**Effect of Intravenous Ethanol on Cerebral Vasospasm Produced by Subarachnoid Blood**

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**SUMMARY** The cat basilar artery was exposed using the transclival approach. After administration of 5% ethanol via intravenous infusion, vasospasm was produced by applying the animal's fresh arterial blood to the exposed artery. The resultant vasospasm was of markedly reduced intensity and duration as compared to vasospasm in control animals. In ethanol-treated animals with spasm induced from non-autogenous fresh arterial blood free of ethanol, a reduction in the duration of vasospasm was noted although the initial intensity of spasm was similar to control animals. There was no anti-spasm effect if the ethanol infusion followed the production of vasospasm.

THE ETIOLOGY of cerebral vasospasm following a subarachnoid hemorrhage remains under intense investigation. Approaches to this problem have involved the study of a variety of vasoactive agents including the beta adrenergic drug isoproterenol, the alpha adrenergic blocking drug phenoxybenzamine, the monoamine inhibitor reserpine, and the direct smooth muscle relaxant nitroprusside.

Ethanol is another potential vasodilating agent of the cerebral circulation. Thomas reported that ethanol caused dilatation of pial arteries in cats and rabbits, preceded sometimes by slight constriction. Miyazaki's data indicated that ethanol produced a significant increase in cerebral blood flow in 50% of the cases studied. In contrast, Battey, et al. found ethanol to cause no significant change in cerebral blood flow.

The purpose of the present study was to determine if ethanol could alter the vasospasm induced by the application of arterial blood to the exposed basilar artery.

**Methods and Materials**

Adult cats weighing from 2-5 kg were anesthetized with an intraperitoneal injection of sodium pentobarbital at a concentration of 30 mg/kg body weight and placed in the supine position on an electric heating pad which maintained rectal temperature between 37°C and 39°C. Catheters were inserted in the femoral artery for continuous recording of arterial blood pressure and in the femoral vein for administration of fluids; respiration was continuously monitored. The basilar artery was approached transclivally. After the arachnoid had been opened atraumatically, the exposed basilar artery was kept undisturbed for 30 min to allow any mechanically induced vasospasm to dissipate. To produce arterial vasospasm, 0.5 ml of fresh arterial blood obtained from the femoral artery was applied to the basilar artery and allowed to clot for 10 min. Using irrigation with warm (38°C) lactated Ringer's solution, the clot was removed. To determine sequential changes in vessel size, the artery was photographed using Kodak 200 ASA Ektachrome film with a Nikon camera attached to the operating microscope. Control photographs were taken before the application of blood, followed by serial pictures every 10 min for either a 50 or 90 min period after the blood clot was removed. The photographs were projected and traced onto paper, and the area of each photographed artery was determined by a planimeter. The degree of spasm was expressed as percent change in area over control values.

The ethanol-treated cats received 26 ml of 5% ethanol/kg body weight, and the control animals were given 26 ml of lactated Ringer's solution/kg body weight. All solutions were infused into the femoral vein at a rate of 1.91 ml/min using a Harvard pump. Throughout the experimental period, 1 ml samples of arterial blood were drawn from the femoral artery for analysis of blood ethanol levels.

Three experimental groups were studied. The first received intravenous ethanol or lactated Ringer's solution prior to the application of blood to the basilar artery. A second group also received intravenous ethanol or lactated Ringer's solution prior to the application of blood, but for this group the blood came from non-ethanol treated cats. The third group received the ethanol or lactated Ringer's solution infusion after the production of vasospasm with autogenous arterial blood.

**Results**

The results in the first group, in which the effectiveness of systemically infused ethanol in preventing acute vasospasm was studied, are shown in figure 1. At every time point following the removal of the blood clot from the basilar artery, there is significantly more spasm in untreated animals (p < 0.05). In animals having received ethanol, the minimal vasospasm produced is almost completely relieved within 10 min, while the non-ethanol-treated animals continued to have marked vasospasm after 50 min. The initial mean blood ethanol concentration of 240 ± 35 mg/100 ml (mean ± SEM) decreased rapidly to a level of approximately 150 mg/100 ml (the human intoxication level is 150 mg/100 ml of blood). Figure 2 shows the results when fresh arterial blood, obtained from non-treated cats, is applied to the basilar arteries of cats that had been infused with ethanol. Initially, there...
is substantial vasospasm, not significantly different from controls; between 10 and 20 min after removing the blood clot, however, the spasm in the ethanol-treated animals begins to subside, and it completely disappears by 50 min.

The results from the last group of animals are shown in figure 3. Here the infusion of ethanol or lactated Ringer’s solution alone was begun immediately following the removal of the blood clot from the basilar artery. Throughout the entire 90 min period after removing the blood clot, there was no significant difference in degree of vasospasm between the ethanol-treated animals and the controls (p > 0.4).

In all experimental groups, arterial blood gases, pH, and blood pressure remained unchanged throughout the procedure. At the termination of each experiment, all basilar arteries displayed vasospasm when lightly stroked indicating that ethanol had not irreversibly impaired the arteries’ physiological mechanisms of contraction.

**Figure 1.** Effects of ethanol infused before the application of autogenous arterial blood to the exposed cat basilar artery. In the lower portion, the percent change in vessel size (cm²) is plotted vs time (minutes) after the removal of the blood clot. The curves shown represent animals that had been treated with ethanol (n = 8, ○ ○ ○ ○) or lactated Ringer’s solution alone (n = 6, • • • •). In the upper portion mg of ethanol/100 ml blood from ethanol treated cats are plotted vs time (minutes) following the blood clot removal (n = 8, • • • •). All points represent a mean ± SEM.

**Figure 2.** Effects of ethanol infused before the application of non-autogenous arterial blood to the exposed cat basilar artery. The lower portion is plotted as in fig. 1 with the curves representing animals treated with ethanol (n = 3, ○ ○ ○ ○) or lactated Ringer’s solution alone (n = 6, • • • •). In the upper portion the curve represents the ethanol blood concentrations after the blood clot removal and is plotted as in fig. 1 except that n = 3 (• • • •). All points represent a mean ± SEM.

**Discussion**

The results of this study demonstrate that ethanol infused prior to the application of blood to the exposed cat basilar artery can significantly reduce the resultant vasospasm. This anti-spasm effect cannot primarily be attributed to vaso-paralytic properties of ethanol present in the topically applied arterial blood, since vasospasm caused by ethanol-free blood is also quickly relieved. Once vasospasm has been induced, however, the subsequent intravenous infusion of ethanol cannot significantly reduce it.

The anti-spasm effects of ethanol are not related to changes in systemic blood pressure, as these were
minimal (± 10 mm Hg) following infusion of the experimental solutions. This finding is in agreement with several other studies in which there also was no correlation between ethanol's effect on the systemic circulation and the cerebral circulation.7, 8, 10

Ethanol influences many physiological processes in muscle and nerve14-16 including catecholamine metabolism. Klingman and Goodall suggested that ethanol depletes norepinephrine stores in adrenergic nerves.17 The presence of adrenergic nerve plexuses has been demonstrated in cerebral vessels18 and the depletion of catecholamines from these stores following vasospasm has been reported.19 Disulfuram, an inhibitor of norepinephrine synthesis through its action on dopamine beta-hydroxylase, has also been used to prevent spasm in cat basilar artery,20 and the combination of ethanol and disulfuram has been found to act synergistically in depleting norepinephrine in animals.21 The combination of ethanol and disulfuram in humans, however, elicits profound nausea and vomiting and this combination certainly could not be synergistically in depleting norepinephrine in animals.21

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References

Effect of intravenous ethanol on cerebral vasospasm produced by subarachnoid blood.

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