Ethanol-induced acute pulmonary hypertension and right ventricular dysfunction in pigs

Editor—Absolute ethyl alcohol (ETOH) is used with increased frequency in the treatment of conditions such as percutaneous ablation of unresectable hepatic tumours, sclerotherapy of oesophageal varices, ventricular septal ablation, and i.v. embolization of arteriovenous malformations.1–3 Although the incidence of complications with the use of ETOH is relatively low, episodes of cardiopulmonary collapse have been described.4 The postulated mechanism is severe pulmonary vasoconstriction from the sudden passage of ETOH into the pulmonary circulation, causing pulmonary hypertension (PHTN) and right ventricular (RV) strain.5 However, there is limited information on the effects of i.v. ETOH on heart function, pulmonary and systemic haemodynamics,6,7 and in clinical conditions similar to those encountered during therapeutic procedures.

We have studied the causal relationship between the i.v. administration of ETOH and alterations in systemic and pulmonary haemodynamics, and examined the duration of such changes in an intact porcine model. An additional purpose was to create a basis for investigating possible treatment in such catastrophes.

After approval by the University of Florida Institutional Animal Care and Use Committee, eight domestic pigs (45–50 kg) were studied and handled according to NIH Animal Care and Use Committee, and in clinical conditions similar to those encountered during therapeutic procedures. After discontinuation of ETOH, the animals were euthanized and the animals observed until haemodynamics returned to within 10% of baseline.

Data were collected at baseline, when the target MPAP was achieved, and after discontinuation of the infusion until haemodynamics returned to within 10% of baseline. After discontinuation of ETOH, the animals received only an infusion of 2 ml kg−1 of normal saline (NS). At the end of the experiment, the animals were euthanized. Data were expressed as mean (SD). A two-way analysis of variance was used, followed by Student–Newman–Keuls test for multiple comparisons. A P-value of <0.05 was considered significant.

A rate of 50 mg kg−1 (approximately 2.5 ml of ETOH per min) was sufficient to induce significant PHTN within 3 min. The infusion of ETOH achieved a two-fold elevation in MPAP at a mean dose of 188 (22) mg kg−1. During the ETOH infusion, CO was maintained (Table 1), heart rate (HR) increased, and stroke volume remained stable. After ETOH infusion, CVP and MPAP increased significantly (Table 1), resulting in significantly increased PVR [from 289 (94) to 564 (118) dyn s cm−5; P<0.05], although MAP and PAOP (Table 1) and SVR remained relatively unchanged. The SVR/PVR ratio decreased by

Table 1 Haemodynamic data before and after ETOH administration. aP<0.05 compared with baseline. bP<0.05 compared with ETOH effect. Values represent mean (SD). ETOH, absolute ethyl alcohol; NS, normal saline; CVP, central venous pressure; PAOP, pulmonary artery occlusion pressure; MAP, mean arterial pressure; MPAP, mean pulmonary artery pressure; CO, cardiac output; HR, heart rate; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; PHTN, pulmonary hypertension (when target MPAP was achieved)

<table>
<thead>
<tr>
<th></th>
<th>CVP (mm Hg)</th>
<th>PAOP (mm Hg)</th>
<th>MAP (mm Hg)</th>
<th>MPAP (mm Hg)</th>
<th>CO (litre min−1)</th>
<th>HR (beats min−1)</th>
<th>Stroke volume (ml beat−1)</th>
<th>SVR/PVR ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>8.1 (2.2)</td>
<td>10.2 (1.7)</td>
<td>70.3 (6)</td>
<td>20.7 (2)</td>
<td>3.0 (0.3)</td>
<td>96 (9)</td>
<td>32 (2.6)</td>
<td>5.1 (1.2)</td>
</tr>
<tr>
<td>Target PHTN</td>
<td>12.4 (1.9)*</td>
<td>12.8 (1.9)</td>
<td>74.5 (11)</td>
<td>38.8 (4.3)*</td>
<td>3.4 (0.5)</td>
<td>122 (10)*</td>
<td>31 (3.4)</td>
<td>2.6 (1.0)*</td>
</tr>
<tr>
<td>10 min after ETOH</td>
<td>12.1 (2.0)*</td>
<td>10.4 (0.8)</td>
<td>69.3 (6)</td>
<td>19.8 (1.9)</td>
<td>3.1 (0.3)</td>
<td>101 (8)*</td>
<td>32 (3.8)</td>
<td>5.8 (0.9)*</td>
</tr>
</tbody>
</table>
49%, after ETOH infusion \( (P<0.05; \text{Table 1}) \). RV \( dP/dT \) decreased by approximately 41% during ETOH infusion, with recovery noted 10 min after the infusion was stopped. The effects of ETOH were relatively short-lived because baseline haemodynamic values (MPAP, HR, PVR, SVR/PVR ratio, but not CVP) (Table 1) returned to baseline approximately 10 min after the drug was stopped.

The results of this study demonstrate that the intravascular infusion of a small dose of ETOH can trigger severe pulmonary vasoconstriction, leading to RV dysfunction. Ethanol has been shown to cause pulmonary vasoconstriction in several species. Several investigators documented variable increases in PAP and PVR with i.v. infusions of ETOH, the magnitude of which are dose- and concentration-dependent. The mechanisms for ETOH-induced pulmonary vasoconstriction are believed to involve the release of secondary mediators such as catecholamines or histamines, or arachidonic acid metabolites. The effects of ETOH in the vasculature are complex and involve both vasoconstriction and vasodilatation. It was demonstrated that intracellular \( \text{Ca}^{2+} \) in a vascular smooth muscle cell preparation increased with ETOH, even in the presence of \( \text{Ca}^{2+} \) channel blockade.

The effects of ETOH on pulmonary and systemic haemodynamics in our study were short-lived and vascular resistances returned to baseline values approximately 10 min after the discontinuation of ETOH, whereas depression of RV contractility persisted. The absence of hypotension and preservation of CO during the phase of marked PHTN and RV dysfunction can be explained by the increased sympathetic outflow, as evidenced by a 40% increase in HR, with the calculated stroke volume essentially unchanged.

Our study differs from previous investigations in that the concentration of ETOH used is that commonly used in ablation procedures. We established that 50 mg kg\(^{-1}\) given at approximately 2.5 ml min\(^{-1}\) was sufficient to induce significant PHTN within 3 min. This result, extrapolated to clinical use, suggests that a slow rate of ETOH infusion should be considered, in conjunction with careful monitoring of the patient’s haemodynamic status, in conditions where the risk of intravascular absorption is high.

In our study, systemic haemodynamics were relatively preserved probably because of an otherwise intact cardiovascular system in our experimental animals. We postulate that in otherwise healthy patients, small amounts of ETOH may not have a measurable clinical effect, as brief, moderate increases in PVR may be tolerated without haemodynamic compromise. In contrast, patients with pre-existing PHTN or myocardial disease will be more susceptible to haemodynamic instability.

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Placement of enterogastric tubes

Editor—Enterogastric tubes are widely used in clinical practice to facilitate gastric emptying or the administration of enteral feed and oral medication. Morbidity associated with their use is uncommon but is well recognized. A report from the National Patient Safety Authority (NPSA) states that 11 deaths occurred from misplaced NG tubes between 2003 and 2004. A fatal cardiovascular collapse during percutaneous ethanol injection of a hepatocellular carcinoma under general anesthesia. Anesthesiology 2004; 100: 1307–8


doi:10.1093/bja/aen047


4 Naik B, Lobato EB, Urdaneta F. Acute cardiovascular instability during percutaneous ethanol injection of a hepatocellular carcinoma under general anesthesia. Anesthesiology 2004; 100: 1307–8


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