Proceedings of Frontiers in Critical Care 2013. Resuscitation - which type of fluid?

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Introduction and background

The choice of fluid for volume resuscitation is a difficult one. No definite indication of the superiority of one fluid over others is available. Research provides some implications for practice. Professor Gattinoni comprehensively compared albumin, artificial colloids, and various crystalloids in the light of recent literature and the expected results of his ALBIOS Trial.

Methods

Analysis of professor Luciano Gattinoni's presentation on the first Frontiers in Critical Care congress on the 12th of April 2013 in Amsterdam, The Netherlands, complemented by a review of relevant papers.

Results and main message

At the Frontiers In Critical Care congress in Amsterdam, Professor Gattinoni compared albumin to synthetic colloids and crystalloids for volume resuscitation. The common physiological response to different types of shock, characterized by pressure reduction, with or without absolute volume deficit in the arterial tree, is a direct and sympathetically mediated activation of the renin-angiotensin-aldosterone (RAAS) system and anti diuretic hormone (ADH) release. This results in the adaptive response of water re-absorption and sodium retention in the kidney leading to plasma volume (re-)expansion [3]. Suppressing this homeostatic response (baroreceptor stimulation) depends on the amount of infused fluid, not on the type of fluid.

The ratio of the amounts of colloids to crystalloids needed to achieve the same amount of intravascular volume expansion is thought to be 1:1.5 [3]. Benefits and risks only play a part when large volumes are infused in a relatively short time [3]. These benefits and risks depend on physical and chemical effects of infused solutions and include transportation, antioxidant features, nitrix oxide (NO)-modulation and effects on acid-base status.

Albumin is a versatile molecule. It serves as a carrier molecule for calcium, hormones (e.a. thyroid and steroid), fatty acids and protein. It also serves as a oxygen radical and NO scavenger by its cysteine residues exposing a thiol (SH-radical) group, while its 16 histidine imidazole residues serve as a buffer with a pH of about 6.75 (weak acid) [1]. Albumin is thought to aid in the normalization of inflammatory parameters in sepsis by modulating NO metabolism and free radical production [1]. Albumin is also the major determinant of the oncotic pressure in plasma, whereby the concentration-pressure relationship is a nonlinear, exponential one.

On altered capillary permeability (i.e. in full blown sepsis) none of the fluids, colloid nor crystalloid, have beneficial or negative effects. In battling low pressure this is probably the same, showing an equally indifferent effect of crystalloid and colloid solutions, except for albumins potential scavenging of NO, lessening vasoplegia in sepsis.

Crystalloids would be expected to have a worsening effect on (pulmonary) edema formation, while an indifferent effect of colloids is expected. Regarding kidney function, the 6S-Trial sends a clear signal that synthetic colloids (eg hydroxyl-ethyl starches, HES) are detrimental to kidney function compared to Ringers solution, leading to increased mortality [7]. The CHEST trial shows more renal replacement therapy and consistently higher creatinine levels in patients treated with HES than in those treated with saline [6]. Saline [3] and possibly hyperoncotic albumin [9] might also worsen renal insufficiency, leaving

lactated Ringers and Rehydrating III as safe choices.

Another important side-effect of volume loading is the alteration of acid-base status of the blood, an effect that becomes clinically relevant when an extracellular volume is diluted by about 10% [3]. Acid-base status can be understood by the Steward Equations. The difference in concentrations (mEq) between fully dissolved (strong) cations (sodium, potassium, calcium and magnesium) and anions (chloride and other strong anions) is the strong ion difference (SID). The SID is about equal to the Buffer Base (BB), defined as the sum of the molar charge of the bicarbonate and non-volatile weak acid buffers ([A-]) which are largely determined by total protein content (mainly being albumin). Both influence proton concentrations because of constant physiological electro-neutrality. Independent determinants of pH are: SID, pCO_2 and [A-].

Since the publication of Scheingraber in 1999 it is known that infusing large amounts of saline results in acidosis, while infusing the same amount of Ringers solution does not seem to alter pH [8]. This can be explained by in vitro experiments diluting plasma with a solution with a SID of 0 (water or normal saline) showing the determinants of pH being evenly diluted in a closed system leading to no pH change [4]. Dilution under a constant $pCO2$ (open system) on the other hand will lead to acidosis, because carbon dioxide content (volatile acid load) increases to pre-dilution value, while SID and protein content remain diluted. When, in vivo diluting plasma in an open system with a substance that has a strong ion difference similar to the baseline $HCO3-$, pH will remain constant, a diluent with a SID lower than baseline bicarbonate produces acidosis and one with a higher SID produces alkalosis [2].

In a swine model with an average baseline serum bicarbonate of 29.2 mEq/l, Ringers lactate having a SID of 28 mEq/l after lactate metabolism produces no pH change, while dilution with rehydrating III solution, having a SID of 55 mEq/l after metabolism of acetate leads to alkalosis, and saline (SID=0 mEq/l) produces acidosis [5]. So saline and starches in a saline solution worsen acidosis and are possibly the worst choice for large volume resuscitation in this respect [3]. Rehydrating III solution and albumin with its buffering properties improve acidosis and balanced solutions have an indifferent effect. Finally synthetic colloids all have a negative impact on hemostasis.

Discussion

With regards to volume expanding properties, solutions are equal when given in the right amount. In septic patients albumin has a theoretical advantage over other solutions owing to its modulating properties of the inflammatory response. Synthetic colloids may be dangerous because of their negative impact on kidney function. Acid-base status is determined by the strong ion difference (SID) of the infused fluid. In vivo when diluting plasma with a fluid with a SID less than baseline bicarbonate, acidosis will result. This makes saline the worse choice for large volume resuscitation. No clear recommendations can be made, yet albumin seems promising. Although albumin has advantages over synthetic colloids and normal saline, its additional value and possibly even superiority to balanced solutions with a SID equal to baseline bicarbonate, remain to be proven. In this respect its function as a transport molecule, weak acid buffer, radical scavenger and NO modulator suggest potentially beneficial effects in sepsis. The results of the ALBIOS Trial, investigating effect of albumin for volume replacement in severe sepsis, currently awaits publication, shedding more light on the promise of albumin. There might be a beneficial effect in septic shock.

Conclusion

Negative effects on renal function and coagulation make synthetic colloids dangerous. Within crystalloids saline is the worse choice due to the risk of dilutional acidosis, which can be avoided by choosing a (balanced) crystalloid solution with a SID similar to baseline bicarbonate concentration. Albumin has potential beneficial effects in sepsis and theoretically compares favorably to artificial colloids and normal saline, yet this remains to be proven.

Key messages

The common denominator of different types of shock is the activation of the RAAS system and ADH release. A solution with a SID lower than baseline bicarbonate concentration produces acidosis. In large volume resuscitation saline is the worst choice amongst crystalloids. Albumin being a non-volatile weak acid buffer, a relatively harmless colloid, an endogenous transport molecule and a radical scavenger is theoretically promising. It is a long way to a firm recommendation on the choice of fluid for volume resuscitation.

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