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In Reply: Deem raises important questions that provide an opportunity to clarify certain aspects of our data. The small increase in cardiac output produced by 6.0 ml · kg^{-1} of 7.2% hypertonic saline in our study[1] is predictable. We compared equal *quantities* of sodium chloride dissolved in different *volumes* of water, *i.e.*, 6.0 ml · kg^{-1} of 7.2% saline *versus* 54 ml · kg^{-1} of 0.8% saline.[1] In contrast, when equal volumes of hypertonic salt solutions and 0.9% saline or lactated Ringer's solution were compared,[2,3] cardiac output was higher, not surprisingly, in animals that received hypertonic solutions.[3] Traverso *et al.*[4] compared different volumes of different solutions (lactated Ringer's solution and 7.5% saline) administered over different time courses, thereby confounding easy interpretation. We conclude that it is not anomalous that cardiac output acutely was better restored by a much larger volume of 0.8% saline than by a smaller volume of 7.2% saline.

Perhaps a more important question is why some authors[2–4] report relatively sustained improvement in cardiac output after hypertonic saline while others[1,5–8] demonstrate only a transient increase. In fact, if one assumes that sodium (Na^+) is the predominant cation in the extracellular volume (ECV), that potassium (K^+) is the primary cation in the intracellular volume (ICV), and that extracellular and intracellular osmolality must remain equal, the effects of hypertonic saline on plasma volume can be predicted easily[9]:

$$\frac{\text{original extracellular } Na^+ + \text{added } Na^+}{\text{original ECV} + x} = \frac{\text{original intracellular } K^+}{\text{original ICV} - x}$$

where x = fluid osmotically translocated from the ICV to the ECV. For example, one would calculate the effect of an infusion of 0.6 ml · kg^{-1} of 7.2% saline as follows, assuming that animals weighed approximately 20 kg, that plasma volume equaled 4.0% of total body weight, ECV equaled 20% of total body weight (4 l), and ICV equaled 40% of total body weight (8 l):

$$\frac{140 \text{ mEq} \cdot l^{-1}(4 \text{ l}) + 1232 \text{ mEq} \cdot l^{-1}(0.12 \text{ l})}{(4 \text{ l}) + x} = \frac{140 \text{ mEq} \cdot l^{-1}(8 \text{ l})}{(8 \text{ l}) - x}$$

Based upon this calculation, the total ECV expansion expected from the addition of 148 mEq of sodium in the form of hypertonic saline would be 0.65 l, which in turn would be expected to expand plasma volume by only 0.13 l. Before complete equilibration, acute plasma volume expansion would be somewhat greater. The infusion of a 9-fold greater volume of 0.8% saline should result in plasma volume expansion exceeding 200 ml after complete redistribution throughout ECV. We are therefore intrigued that other investigators[10,11] demonstrate prolonged expansion of plasma volume.

Deem's concern that effects on cerebral perfusion pressure might influence cerebral blood flow measurements is important. Hemodilutional resuscitation, whether or not accomplished using hypertonic solutions, reduces systemic vascular resistance and usually reduces mean arterial pressure[2,4–8] because of a decrease in viscosity. Certainly, if cerebral vascular resistance is abnormally high, lower mean arterial pressure should limit the improvement in cerebral blood flow observed in our present study.

The effect of hypertonic solutions on myocardial contractility represents another intriguing question. Hypertonic sucrose, incrementally given to increase *systemic* osmolality up to 390 mOsm · kg^{-1}, produced dose-dependent increases in myocardial contractility in an *in vivo* preparation[12]; in an *ex vivo* preparation, an increase of 100 mOsm · kg^{-1} increased isometric tension, whereas greater osmolality decreased tension or exerted variable effects.[13] For comparison, the usual increase in osmolality associated with hypertonic resuscitation ranges from approximately 40 to 60 mOsm · kg^{-1} (final serum osmolality equalling 320 to 340 mOsm · kg^{-1}). Ionic solutions (such as those containing sodium) do appear to reduce myocardial contractility more than nonionic solutions. In intact animals, however, myocardial depression has been associated with changes in osmolality much greater than those produced by usual systemic doses of hypertonic saline, *i.e.*, acute intracoronary administration of a 450-mOsm · kg^{-1} solution of sodium chloride.[14] In anesthetized dogs, 3.0 ml · kg^{-1} of 7.5% saline produces an apparent improvement in myocardial contractility.[15]

In summary, we appreciate Deem's comments. Major questions remain to be answered about both the systemic and cerebrovascular effects of hypertonic resuscitation solutions. We agree, based on our data, that there is little evidence for any major systemic physiologic effect of hypertonic saline other than a modest, mathematically predictable, and transient improvement in preload.

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Is the Risk of Using a "Basal" Infusion with Patient-controlled Analgesia Therapy Justified?

To the Editor:—Patient-controlled analgesia (PCA) has become a widely accepted technique for managing postoperative pain following elective surgical procedures.[1] Many of the modern computer-based PCA delivery systems have the capability of administering basal (background) infusions to supplement conventional PCA therapy.[2] Although some studies have suggested that the use of a basal infusion might decrease the pain associated with physical activity and improve the quality of sleep,[3–5] other studies have questioned the routine use of background infusions.[6–8]

In contrast to "on-demand" PCA therapy, the use of a continuous infusion obligates the patient to receive a *minimum* amount of opioid medication. While mistakes in programming with on-demand therapy can result in an excessively large bolus dose being administered, the risk of a serious overdose is reduced because it is necessary that the patient activate the device in order for each bolus dose to be administered. The consequences of a mistake in programming a continuous infusion are potentially more serious because the opioid medication is administered *without* the patient having to activate the PCA device.

As suggested by McKenzie,[9] whenever the continuous (or continuous plus PCA) infusion mode is used, "a danger of overdose is present." During a recent study involving the use of a nighttime basal infusion,[8] a patient received a near-fatal overdose as a result of a human programming error at our institution. This 69-yr-old woman received 10 times the prescribed dosage of morphine when the PCA device was misprogrammed after the battery expired during the early morning hours of the third postoperative day following a radical abdominal hysterectomy procedure. She received approximately 50 mg morphine over a 5-h period before she was found with bradypnia (one to two breaths per minute). She was resuscitated with naloxone 0.4 mg intravenously (twice), and tracheal intubation was performed to treat hypoxemia secondary to pulmonary aspiration. Her aspiration pneumonia required ventilatory support for 5 days in the intensive care unit. Following discharge from the intensive care unit, the patient experienced an uneventful recovery. The occurrence of mishaps due to human errors remains a serious concern with PCA therapy,[10] particularly when using the continuous infusion modes available with the sophisticated, computer-based PCA delivery systems.[2]

Because only a small proportion of patients ($\approx$ 5%) appear to benefit from the addition of a continuous infusion with PCA therapy after abdominal hysterectomy procedures,[7] we question the *routine* use of this PCA modality in that patient population. Nevertheless, there are specific situations (*e.g.*, patients who experience inadequate pain control with physical activity or at night) in which the continuous infusion mode may be useful. Prior to instituting a new mode of postoperative PCA therapy, carefully controlled studies should be performed to determine the risk-to-benefit ratio in the patient population receiving the analgesic therapy.

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