The Effect of Clenbuterol on Acetylcholine Induced Dyspnoea in Calves

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Introduction

Respiratory diseases are very common in calves and cause considerable economic losses. Curative therapy consists mainly in the administration of antibiotics and anti-inflammatory drugs. Broncholytic drugs such as beta-2-sympathetic agents were until now only occasionally used in calves. In horses these drugs are currently used in the treatment of COPD and acute bronchopneumonia (3).

The aim of this experiment was to evaluate the effect of clenbuterol, (Ventipulmin Boehringer), a beta-2-sympathetic drum on the acetylcholine-induced dyspnoea in calves.

Materials and Methods

Eleven calves (mean bodyweight 157 ±68 kg) were used in this experiment. Seven of these calves were suffering from chronic bronchopneumonia. During the experiment the calves were fixed in a wooden stanchion and were not sedated.

Intrapleural pressure difference (ΔPPl) was measured by direct puncture of the pleural cavity. The intrapleural catheter (Sherwood Medical Industries Inc.) was continuously flushed with a slow-dripping physiologic saline solution and was connected to a pressure transducer amplifier (Siemens Elema 863).

Pulmonary haemodynamics were measured by means of a 160 cm Swan-Ganz catheter (Edwards Laboratories), which was inserted in the jugular vein and introduced into the pulmonary artery until it wedged the arterial lumen. The Swan-Ganz catheter was filled with heparinised physiologic saline and connected to a pressure transducer amplifier (Siemens Elema 863). Zero pressure was at the level of the shoulder joint.

Mean pulmonary artery pressure ($\overline{PAP}$) and mean capillary wedge pressure ($\overline{CWP}$) were measured. Afterwards the pulmonary driving pressure (PDP) was calculated from the following equation : $PDP = \overline{PAP} - \overline{CWP}$.

ΔPpl, pulmonary haemodynamics and an ECG were recorded with a direct writing Elema Mingograph Cardirex 6T (Siemens).

Measurements were made before (A) and immediately after acetylcholine challenge (B). Acetylcholine (2 g%) was nebulised into a facemask with an inhalator (Werner Kegel, GMBH). Acetylcholine was given until dyspnoea was evident (a 2- to 3-fold increase in ΔPpl as seen on the registration). Expired air was captured by a movable ventilator. After all parameters had returned to their prechallenge level (+2 hours) clenbuterol (10 mg%) at a dose rate of 0.8 ug/kg was nebulised. Immediately after this, calves were challenged with the same dose of acetylcholine as given before clenbuterol administration and measurements were made immediately after this nebulization (c). The results of the three groups (A, B, C) were analysed by analysis of variance, followed by a multiple t test.

Results

Nebulisation of acetylcholine resulted in dyspnoea, coughing, hypersalivation and nasal discharge. The overall dose of acetylcholine (0.43 ±0.63 mg/kg) required for inducing a threefold increase in ΔPpl, differed strongly between calves and was about ten times lower ($P<0.05$) in the diseased group (0.11 ±0.11 mg/kg) as compared to the normal group (0.99±0.81 mg/kg).

Acetylcholine challenge resulted in a significant increase in RR (respiratory rate), $\overline{PAP}$ <0.01), $\overline{CWP}$ and PDP (<0.05). HR (heart rate) was only slightly increased. Nebulisation of clenbuterol partially prevented the acetylcholine-induced increase in $\overline{PAP}$, $\overline{CWP}$, PDP, RR and ΔPpl (A-C). The effect on Ppl was significant (B-C).

Discussion

Invitro experiments conducted by Mirbahar and Eyre, showed the constrictory effect on strips of bovine airway muscle, pulmonary artery and vein (1). Our findings demonstrate that nebulisation of acetylcholine in conscious calves induces an identical effect. The much higher sensitivity of diseased calves is of particular interest. The increase in ΔPpl, reflects constriction of airways and correlates well with the increase in airway resistance and

decrease in dynamic compliance as seen after the administration of other bronchoconstricting agents (2, 4).

The increase in $\overline{CWP}$ is probably due to a constrictory effect of acetylcholine on the pulmonary venous system. The high $\overline{PAP}$ value results partly from the increased $\overline{CWP}$ and partly from the augmented PDP. PDP may be increased by the reflex constriction of pulmonary arterioles as a consequence of alveolar hypoxia.

TABLE 1. Parameters in all calves (n=11).

	A	B	C	A-B	A-C	B-C
$\overline{PAP}$ (kPa)	3.78±0.87	5.79±2.08	4.92±1.58	xx	x	o
$\overline{CWP}$ (kPa)	1.75±0.69	2.62±1.08	2.11±0.77	x	o	o
PDP (kPa)	2.03±0.56	3.17±1.62	2.81±1.13	x	x	o
HR	114±23.6	134±45.9	135±41.6	o	o	o
RR	50±21.9	97±39.5	79±34.8	xx	x	o
ΔPpl (kPa)	0.84±0.20	2.44±1.17	1.20±0.33	xx	xx	xx

TABLE 2. Parameters in normal calves (n=4).

	A	B	C	A-B	A-C	B-C
$\overline{PAP}$	2.90±0.60	4.01±1.84	3.54±0.92	o	o	o
$\overline{CWP}$	1.34±0.48	1.81±0.61	1.68±0.95	o	o	o
PDP	1.56±0.48	2.20±0.67	1.86±0.65	o	o	o
HR	128±30.8	168±63.5	159±57.0	o	o	o
RR	36±9.6	102±62.1	68±26.2	o	o	o
ΔPpl	0.72±0.05	2.19±0.98	1.10±0.23	x	x	o

TABLE 3. Parameters in diseased calves (n=7).

	A	B	C	A-B	A-C	B-C
$\overline{PAP}$ (kPa)	4.29±4.90	6.80±1.84	5.71±1.31	xx	x	o
$\overline{CWP}$	2.00±0.62	3.05±1.05	2.35±0.58	x	o	o
PDP	2.29±0.43	3.75±1.75	3.36±0.99	x	x	o
HR	108±18.6	117±26.7	123±30.6	o	o	o
RR	57±24.0	95±25.5	86±39.1	x	o	o
ΔPpl	0.91±0.22	2.88±1.32	1.26±0.37	xx	x	x

A control parameters
B parameters after administration of acetylcholine
C influence of clenbuterol on acetylcholine challenge
x $P<0.05$
xx $P<0.01$

As shown in Table 2 and 3, pretreatment with clenbuterol abolishes at least partly the acetylcholine induced effects in both healthy and diseased calves. Clenbuterol is known to exercise a bronchodilating activity. Bronchodilatation ameliorates alveolar ventilation and may in this way decrease PDP. The effect of clenbuterol in decreasing $\overline{CWP}$ is in agreement with the relaxing effect of isoproterenol on pulmonary vein strips (1).

From these results we may conclude that clenbuterol reduces the acetylcholine induced dyspnoea in calves.

Summary

The effect of clenbuterol (Boehringer Ingelheim) was measured on acetylcholine induced dyspnoea in calves.

Acetylcholine was nebulised in 4 normal calves and in 7 calves suffering from chronic bronchopneumonia. The animals were not sedated. Lung-function was evaluated by measuring the pulmonary driving pressure ($PDP=\overline{PAP} - \overline{CWP}$) and the changes in intrapleural pressure (ΔPpl). Nebulisation of acetylcholine (2 g%) provoked a significant increase in ΔPpl, $\overline{PAP}$ and RR ($P<0.01$), in PDP and $\overline{CWP}$ ($P<0.05$). HR was not significantly increased.

Nebulisation of clenbuterol, a beta-2-sympathomimetic drug, partially prevented the acetylcholine-induced increase in PAP, CWP, PDP, RR and ΔPpl. The results indicate that B-adrenergic receptors are active in bovine airways and that the use of clenbuterol may be indicated in clinical respiratory disease such as bronchopneumonia in calves.

References

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