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Comparison of Reflex Responses on Administration of Lactic Acid in Pulmonary and Systemic Circulation in Cats

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ABSTRACT

Background : There are variety of chemicals that, when administered intravenously, are capable of inducing bradycardia, hypotension, and apnea by activating pulmonary C-fiber (type J) receptors (Paintal, 1973). The present study was planned to compare the reflex responses to bolus injections of lactic acid into pulmonary and systemic circulation in anaesthetized cats. **Methods:** The present study was conducted in the department of Physiology, Vallabhbhai Patel Chest Institute, New Delhi during 1999 – 2000. The cats were anaesthetized and the tip of venous cannula on one side was advanced as far as right atrium (confirmed at post-mortem). Left side of the chest was opened at the third intercostal space after connecting the animal to the ventilator. Lactic acid was injected into the right atrium and then left atrium followed by the recording of response. **Results:** The right atrial injection of a small dose(0.2mmol/kg) elicited either tachypnea or apnea. However, on increasing dose to 0.3mmol/Kg, tachypnea was more pronounced or replaced by apnea. The cardiac (bradycardia & hypotension) and respiratory responses occurred within pulmonary circulation time. Left atrial injection of lactic acid produced apnea, bradycardia and hypotension within systemic circulation time. **Conclusion:** The effect of lactic acid injection into right atrium or left atrium injections is due to stimulation of pulmonary receptors or cardiac receptors respectively.

Keywords: Pulmonary C-fiber receptors, Right atrial injection, Left atrial injection, Vagotomy, J receptors.

INTRODUCTION

Lungs and airways are extensively innervated by non-myelinated (C-fiber) vagal afferents that play an important role in regulating various airway functions (Coleridge & Coleridge, 1977). Two populations of C-fiber endings have been described in the respiratory tract: bronchial and pulmonary (Coleridge & Coleridge, 1977). The primary criterion for their identification as bronchial or pulmonary is based on their preferential circulatory accessibility through the systemic or the pulmonary circulation, respectively. There are variety of chemicals that, when administered intravenously, are capable of inducing bradycardia, hypotension, and apnea by activating pulmonary C-fiber (type J) receptors (Paintal, 1973).In humans, there are two distinct by products of energy generation during exercise that give an acid reaction i.e. carbonic acid & lactic acid. A previous study has shown that lactic acid activates pulmonary C-fiber receptors in rats (Lee et al, 1997). However, it is not known whether lactic acid can stimulate pulmonary C-fiber receptors and produce pulmonary chemoreflex in a species other than rat.Therefore, the present study was planned to compare the reflex responses to bolus injections of lactic acid into pulmonary and systemic circulation in anaesthetized cats.

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MATERIALS AND METHODS

The present study was conducted in the department of Physiology, Vallabhbhai Patel Chest Institute, New Delhi during 1999 – 2000.

Experiments were performed on healthy cats (n = 18) of either sex between 2.5 – 4.5 Kg. The cats were anaesthetized giving trichloroethylene vapours initially and later by injecting α-chloralose. The polyethylene cannula were introduced into the femoral vein and artery on both the sides. The tip of venous cannula on one side was advanced as far as right atrium (confirmed at post-mortem). The trachea was cannulated and artificial ventilation when needed was provided by a Starling ideal pump (rate 24 breaths/min, tidal volume 10 – 12 ml/Kg). The arterial pCO2 and pH were maintained within the normal range by adjusting the tidal volume and by infusing sodium bicarbonate.

Left side of the chest was opened at the third intercostal space after connecting the animal to the ventilator. A polyethylene cannula was introduced into the left atrium through the left auricle appendage. Finally, the chest was closed in layers. The cannula in left atrium was used for the left atrial injections of lactic acid.

A wide bore cannula connected to a pressure transducer was inserted into the pleural space on the right side after making a small slit. The intrapleural pressure tracing was used as an index of respiration (Anand & Paintal, 1980). Pneumothorax was minimised by periodic suctions.

Intrapleural pressure and arterial blood pressure were recorded using strain gauges (P23DC, Statham Instruments Ltd., Puerto Rico). Mean pressure was obtained by electronic damping of the pulsatile signals. An ECG (lead II) was recorded. Instantaneous heart rate was obtained by a cardiotachometer triggered by the R wave of the ECG. All variables were recorded in an ink writing recorder (Grass 7D Polygraph).

0.2 & 0.3 mmol/Kg of lactic acid were injected into the right atrium and the cardiorespiratory responses elicited were recorded. Similarly, 0.2 & 0.3 mmol/Kg of lactic acid were injected into the left atrium and the cardiorespiratory responses elicited were recorded. An interval of 15 – 20 min was given between lactic acid injections.

Analysis of Data

The group data were expressed as mean ± SEM. A p value < 0.05 was considered as significant.

RESULTS

Table 1: Changes in respiration following injections of graded doses of lactic acid into the right atria of anaesthetized cats

Primary respiratory responses				
Dose (mmol/Kg)	**Tachypnea**		**Apnea**	
	% Increase	**Latency (sec)**	**Duration (sec)**	**Latency (sec)**
0.2	61±12 (n=6)	2.2±0.3	6.7±1.0 (n=4)	0.9±0.3
0.3	76±15 (n=5)	2.1±0.3	6.8±0.8 (n=7)	1±0.2

- Values are mean ± SEM. The number of animals tested for each dose is the sum of n values in the corresponding row.
- ($P < 0.05$)

Table 2: Changes in heart rate and mean arterial blood pressure following injections of graded doses of lactic acid into the right atria of anaesthetized cats

Primary cardiovascular responses				
Dose mmol/Kg	**Heart rate**		**Mean Arterial Blood Pressure**	
	% Fall	**Latency(sec)**	**% Fall**	**Latency (sec)**
0.2	25±6 (n=6)	0.9±0.4	20±3 (n=6)	3.8±0.4
0.3	31±7 (n=9)	1.6±0.42	26±2 (n=9)	3.1±0.5

- Values are mean ± SEM. The number of animals tested for each dose is the sum of n values in the corresponding row.
- ($P < 0.001$)

Table 3: Changes in respiration following injections of graded doses of lactic acid into the left atria of anaesthetized cats

Primary respiratory responses				
Dose (mmol/Kg)	**Tachypnea**		**Apnea**	
	% Increase	**Latency (sec)**	**Duration (sec)**	**Latency (sec)**
0.2	29 (n=1)	1.4	4.7±0.3 (n=2)	1.2
0.3	79 (n=1)	1.0	5.1±0.4 (n=3)	1.3±0.1

- Values are mean ± SEM. The number of animals tested for each dose is the sum of n values in the corresponding row.

Table 4: Changes in heart rate and mean arterial blood pressure following injections of graded doses of lactic acid into the left atria of anaesthetized cats

Primary cardiovascular responses				
Dose mmol/Kg	**Heart rate**		**Mean Arterial Blood Pressure**	
	% Fall	**Latency(sec)**	**% Fall**	**Latency (sec)**
0.2	25±6 (n=2)	1.1±0.1	23 (n=1)	1.4
0.3	27±5 (n=3)	1.0±0.1	18 (n=1)	2.0

- Values are mean ± SEM. The number of animals tested for each dose is the sum of n values in the corresponding row.

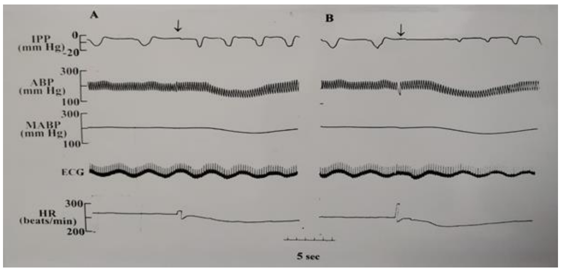

Figure 1: Cardiorespiratory responses following right atrial injections of graded doses of lactic acid in anaesthetized cats. Lactic acid was injected at the arrows and dose administered in A - 0.2mmol/kg & B - 0.3mmol/Kg).

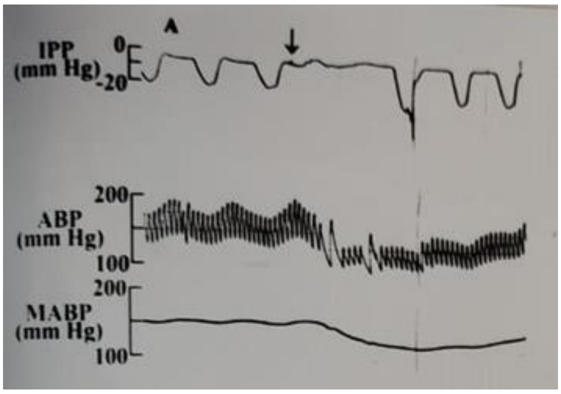

Figure 2: cardiorespiratory responses following left atrial injections of lactic acid (0.3mmol/Kg) in anaesthetized cats.

In these cats the control respiratory, heart rate & mean arterial blood pressure were 13± 1 breaths/min, 220±10 beats/min and 149±11 mmHg respectively. The arterial pH, pO2 and PCO2 were 7.33±0.01, 156±23 mmHg and 39±3.26 mmHg respectively.

A dose of 0.2 mmol/Kg (n=11) lactic acid was injected into the right atrium of cats. This dose was sufficient enough for eliciting a cardiorespiratory response. At this dose, there was tachypnoea in six whereas apnea in remaining animals [Table 1]. Bradycardia and hypotension occurred in six and no change were noticed in the remaining animals [Table 2]. With a higher dose of lactic acid (0.3mmol/Kg) (n=12), tachypnea occurred in five and apnea in the remaining animals [Table 1]. Bradycardia and hypotension occurred in nine and no change were noticed in the remaining animals [Table 2].

Left atrial injection of 0.2 mmol/kg of lactic acid elicited tachypnea or apnea with a latency of 1.4 and 1.2 sec respectively. The respiratory responses were more pronounced on increasing the dose to 0.3 mmol/kg and were accompanied by hypotension and bradycardia [Table 3 & 4].

DISCUSSION

It has been well established in cats that intravenous/right atrial injections of phenyldiguanide and capsaicin produce apnea, bradycardia and hypotension by stimulating pulmonary C-fiber receptors (Dawes 1951; Fastier 1959; Paintal 1955, 1957; Ravi and Dev, 1988). The latency for cardiorespiratory responses was 0.9 – 3.3 sec(mean 2.1 sec) that is within pulmonary circulation time(Colerdge and Coleridge, 1977).the primary respiratory responses produced by pulmonary C-fiber receptor stimulation has been considered to be tachypnoea (Anand and Paintal, 1980; ravi, 1988; ravi and Singh,1996). However, on increasing the dose, tachypnea was replaced by apnea.

As observed with phenyl diguanide and capsaicin (Paintal, 1955) the right atrial injection of a small dose (0.2mmol/kg) elicited either tachypnea or apnea. However, on increasing dose to 0.3mmol/Kg, tacypnea was more pronounced or replaced by apnea. The respiratory responses occurred within pulmonary circulation time. Along with the respiratory responses, bradycardia and hypotension were also elicited [Figure 1].

Left atrial injection of lactic acid also produced apnea, bradycardia and hypotension [Figure 2]. The results (latency-1.3 sec) suggest that the cardiorespiratory responses elicited were due to stimulation of receptors perfused by systemic circulation, notably the cardiac receptors. Bilateral vagotomy abolished cardiorespiratory responses to both right atrial and left atrial lactic acid.

CONCLUSION

Right atrial injection of lactic acid produced cardiorespiratory reflex response by stimulating receptors with vagal afferents perfused by pulmonary circulation. The study suggests that the lactic acid is producing the similar reflex response as with phenyldiguanide and capsaicin by stimulating pulmonary C- fiber receptors (Dawes 1951; Fastier 1959; Paintal 1955, 1957; Toh 1955). However left atrial injection of lactic acid produced the cardiorespiratory effects by stimulating cardiac receptors which are perfused by systemic circulation. Both the responses were mediated by vagus nerves. The further study required to demonstrate the effects of lactic acid in other species as well as in humans and its significance in exercise physiology.

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