TABLE 2. Antithrombin III Activity (Percent)

<table>
<thead>
<tr>
<th>Nitroglycerin Concentration (ng/ml)</th>
<th>Subject</th>
<th>Row Average (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>74.6</td>
<td>69.8</td>
</tr>
<tr>
<td>2</td>
<td>79.0</td>
<td>87.6</td>
</tr>
<tr>
<td>10</td>
<td>91.0</td>
<td>63.8</td>
</tr>
<tr>
<td>20</td>
<td>65.5</td>
<td>81.3</td>
</tr>
<tr>
<td>Mean (n = 12)</td>
<td>77.5</td>
<td>94.6</td>
</tr>
</tbody>
</table>

Each entry is the mean of three observations, except where noted.
* n = 36.
All samples have essentially identical heparin concentrations.

Effect on either AT3 concentration or its activity. It is possible that an in vivo study might yield different results.

The mechanism explaining the nitroglycerin-induced heparin resistance seen by Habib et al.5 remains to be delineated. Nitroglycerin may inhibit hepatic synthesis or release of AT3. Perhaps nitroglycerin alters the configuration of AT3, thus impairing its critical interaction with heparin. Nitroglycerin may activate the heparinase enzyme system, thereby causing an accelerated decline in plasma heparin. Simple competition of nitroglycerin with heparin for limited AT3 binding sites also may explain this phenomenon, although data presented here argue against this possibility.

Excessive heparinization and incomplete anticoagulation may each have disastrous consequences. It is clear that nitroglycerin antagonism of heparin requires further investigation.

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Anesthesiology

Prostacyclin Infusion in ARDS

To the Editor:—The recent study by Radermacher et al.1 raises several interesting points. Of particular interest are the observed effects of prostacyclin administration on oxygen transport (O2T) variables and the observation that most patients did not demonstrate supply-dependent oxygen uptake. This is an important finding both because of the rigorous criteria for defining ARDS and because of the meticulous attention to accuracy in measurement techniques.

The failure of oxygen consumption (VO2) to increase in response to oxygen delivery (DO2) is interesting. As pointed out by the authors, this has been observed previously by Annat et al.,7 who demonstrated maintenance of VO2 when DO2 was reduced by positive end-expiratory pressure (PEEP) in ARDS patients. The PEEP-induced decrease in DO2 in Annat’s series was in fact small, and few patients were studied. Gilbert et al.8 also demonstrated that supply dependency did not occur in septic patients with normal lactate concentrations in whom DO2 was increased by transfusion with blood or colloid. Both of these studies, however, had limitations, a major problem being the use of calculated oxygen saturation to determine oxygen content. The majority of authors have confirmed supply dependency of oxygen consumption in patients with ARDS or sepsis. The identification of an adequate level of VO2 in this population has remained problematic, however.

In the study by Radermacher et al., VO2 did not increase in seven of the nine patients. The authors postulate that these patients may not have had a significant oxygen debt. An alternative explanation could be that prostacyclin worsened the efficiency of vaso-regulation at the periphery: the oxygen extraction ratio fell from 24 to 19% during infusion. The increase in mixed venous oxygen tension may suggest an increase in flow to well-perfused tissues, with no increased flow to ischemic tissue.9

Optimization of O2T variables is an important therapeutic maneuver in the critically ill. In ARDS and sepsis, adequate levels of DO2 and VO2 are difficult to define as are reliable markers of tissue hypoxia, hence the development of dynamic tests with prostacyclin and dobutamine.6 While the failure of VO2 to increase may imply that there was no oxygen debt, it equally may reflect a failure of the prostacyclin to improve the extraction defect. This feature, in combination with the demonstrated effect on the intrapulmonary shunt and systemic arterial pressure, may prove to be a major limitation of prostacyclin administration.

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Preservative-Free Is Not Antioxidant-Free

To the Editor—In recent years the practice of giving a small (3-ml) test dose injection of lidocaine containing a 1:200,000 dilution of epinephrine before giving a larger epidural dose has become popular.

The purpose of test-dosing with lidocaine and epinephrine is to determine whether the epidural catheter tip is misplaced either in the subarachnoid space or the intravascular space. There are epidural kits being manufactured that provide the anesthetist with premade "test-dose" solutions of lidocaine with epinephrine (1:200,000). In at least one of these kits the label on the test dose vial states: "No preservatives added." This may be misleading to the anesthetist, in that the sodium metabisulfite is considered an antioxidant for epinephrine and not a preservative for the lidocaine. All prepackaged local anesthetic solutions containing epinephrine contain sodium metabisulfite.

In 1980 case reports began to appear implicating 2-chloropropracaine as neurotoxic. Subsequent clinical reports and animal studies suggested that the low pH and metabisulfite are possible causes of neurotoxicity and that the spinal nerve roots are more susceptible than peripheral nerves. The standard epidural kit containing the lidocaine with epinephrine used for giving a test dose contains 0.5 mg/ml sodium metabisulfite and has an acidic pH. If 3 ml is given as a test dose, a total of 1.5 mg sodium metabisulfite is given. If, however, a fresh solution of lidocaine with epinephrine (1:200,000) is made (obtaining the epinephrine from the standard 1-ml vial of epinephrine, which itself contains 1 mg/ml sodium metabisulfite), then only 0.015 mg sodium metabisulfite per 3 ml would be given. Hence, by making a fresh solution, 100-fold less sodium metabisulfite is injected.

To my knowledge, no case reports of neurotoxicity have been reported after inadvertent subarachnoid injection of a test dose using a prepackaged test-dose solution containing lidocaine with epinephrine.

Reference:


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