

Title : The Effects of Tolazoline on Intravascular Pressures and Cardiac Output and its Distribution During Hypoxemia

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Introduction: Pulmonary hypertension is frequently found in neonatis and is exacerbated by certain diseases such as diaphragmatic hernia or severe birth asphyxia. Neonatal pulmonary hypertension often is treated with Tolazoline. Evidence for the efficaciousness of Tolazoline lies in anecdotal case reports. No systematic study of its effects has documented its usefulness. Since Tolazoline is not an innocuous drug (complications include gastrointestinal and intracranial bleeding and renal failure) we have examined its effects on pulmonary hypertension and distribution of blood flow.

Methods: We studied 7 awake, normoxic and subsequently hypoxemic unmedicated lambs. Under local anesthesia, catheters were inserted into the left ventricle, ascending and descending aorta (below the ductus arteriosus) and the pulmonary artery. Cardiac output and its distribution was measured by the microsphere technique¹ during normoxia (PaO₂ 75 torr). Then the PaO₂ was reduced to 23±4 torr. CO₂ was not added to compensate for the fall in PaCO₂. Cardiovascular measurements were repeated during both hypoxemia and hypoxemia plus a continuous infusion of 1, 5, and 10 mg/kg/hr of Tolazoline.

Results: Cardiac output (\dot{Q}) was 956±199 ml/min, heart rate (HR) 190±48 beats/min, mean arterial pressure (MAP) 81±9 torr during the normoxic control period. These changed to 1366±573 ml/min, 237±58 beats/min, 77±14 torr and 41±6 torr during hypoxemia. The addition of Tolazoline to the hypoxemic, awake lamb did not reduce pulmonary artery pressure nor did it alter the cardiac output, heart rate or mean arterial pressure (Table I). Blood flow to gut, spleen, and kidney was reduced by hypoxemia and was reduced even more during Tolazoline infusion. (Table II). Brain blood flow increased 34% with hypoxemia and returned towards normal with increasing doses of Tolazoline. Cardiac blood flow increased 300% from control during hypoxemia and did not decrease with Tolazoline infusion. We also made 3 animals hypoxemia (PaO₂ 25±4 torr) for 1.5 hours and found no deterioration of the preparation (Table III).

Discussion: Our data do not indicate that an infusion of Tolazoline decreases pulmonary artery pressure when pulmonary receive Tolazoline. Thus our data do not support the use of Tolazoline in the treatment of neonatal pulmonary hypertension.

References:

1. Rudolph AM, and Heymann MA: The circulation of the fetus in utero: methods of studying distribution of blood flow, cardiac output and organ blood flow. Circ Res 21:163, 1967.

Table I

Cardiovascular Measurements During Tolazoline Infusion as a % of the Measurement During Hypoxemia

Tolazoline Dose (mg/kg/hr)	\dot{Q}	HR	MAP	MPA
1	93	107	101	107
5	107	105	79	112
10	105	104	91	103

Table II

Organ Blood Flow (% of Control)

	Gut	Spleen	Kidney	Brain	Heart
Hypoxemia	80	36	83	134	308
Tol					
1 mg/kg/hr	63	36	74	146	285
Tol					
5 mg/kg/hr	68	32	60	119	310
Tol					
10 mg/kg/hr	67	31	50	104	385

Table III

Effects of Hypoxemia and Time

	PaO ₂	pH	MPA	HR
Hypoxemia				
30 min	25	7.48	51	175
60 min	29	7.44	54	195
90 min	32	7.35	56	191