Role of acidic pH of intravenous fluids in subsequent development of metabolic acidosis- may not be what it seems

Sir,

We extend our thanks to Singh *et al.* for drawing attention toward the controversies surrounding the use of acidic intravenous fluids (IVFs) infusion.[1] They have rightly mentioned the propensity of 5% dextrose (D5) and 0.9% saline (NS) to cause thrombophlebitis and other deleterious effects.[1] But unlike mentioned by the authors, current literature discusses the known and putative reasons for the pH of 5.5 of NS.[2] Dissolved CO_2 from atmosphere, the ionic composition of the solution and inherent properties of the packaging material in which the solutions are supplied, are thought to determine it.[2] We believe that the same set of reasons may also explain the acidic pH (4.2) of D5.

Free acid activity is indicated by pH but the nondissociated acid molecules in a solution may not be characterized by the pH value.[2,3] Thus solutions with high titratable acid have

reservoir of hydrogen ion (H^+) irrespective of pH.[3] Citing the work of Gaudry *et al*. the authors attribute the acidity of IVFs to their method of sterilization, Gaudry *et al*. in their manuscript mentioned that the titratable acidity of majority of solutions under study (e.g. D5, NS) varied between 0.063 to 9.480 meq acid/l, depending on the method used for preparation and sterilization.[1,4] Gaudry *et al*. also mention that though many have measured the pH of common IVFs, not much data are available regarding their titratable acidity.[4] The work of Gaudry *et al*. dates back to 1972 and a PubMed search by us with the term 'titratable acidity fluid/titratable acidity solution/titratable acidity infusion' revealed only two studies relevant to this discussion. These studies date back to 1973 and 2005 and only the abstracts could be retrieved by us.[3,5] Though the *in vitro* pH of D5 and NS is acidic, their effect on H+ balance is probably negligible.[2,4] It may be because of their low titratable acid content.[4] But metabolic acidosis accompanies infusion of these solutions.[1,2,4,6,7] This acidosis was explained by dilution of bicarbonate content in plasma.[2,6,7] Subsequently Stewart's physiochemical approach was used to describe the *in vivo* effect on acid base status by IVFs.[6,7] According to the later concept, the acid–base effect of an IVF is determined by the strong ion deference (SID) and the total weak acid concentration (A_{TOT}) of the fluid.[6,7] pH falls with decreasing SID, increasing A_{TOT} or CO_{2TOT} (total CO_2 content) / PCO_2.[6,7] As the IVFs equilibrate with ECF, they alter SID of ECF, as SID of these IVFs defers appreciably from that of plasma.[6,7] SID of D5 and NS is 0, they decrease the SID of plasma and exert an acidifying effect.[6,7] These crystalloids are devoid of any weak acids and decrease A_{TOT} of plasma due to its diluting effect causing alkalosis.[6,7] Whereas some colloids (e.g. albumin, gelatin) itself may contribute toward A_{TOT} of plasma, thus, acidifying it.[6,7] Although CO_{2TOT}/PCO_2 also independently influences the pH of a biological system, its contribution in determining *in vivo* acid base activity of an IVF is generally regarded to be low as the concentration of dissolved CO_2 is itself low (about 0.012 mmol/l).[2,6,7] But it should be kept in mind that IVFs with high CO_{2TOT} have impact on intracellular acid base status, more during rapid administration or low perfusion states.[6,7] Contrary to the prediction by Singh *et al*. the pH of hypertonic saline (3%) is 5.8 and it causes more acidosis than NS because of its higher osmolarity that draws more water from other body fluid compartments.[6,7] Although the pH of Hartmann`s solution is 5, its *in vivo* SID is 27 meq/l, which is close to the ideal SID of 24 meq/l.[2,6,7] And despite its pH of 5, it is known to prevent infusion-related metabolic acidosis.[2,6,7] In-depth discussion on application of the concept of quantitative physical chemistry on the *in vivo* effect of acid base homeostasis is available.[6,7] The effect on plasma pH by solutions with same pH may be different and differing pH can have similar acid–base effects.[2,6] Thus, the effect of an IVF on plasma/ECF SID, A_{TOT} and CO_{2TOT} depending on the amount infused should be considered while predicting its possible *in vivo* effect on acid base status, not merely its *in vitro* pH.[1-7]

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