Does Acute Normovolemic Hemodilution Work in Cardiac Surgery?

To the Editor:—In a recent article by Höhn et al., it was concluded that acute normovolemic hemodilution (ANH) in addition to aprotinin was not beneficial in preventing allogeneic blood transfusions compared to aprotinin alone in cardiac surgery. In this randomized, controlled trial, the patients were hemodiluted to a hematocrit of 28% pre-cardiopulmonary bypass (CPB). The transfusion threshold was set at 17% during CPB and at 25% for post-CPB. The total fluid replacement was in excess relative to the amount of ANH (autologous blood) removed (6.4 ± 2.11 of crystalloid, 2.0 ± 0.7 l of colloid). This led to excessive hemodilution, reducing the hematocrit below the transfusion threshold in the ANH group. Indeed, 50% of the patients in the ANH group required either all (33%) or a portion (22%) of the autologous blood to be transfused during CPB, thus negating its positive effects on erythrocytes and coagulation protection. Consequently, allogeneic erythrocyte transfusion rates and the indirect clinical markers for surgical bleeding (cell saver and 24-h chest tube drainage) were not different between the two groups. One of the goals of ANH is to prevent the autologous blood from the negative effects of CPB and to return it after heparin neutralization. Additional hemodilution occurs with the onset of CPB; therefore, hemofiltration or ultrafiltration and/or diuresis should have been employed to remove excess fluids. Alternatively, ANH can be performed just prior to the onset of CPB (by diverting heparinized blood into a storage bag), thus preventing excessive dilutional anemia.

The criteria for exclusion from this study were left main disease, severe aortic stenosis, recent myocardial infarction, unstable angina, ejection fraction below 30%, severe carotid stenosis, combined coronary artery bypass grafting and valve cases, respiratory insufficiency, renal insufficiency, and anemia (hemoglobin < 12 g/dl). This exclusion process resulted in the selection of a group of patients that we know are at low risk for allogeneic transfusions. Our data (shown below) and those of other investigators demonstrate that patients presenting with renal insufficiency, and anemia (hemoglobin < 12 g/dl) do not benefit from ANH.

At our institution, the cardiac surgery program utilizes a multidisciplinary approach to blood conservation. In over 300 cardiac surgery cases (coronary artery bypass grafting, valves, and combined procedures), we remove on average 1280 ml of ANH blood per case (based on a formula to reach a target hematocrit on bypass of 20%). The average amount of fluid used for replacement was 1680 ml of crystalloid and 591 ml of colloid (Hextend®, Abbott Laboratories, North Chicago, IL). Hemofiltration or ultrafiltration and/or induced diuresis is frequently utilized on CPB to remove excess fluids and to reduce the dilutional effect from the CPB prime. The starting hematocrit averages 39%. We use e-aminoacaproic acid for low-risk cases and reserve aprotinin (Trasylol®, Bayer, West Haven, CT) for high-risk cases. The total amount of cell saver returned is approximately 200 ml, and 24-h chest tube drainage is 428 ml. Allogeneic transfusion rates for packed erythrocytes, fresh frozen plasma, and cryoprecipitate are 11%, 3%, and less than 1%, respectively.

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Finally, as suggested by Dr. Moskowitz and others, we agree that the implementation of a standardized, multidisciplinary approach, including definition of transfusion criteria, administration of antifibrinolytic drugs, use of cell saver devices, and external heating, is most helpful to reduce transfusion of allogeneic blood products in patients undergoing cardiac surgery. However, evidence supporting the addition of ANH as a blood-sparing technique is still lacking, although a consensus is based on data from observational studies and prospective, unblinded, randomized trials.7

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To the Editor.—In the article by Njoku et al.1 in the March 2002 issue of Anesthesiology, they describe a patient who developed nonfatal hepatic failure 24–48 h after coronary artery surgery on cardiopulmonary bypass. The authors suggest, “that the hepatitis may have been caused by isoflurane.”

The patient was a 66-yr-old man with arteriopathy who had non-insulin-dependent (type 11) diabetes mellitus, chronic obstructive pulmonary disease, hypertension, coronary artery disease, and carotid artery disease. Two months prior to his coronary artery surgery, the patient had been anesthetized with isoflurane for a carotid endarterectomy.

During his operation, but prior to the establishment of cardiopulmonary bypass, the patient received norepinephrine and nitroglycerin to support his circulation and hemodynamic performance. His bypass time was 110 min, and his aortic cross-clamp time was 89 min.

The authors of this case report state, “we provide clinical, histologic, and immunohistochemical evidence supporting a possible role of trifluoroacetylated protein (TFAMPs) in hepatitis associated with isoflurane.” I believe that the patient’s postoperative hepatic failure was much more likely to be caused by an operative hepatic perfusion problem than from any event initiated by isoflurane.

The National Halothane Study2 investigated the administration of 254,896 halothane anesthesics. There were 14,100 patients who received halothane on two or more occasions. In this study, it was calculated that the mortality rate following multiple exposure to halothane within a 6-week period was 1 in 3,525. The incidence of hepatic failure after a second isoflurane anesthetic within 2 months is unknown, although it is universally agreed that the incidence of hepatic failure after halothane anesthesia is much less than the incidence of hepatic failure after halothane anesthesia. The incidence of hepatic failure after isoflurane anesthetics would be much less than 1 in 3,525. This should be compared with the incidence of hepatic failure following cardiopulmonary bypass, from low regional blood flow, of 1 in 1,500.3

The biopsy findings presented in the case report are equally compatible with hepatic failure that has been caused by hepatic artery hypotension, hepatic or portal vein hypertension, and toxic or immuno logic injury to the hepatocyte. It is generally agreed that anesthetic agent hepatitis cannot be confidently diagnosed from an examination of a patient’s hepatic histopathology.

It would seem that the authors’ claim that the patient’s postoperative hepatic failure was due to isoflurane hepatitis rests heavily on the immunohistologic studies. These studies show that the trifluoroacetyl moiety was demonstrated in the mitochondria, the endoplasmic reticulum, the nuclear membrane, and the nucleus of the hepatocyte. The presence of the trifluoroacetyl moiety at these sites does not prove that the trifluoroacetyl moiety induced any injury in the hepatocyte. In every patient anesthetized with isoflurane, a small amount of the absorbed isoflurane is metabolized in the liver to trifluoroacetic acid, which is then excreted in the urine. During the metabolism of isoflurane to trifluoroacetic acid in the liver, intermediate metabolites are produced, and it would seem likely that the hepatic metabolites of isoflurane that have been identified by the authors are of no pathologic significance.

On the balance of probability, it is 100 times more likely that this patient’s hepatic failure was related to some intraoperative event rather than to isoflurane hepatitis. The connection between the hepatic failure and the isoflurane administered during this patient’s anesthesia is merely coincidental.

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In Reply.—In Dr. Wark’s letter, he states, “hepatic failure after cardiopulmonary bypass is unlikely to be isoflurane hepatitis.” In response, I will borrow an Asian proverb: “A journey of a thousand miles must begin with a single step.”

Dr. Wark introduces alternative views of a classic argument. We both agree that hepatotoxicity can occur following halothane administration. However, we disagree about hepatotoxicity when other halogenated volatile anaesthetics are considered. Nonetheless, hepatotoxicity following halogenated volatile anaesthetics, including isoflurane, is believed to be idiosyncratic, and immune-mediated processes are believed to have a role in this injury, similar to other forms of idiosyncratic drug-induced hepatotoxicity. There are several reports of immune responses and hepatotoxicity following isoflurane administration. More importantly, in this case report, isoflurane was implicated after critically examining other possible causes of hepatotoxicity and was not based on histologic findings alone.

This case report takes forward steps in the journey of a thousand miles to the discovery of the etiologies of drug-induced hepatotoxicity. The first step was also taken by those before us. We demonstrated liver injury following isoflurane administration. Norepinephrine and nitroglycerin were administered, but hypotension or other evidence of ischemia was not demonstrated. The article from 1996 referenced by Dr. Wark clearly states the risk factors for gastrointestinal complications after cardiopulmonary bypass: advanced age, combined coronary artery bypass grafting–valve operation, postoperative low cardiac output, prolonged ventilation time, reexploration of the chest, sternal infection, and a history of peptic ulcer. In our report, the patient was 66 yr old, underwent a three-vessel coronary artery bypass graft, and maintained mean arterial pressures ≥ 70 mmHg for > 48 h intraoperatively and postoperatively during the initial demonstration of increased aspartate aminotransferase. Therefore, if Dr. Wark’s probability was correct, the only risk factor was age.

By showing that the patient had several risk factors for volatile anesthetic-induced liver injury, additional steps were taken. The patient had received two anesthetics in 5 months; developed a relapsing fever postoperatively, which could suggest the presence of an immune-mediated process; and also developed significant increases in serum transaminases. The immunohistochemical evidence was supportive since the trifluoroacetyl-modified proteins were detected in centrilobular areas, suggesting drug-induced liver injury, and were associated with cytoplasmic organelles, suggesting specificity. Surprisingly, the trifluoroacetyl-modified proteins were detected after 72 h at concentrations previously not seen with isoflurane. Surely, the increased amount of trifluoroacetyl-modified proteins may have been caused by reduced hepatic clearance from global hepatic dysfunction induced by other causes. However, if this was the case, anesthetic metabolism should have been impaired as well.

Our gastroenterology colleagues completed another step in the journey by documenting identical histologic evidence of hepatotoxicity in a patient 5 days after isoflurane exposure for a different surgical procedure. We would like to thank Dr. Wark for his comments. We will only move forward by having these kinds of discussions.

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Use of the Arndt Wire-guided Endobronchial Blocker

To the Editor—The Arndt fiberoptically directable, wire-guided endobronchial blocker (William Cook Europe A/S, Bjaeverskov, Denmark) is a useful tool to achieve one-lung ventilation with an endotracheal tube in a variety of clinical settings. The endobronchial blocker is placed coaxially through a conventional endotracheal tube using a pediatric bronchoscope and a special bronchoscopy port. The special bronchoscopy port offers multiple access ports, allowing simultaneous introduction of the bronchoscope and the endobronchial blocker while the airway anatomy is distorted.

Our patient was a child with major airway abnormalities. This resulted in the following problems: (1) the maneuvers designed to aid oral and nasal flexible fiberoptic bronchoscopy were inapplicable, (2) we could not have kept the child awake before airway control, and (3) nasotracheal intubation was necessary. The former two presumably led to the failure of our FFB-aided intubation attempts. The last problem posed a significant challenge. We were able to convert the existing oral ETT to a nasotracheal tube with the help of the FFB, but the limitations of this method can be manifold, such as breakage of optical fibers, trauma, failure, and inadvertent extubation. An uncuffed polyvinyl chloride ETT is flexible enough to allow bending without transmitting tension to the FFB. The absence of jaw and tongue retraction led to minimal oral space in our patient, which significantly decreased the arc of negotiation of the FFB-ETT unit and consequently prevented damage to the optical fibers. Moreover, the possibility of accidental extubation was lessened, as the tube and the FFB were firmly grasped, the tip of the fiberscope was anteriorly flexed, and the pull of the FFB through nose was gentle. FFBs have been utilized previously to effect safer conversion of a nasal tube to an oral tube. Ours is probably the first case in which an oral to nasal ETT conversion was carried out with the help of a FFB. This case not only reiterates the few significant limitations of the FFB while gaining a difficult airway, but it also shows that deft handling of this delicate equipment may improve outcome.

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Fig. 1. Sheared balloon of the Arndt endobronchial blocker. Insert shows the endobronchial blocker passing through the Tuohy-Borst valve (arrow) of the special bronchoscopy port.
To the Editor:—For difficult airway management in pediatric patients, a technique using a laryngeal mask airway (LMA™; Laryngeal Mask Company, Nicosia, Cyprus), a fiberoptic bronchoscope (FOB), wire insertion, and an endotracheal exchange catheter has been described.1,2 We have employed a similar technique in adults when dealing with an unanticipated difficult airway after induction of anesthesia. In an anesthetized patient, the technique is as follows: insertion of an appropriate-sized LMA™ and ventilation of the patient; passage of a FOB through a collapsible elbow connector, through the LMA™, and into the trachea; passage of a guide wire (0.081-cm diameter, 145-cm length; Cook Urological, Spencer, IN) through the FOB suction port and into the trachea; withdrawal of the FOB, leaving the wire in place; passage of an endotracheal tube exchange catheter (Cook Critical Care, Bloomington, IN) over the wire and into the trachea; withdrawal of the LMA™, and insertion of a standard endotracheal tube over the exchange catheter. Direct laryngoscopy is useful at this point to guide the endotracheal tube through the mouth and under the epiglottis. Assuming that ventilation with a LMA™ is successful, this technique allows almost continuous control of the airway with manual or mechanical ventilation except during the last step; an unhurried sequential approach allowing deliberate use of the FOB; minimal trauma, as the devices employed are designed for soft tissue use; and final intubation with a conventional endotracheal tube of adequate size. Of note, we have observed that a standard LMA™ works best rather than an intubating type.

Larger endotracheal tubes (sizes ≥ 7.0) may be difficult to insert directly through a LMA™ over a FOB, and the endotracheal tubes used with intubating airways have a higher pressure cuff than standard tubes. This is of greater importance when postoperative ventilation is anticipated. Smaller endotracheal tubes placed over a FOB and through a LMA™ may secure an airway but may result in problems with weaning or may be generally unsuitable for prolonged ventilation, especially in large patients.

We have used this technique successfully many times during the last 3 yr, and it is now our initial approach to the unanticipated difficult airway in patients undergoing cardiovascular surgery.

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