehospital period: a pliot study. JEUR, 1999; 3: 99-104

12. Wade CE, Kramer GC, Grady JJ, Fabian TC, Younes RN: Efficacy of hypertonic 7.5% saline and 6% dextran-70 in treating trauma: a meta-analysis of controlled clinical studies. Surgery 1997; 122: 609-16

13. Wade CE, Grady J, Kramer G : Efficacy of hypertonic saline dextran in patients with traumatic hypotension : meta-analysis of individual patient data. Acta Anaesthesiol Scand; 1997; 110 Suppl: 77-9

14. Wade CE, Grady JJ, Kramer GC, Younes RN, Gehlsen K, Holcroft JW : Individual patient cohort analysis of the efficacy of hypertonic saline/dextran in patients with traumatic brain injury and hypotension. J Trauma, 1997; 42 (Suppl): S61-S65