**Table 1** - Cochrane Database Systematic Review result on albumin use in critically ill patients from 32 trials (updated August 2004)\*:

Patients category	Relative risk of death	95% Confidence interval		
Hypovolemia	1.01	0.92 - 1.1		
Burns	2.4	1.11 - 5.19		
Hypoalbuminemia	1.38	0.94 - 2.03		

<sup>\*</sup>The pooled relative risk of death with albumin administration was 1.04.

translated to a better outcome in terms of shorter hospital ICU/hospital stay or discharge. Furthermore, the albumin used by the trials included from 2-25% albumin concentration. Although they calculated the total amount of albumin received in grams, the question remains whether it is the concentration of albumin preparation used, the target serum albumin level or the total grams of albumin received, that matters? Albumin has been used for over 50 years for fluid resuscitation in the ICU, despite the lack of any adequately powered randomized clinical trials. As yet, there is no evidence to support the widespread use of albumin. There is no convincing data justifying administration of albumin either for treating hypovolemia or for correcting hypoalbuminemia. Until convincing data pro albumin is presented, injudicious use of albumin is not to be recommended. Further trials are required to form optimal fluid regimens, and indications. That use of albumin in critically ill patients should urgently be reviewed by the critical care practitioner. It should not be used outside the context of rigorously conducted randomized controlled trials.

**Acknowledgment.** We thank all authors of the references used for allowing us to comment on their original work.

Received 25th June 2005. Accepted for publication in final form 16th August 2005.

From Intensive Care Unit, Salmaniya Medical Complex, Ministry of Health, Kingdom of Bahrain. Address correspondence and reprint requests to Dr. Mariam A. Al-Ansari, Consultant Intensivist, Intensive Care Unit, Salmaniya Medical Complex, Manama, PO Box 12, Kingdom of Bahrain. Tel. +973 17255555 Ext. 4205/5205. Fax. +973 17289295. E-mail: icu\_mariam@yahoo.com

## References

- Offringa M. Excess mortality after human albumin administration in critically ill patients. *BMJ* 1998; 317: 223-224.
- Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomized controlled trials. *BMJ* 1998; 317: 235-240.

- Wilkes MM, Navickis RJ. Patient survival after human albumin administration: A meta-analysis of randomized controlled trials. *Ann Intern Med* 2001; 135: 149-164.
- Astiz ME, Rackow EC. Crystalloid-colloid controversy revisited. Crit Care Med 1999; 27: 34-35.
- Haynes GR, Navickis RJ, Wilkes MM. Albumin administration – what is the evidence of clinical benefit? A systematic review of randomized controlled trials. *Eur J Anaesthesiol* 2003; 20: 771-793.
- Finfer S, Bellomo R, Boyce N, French J, Myburgh J, Norton R. SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med 2004; 350: 2247-2256.
- 7. The Albumin Reviewers. Human albumin solution for resuscitation and volume expansion in critically ill patients. The Cochrane Database Systematic Reviews 2004. Available from: http://www.cochrane.org/cochrane/revabstr/AB001208.htm
- 8. Vincent JL, Navickis RJ, Wilkes MM. Morbidity in hospitalized patients receiving human albumin: a meta-analysis of randomized, controlled trials. *Crit Care Med* 2004; 32: 2029-2038.

Use of adrenaline as an adjunct to local anesthetic agent. A cause of concern for the anesthesiologist

Mobarak H. Ansari, MD, Annamma Abraham, DA.

drenaline is an endogenous catecholamine. It is **A** a sympathomimetic agent that has both and adrenergic effects. Physicians mainly use it as a bronchodilator, during cardiopulmonary resuscitation and in the treatment of acute anaphylactic reactions. We often use adrenaline in a concentration of 5 µgm/ml (1:200,000) to reduce blood flow and slow the rate of absorption of the local anesthetic agent, thus reducing the plasma concentration and prolonging the duration of action.1 It has been recognized for a long time that halothane and, to a lesser extent, other volatile anesthetics sensitize myocardium to the arrhythmogenic effects of adrenaline. Sensitization is the interaction between volatile anesthetics and catecholamines that leads to reductions in the threshold for both atrial and ventricular arrhythmias. Sequentially escalating doses of adrenaline produce premature ventricular contractions and sustained ventricular tachyarrhythmias during halothane anesthesia. Pretreatment with thiopentone attenuates halothane-adrenaline induced arrhythmias, presumably via effects on the atrioventricular node or the upper bundle of His. The doses of adrenaline required to produce ventricular arrhythmias during desflurane sevoflurane anesthesia are similar significantly less than those observed during administration of isoflurane and halothane.2 However, Katz and Katz<sup>3</sup> made 3 suggestions for

Table 1 - Studies showing potentially serious hemodynamic side effects of ADR when used as an adjuvant to LDC among patients undergoing various surgical procedures.

Author and reference	Year	Drug combination	Composition	No. of patients	Side effects (%)
Pasternak et al <sup>4</sup>	2004	LDC + ADR		100	Arterial hypertension (58%)
Murthy and Rao <sup>5</sup>	2001	5 Groups		112	
		LDC	LDC-0.5% (Control)	20	No significant hemodynamic change
		LDC + ADR	LDC-0.5%, ADR 1:200,000	23	Biphasic hypotension
		LDC + ADR	LDC-0.5%, ADR 1:100,000	24	Biphasic hypotension
		N. saline + ADR	NaCl-0.9%, ADR 1:200,000	23	Diastolic hypertension
		N. saline + ADR	NaCl-0.9%, ADR 1:100,000	22	Severe tachycardia
Phillips et al <sup>6</sup>	1993	4 Groups		80	
		LDC	LDC-0.5% (Control)	-	No significant hemodynamic change
		LDC + ADR	LDC-0.5%, ADR 1:200,000	-	Hypotension (55%)
		N.Saline	NaCl-0.9% (Control)	-	No significant hemodynamic change
		N. Saline + ADR	NaCl-0.9%, ADR 1:200,000	-	Hypotension (40%)

clinical precautions that have stood the test of time. 1. We should only use solutions of adrenaline of 1:100,000-1:200,000. 2. The dose in adults should not exceed 10 ml of 1:100,000 adrenaline in any 10-minute period. 3. The dose in adults should not exceed 30 ml of 1:100,000 adrenaline in any given 60-minute period. The Ear Nose and Throat, Plastic, Dental and Neurosurgeons mainly use adrenaline mixed with lidocaine. Different studies have revealed that ranges of hemodynamic changes occur by the addition of adrenaline to either lidocaine or normal saline (Table 1).4-6

In a study conducted by Murthy and Rao<sup>5</sup> among 5 groups, 4 groups of patients developed significant hemodynamic changes irrespective of mixtures and the concentrations of adrenaline used. Likewise, in another study conducted by Phillips et al,6 among the 4 groups, 2 of the study groups of patients developed significant hypotension, unlike the control groups when they mixed adrenaline with lidocaine and normal saline. Moreover, in tumescent anesthesia where the volume of the local anesthetic mixed with adrenaline is relatively more, it poses a greater threat to the development of potentially fatal cardiovascular responses, as the likelihood of exceeding the maximum dose of adrenaline increases further.

These hemodynamic changes are typically transient, and pretreatment with metoprolol (1 mg, IV) has been effectively used to alleviate the adverse cardiovascular responses to adrenaline infiltration.7 Nonetheless, they may often be life threatening.<sup>4-6</sup> Currently in the literature, there is a lack of reliable information on measures to prevent or effectively counteract these adverse effects of adrenaline. However, clinical acumen and awareness of the committed anesthesiologists will be the key in prevention and finding an apt solution to this seemingly insignificant yet, potentially hazardous problem.

Received 30th April 2005. Accepted for publication in final form 31st July 2005.

From the Anesthesiology, Prince Saud Bin Jalawi Hospital, Al-Hasa, Kingdom of Saudi Arabia. Address correspondence and reprint requests to Dr. Mobarak H. Ansari, Prince Saud Bin Jalawi Hospital, Al-Hasa 31982, Eastern Province, Kingdom of Saudi Arabia. Tel. +966 (3) 5305094. Fax. +966 (3) 5300070. E-mail: mobarakansari@gmail.com

## References

- 1. Scott B. Adrenaline in local anesthetic solutions. Acta Anaesthesiol Belg 1988; 39: 159-161.
- 2. Hayashi Y, Sumikawa K, Tashiro C, Yamatodani A, Yoshiya I. Arrhythmogenic threshold of epinephrine during sevoflurane, enflurane and isoflurane anesthesia in dogs. Anesthesiology 1988; 69: 145-147.
- 3. Katz RL, Katz GJ. Surgical infiltration of pressor drugs and their interactions with volatile anesthetics. Br J Anaesth 1966; 38: 712-718.
- 4. Pasternak JJ, Atkinson JL, Kasperbauer JL, Lanier WL. Hemodynamic responses to epinephrine-containing local anesthetic injection and to emergence from general anesthesia in trans-sphenoidal hypophysectomy patients. JNeurosurg Anesthesiol 2004; 16: 189-195.
- 5. Murthy HS, Rao GS. Cardiovascular responses to scalp infiltration with different concentrations of epinephrine with or without lidocaine during craniotomy. Anesth Analg 2001; 92: 1516-1519.
- 6. Phillips S, Hutchinson SE, Bayly P, Hollway TE. Adrenaline-induced hypotension in neurosurgery. Br J **Anaesth** 1993; 70: 687-688.
- K, Bhanumurthy S. 7. Muralidhar Attenuation cardiovascular responses to subcutaneous adrenaline in neurosurgical patients. Br J Anaesth 1992; 68: 264-267.