RDIOVASCULAR FUNCTION IN STRESS SENSITIVE PIGS

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UMMARY: The purpose of this experiment was to determine the ways in which catecholamine excess, acidosis and hyperkalaemia could teract in causing stress induced deaths in Stress Sensitive pigs. The cardiovascular responses to intravenous (i/v) injections of radrenaline and isoprenaline were examined before and after infusing 0.3M HCl, KCl or NaCl. The HCl infusion produced a systemic idosis (blood pH = 7.01) and the KCl infusion was designed to maintain an increase in plasma K^+ of 2.8 meq. l^{-1}. The HCl and KCl sions resulted in a reduction in the vasodilatory (and to a less extent) heart rate responses to isoprenaline. KCl resulted in an increase in T segment depression in the electrocardiogram in response to noradrenaline and isoprenaline. It was concluded that a concomittant idosis could provide some protection against catecholamine overloading during stress, but, the effect of K^+ would depend on the degree of hyperkalaemia as at high levels it would cause lethal dysrhythmic episodes.

TRODUCTION: The object of this study was to learn more about the way in which stress leads to death in Stress Sensitive (SS) pigs. e suggested explanation is that SS pigs experience myocardial ischaemia which results in heart failure and myocardial necroses ERGMANN, 1979). The cause of the ischaemia, however, is not certain. It could either be due to catecholamine excess in the circulation OHANSSON et al, 1982) or to a systemic acidosis (SOBEL, 1980; BROOKS, 1967). A completely different explanation is that perkalaemia results in tachycardia, extrasystoles and ventricular fibrillation (COULTER and SWENSON, 1970; COULTER et al, 1975). ll three features (acidosis, high circulating levels of catecholamines and K^+) occur during Malignant Hyperthermia (LUCKE et al, 1979) nd are also thought to be present during the terminal stages of stress induced deaths in SS pigs. This study has looked at the ways in which ese three factors could interact in terms of their effect on myocardial function.

ATERIALS AND METHODS: Twenty pentobarbitone anaesthetised pigs of about 50kg live weight were used in the study. They were echanically ventilated with 3:1 N_2O:O_2 and the ventilation volume was adjusted to achieve normal venous pH and pCO_2. Six pigs were sed in the acidosis treatment, 8 in the KCl treatment and there were 6 NaCl controls. The method used for inducing an acidosis was based n that of KITTLE et al (1965). From preliminary studies it was found that an infusion of 0.3M HCl produced the required fall in blood pH without inducing haemolysis. The 0.3M NaCl control infusion tested for any effects from hypervolaemia or Cl-excess associated with the sions, or from the length of anaesthesia. At the start of the experiment all pigs were atropinised i/v with 0.2 mg atropine kg^{-1} to block any reflex increase in vagal activity in response to the catecholamine injections. Each animal was then subjected to a control set of four eparate i/v catecholamine injections; 200 ng noradrenaline (NA) kg^{-1}, 25 ng isoprenaline (IPR 25)kg^{-1}, 50 ng isoprenaline (IPR 50) and finally 100 ng isoprenaline (IPR 100)kg^{-1}. Heart rate and blood pressure were allowed to return to normal levels between each injection. This series of injections was repeated in each animal when it received either the HCl, KCl or NaCl infusion. HCl (0.3M, pH 5.65) was nfused until the blood pH had fallen to approximately 7 (pH 7.01 ± 0.01). At this point the infusion rate was reduced to maintain a steady blood pH and the catecholamine injections were repeated. KCl (0.3M) was infused at 17.5 ml min^{-1} for about 20 min. until the rhythm of the electrocardiogram (ECG) became irregular. At this point the infusion rate was reduced to 2.24 ml. min^{-1} to retain a steady ECG rhythm during the repeat injections of catecholamines. The plasma K^+ concentration had risen on average by 2.8 meq. l^{-1} at the end of the infusion, nd the venous pH was 7.34 ± 0.03 se. NaCl (0.3M, pH 6.85) was infused at 26 ml. min^{-1} which provided the same net Cl^- and volume of

infusate as the HCl treatment. Mean arterial blood pressure, heart rate and cardiac output were monitored using the methods of GREGORY and WOTTON (1981). S-T segment depression was determined in the KCl experiment by measuring its displacement from the isoelectric baseline in the ECG. On completion of the experiment the pigs were allowed to recover and were slaughtered 7 to 8 days later. Post mortem longissimus dorsi pH_{45} showed that the pigs in all 3 treatments were prone to producing PSE meat; 5.90 ± 0.01, 5.83 ± 0.10 and 5.99 ± 0.14 for the HCl, KCl and NaCl treatments respectively.

RESULTS: Blood pressure and heart rate at the beginning of the experiment were similar in all 3 treatments. The HCl and NaCl infusions had no significant effect on blood pressure, heart rate or stroke volume, but the KCl infusion caused a rise in blood pressure ($p < 0.01$). NA produced a rise in blood pressure and heart rate and IPR caused a rise in heart rate and fall in blood pressure. These effects are expressed as the areas under the response curves in Tables 1 and 2. None of the treatments affected the blood pressure and heart rate responses to NA. Both HCl and KCl caused a reduction in the vasodilatory response to IPR, and in the case of the HCl treatment the blood pressure response to IPR 25 was completely abolished. The heart rate response to IPR tended to be reduced by HCl and by KCl in contrast to NaCl but these effects were not always significant. KCl caused an increase in S-T segment depression in response to NA and IPR 25 (Table 3).

Table 1. Mean areas under the curves for the blood pressure responses (mm Hg.sec) to injections of catecholamines before and after infusions of 0.3M NaCl, 0.3M HCl or 0.3M KCl

	Infusate	Mean area before infusion	Mean area after infusion	Before v after
Noradrenaline	NaCl	(+)1872 ± 137	(+)2007 ± 124	ns
200 ng.kg^{-1}	HCl	(+)2093 ± 80	(+)2502 ± 214	ns
	KCl	(+)1999 ± 70	(+)1846 ± 107	ns
Isoprenaline	NaCl	(-) 979 ± 127	(-)813 ± 102	***
25 ng.kg^{-1}	HCl	(-)1150 ± 65	(+) 11 ± 84	***
	KCl	(-)1168 ± 48	(-)131 ± 120	*
Isoprenaline	NaCl	(-)1325 ± 108	(-)993 ± 77	***
50 ng.kg^{-1}	HCl	(-)1314 ± 124	(-) 28 ± 199	***
	KCl	(-)1403 ± 82	(-)383 ± 163	***
Isoprenaline	NaCl	(-)1701 ± 111	(-)996 ± 94	***
100 ng.kg^{-1}	HCl	(-)1695 ± 103	(-)317 ± 266	ns
	KCl	(-) 1491 ± 183	(-)921 ± 207	

ns P>0.05; *P<0.05; *** P<0.001.

Table 2. Mean areas under the curves for the heart rate response (bpm x sec) to injections of catecholamines before and after infusions of 0.3M NaCl, 0.3M HC1 or 0.3M KC1

	Infusate	Mean area before infusion	Mean area after infusion	Before v after
Noradrenaline 250 ng.kg-1	NaCl	580 ± 86	660 ± 126	ns
	HC1	1107 ± 250	838 ± 192	ns
	KC1	618 ± 120	613 ± 120	ns
Isoprenaline 25 ng. kg	NaCl	712 ± 152	865 ± 194	ns
	HC1	1083 ± 158	688 ± 102	ns
	KC1	902 ± 90	719 ± 70	ns
Isoprenaline 50 ng. kg-1	NaCl	1262 ± 235	1327 ± 232	ns
	HC1	1775 ± 108	1220 ± 93	**
	KC1	1570 ± 91	1375 ± 102	ns
Isoprenaline 100 ng. kg-1	NaCl	2105 ± 361	2261 ± 277	ns
	HCl	2507 ± 251	2064 ± 127	ns
	KC1	3434 ± 83	2031 ± 156	***

ns P>0.05; ** P<0.001.

Table 3. Effect of KC1 infusion on mean change in S - T segment distance from baseline in response to catecholamines

		$\bar{x}$ ± SEM	before v after
Noradrenaline 250 ng. kg-1 Isoprenaline 25 ng.kg-1	Before KC1	2.9 ± 0.9	*
	After KC1	4.8 ± 0.7	
Isoprenaline 50 ng. kg-1	Before KC1	1.0 ± 0.1	**
	After KC1	2.5 ± 0.4	
Isoprenaline 100 ng.kg-1	Before KC1	3.2 ± 0.8	ns
	After KC1	5.8 ± 1.8	
	Before KC1	5.7 ± 0.6	ns
	After KC1	9.3 ± 2.1	

ns P>0.05; *P<0.05; **P<0.01

DISCUSSION: It has been claimed that pigs which die during stressful situations have myocardial necroses which result from excessive exposure to catecholamines (JOHANSSON *et al*, 1982; BERGMANN, 1979). Theoretically the necroses could also be due to acidosis induced ischaemia (SOBEL, 1980; BROOKS, 1967). However, the results from this study indicate that the presence of an acidosis has a protective rather than detrimental effect on the cardiovascular system when it is challenged with catecholamines. The acidosis did not alter

heart rate, stroke volume or blood pressure but it tended to reduce the heart rate response to IPR. It seems likely, therefore, that catecholamine excess is a potentially more important cause of stress induced deaths than the acidosis itself.

In preliminary studies to this experiment it was found in three anaesthetised pigs that infusion of KCl (to give a plasma K^+ concentration of 5.03 ± 0.16 meq.$l^{-1} \pm$ se) caused irreversible alterations in the ECG resulting in death of the pigs. At 2.8 meq. l^{-1} the hyperkalaemia resulted in hypertension, tachycardia and S-T segment depression, and it resulted in an increase in S-T segment depression in response to NA and IPR which suggests that the reduction in myocardial excitability associated with the hyperkalaemia would be exaggerated by any increase in circulating catecholamines.

It is suggested therefore that death could be due to myocardial necroses resulting from overproduction of catecholamines, or cardiac arrest brought on by hyperkalaemia. It is possible that stress induced deaths are not always caused by the same factor. Hyperkalaemia will result in the development of arhythmias and cardiac arrest will occur before homeostasis can be restored. When catecholamine excess is the potentially lethal factor, an accompanying acidosis probably has a protective effect.

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