Title: **INFLUENCE OF ASPIRIN AND METHYL PREDNISOLONE ON ACUTE LUNG INJURY CAUSED BY INTRAVENOUS INJECTION OF THE SCLEROSING AGENT ETHANOLAMINE OLEATE.**

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Introduction. Sclerotherapy is a common mode of treatment for patients with bleeding oesophageal varices due to portal hypertension. It has been noted that some patients develop severe lung injury, resembling the adult respiratory distress syndrome (ARDS), following this therapy. Recently it was shown that some sclerosing agents frequently used for sclerotherapy of bleeding oesophageal varices such as ethanolamine oleate and sodium tetradecyl sulfate can cause severe lung injury (ARDS), if given intravenously in sheep in doses corresponding to 25-50% of what is normally used during sclerotherapy in patients (1). The aim of the present series was to study if corticosteroids or a cyclo oxygenase inhibitor such as aspirin given before injection of the sclerosing agent would modify or prevent the lung injury.

Materials and Methods. Twenty one sheep, weighing 35±4 kg, were intubated (STP 30 mg/kg IV) and ventilated with a mixture of air and oxygen (FiO_2=0.5, Servo 900C). Anesthesia was maintained with IV infusion of ketamine 2 mg/kg/hr and pancuronium, 0.05 mg/kg/hr. Abdominal aortic, pulmonary artery and central venous catheters were inserted for monitoring of heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP) and cardiac output (CO, A Edwards Lab). The total static respiratory compliance (chest wall and lung, C_T), arterial blood gases, platelet (PC) and white cell counts (WBC) were also followed. After one hour of stabilization (t=0) the animals were randomly given either normal saline (NS, 20 ml IV, n=8), methyl prednisolone (MP, 40 mg/kg bwt IV; n=6) or aspirin (ASP, 10 mg/kg bwt IV; n=7) 20 minutes before ethanolamine oleate 5% 5 ml IV was given. At t=180 the animals were sacrificed and the lungs examined and weighed before (wet wt) and after drying (dry wt). Two sided Student's t test for paired data was used to compare changes within groups and the t test for unpaired data was used to compare group MP and ASP with the controls (NS). Data are presented as mean ± 1 SD.

Results. All the animals survived the observation period. None of the groups developed any significant changes in HR, MAP, CVP, PCWP or CO during the study. In the untreated group (NS) the PAP increased three fold immediately after injection of the sclerosing agent, while the respiratory compliance (C_T), arterial oxygen tension, platelet and white cell counts decreased markedly (Table). At post mortem the lungs appeared moderately congested and wet/dry wt ratio of the lungs was significantly higher than in group ASP (5.13±0.24 and 4.68±0.16 respectively, $p<0.01$). In group MP the pulmonary changes were less severe than in group NS, but the PAP icreased markedly and the lung wet/dry weight ratio (4. 95±0.20) was higher than in group ASP ($p<0.05$). C_T, PaO_2 and PC decreased only slightly compared with baseline. In group ASP, however, no hemodynamic or repiratory changes were noted. PAP, PaO_2, C_T, PC and WBC remained virtually unchanged throughout the study.

Table Sclerosing agent

	Group	Baseline	15 min	60 min	120 min	180 min
PAP	NS	12±0.8	34±7.7	16±1.7	15±1.7	15±2.2
	MP	13±1.1	33±5.1	14±3.3	14±3.0	14±2.7
	ASP	12±1.4	12±2.4*	12±2.6†	12±2.8†	12±2.8
CT	NS	29±3.5	15±4.9	17±2.4	19±3.0	22±4.6
	MP	32±4.9	20±7.0	24±7.3	25±6.7	24±7.0
	ASP	29±2.7	29±6.3*	27±4.7*	26±5.5†	25±4.3
PaO2	NS	216±16	122±56	122±45	129±27	122±20
	MP	213±24	143±81	156±69	155±59	157±58
	ASP	207±25	209±40†	196±46†	193±48†	214±23*
PC	NS	408±45	145±54	190±69	238±91	295±104
	MP	361±59	219±99	277±106	305±143	343±167
	ASP	385±42	350±52*	375±40*	420±76*	430±89

† $p<0.05$ and * $p<0.01$ for difference between group ASP and NS.

Discussion. Prostaglandins are known to be involved in the pathogenesis of lung injury (ARDS) associated with shock in animals and man. In this sheep model aspirin effectively prevented lung injury seen after injection of ethanolamine oleate. Since aspirin is a cyclo oxygenase inhibitor these findings suggest that this lung injury was mediated by prostaglandins such as thromboxane A_2. Why MP, which is an inhibitor of phospholipase A_2 and thus inhibits the cyclo oxygenase pathway, was less effective than aspirin in this study is not clear. It can possibly be explained by its limited effects on the phospholipase in platelets. This was supported by a marked drop in platelet counts (an indicator of platelet trapping in the lungs) (1) in group MP while they remained unchanged in group ASP.

Reference. Vallgren S, Sigurdsson GH, Moberger G, Christenson JT. Influence of intravenous injection of sclerosing agents on the respiratory function. Acta Chir Scand, in press 1988.