INFLUENCE OF PHENOXYBENZAMINE AND PROPRANOLOL ON BLOOD SEROTONIN AND pH, PLASMA CORTISOL AND M. LONGISSIMUS pH AND COLOR IN SWINE

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Summary

Blood samples were collected from a catheter placed in the anterior vena cava of 18 Yorkshire x Hampshire crossbred pigs representing the high U.S.D.A. 1 grade. Blood serotonin levels were negatively and significantly correlated with blood pH and plasma cortisol levels for samples collected before the administration of propranolol and phenoxybenzamine. Also, significantly higher levels of blood serotonin were observed in a litter of stress-susceptible pigs when compared with more stress-resistant animals. Pigs treated with phenoxybenzamine had lower blood pH and serotonin levels after stress than did the controls or propranolol-treated pigs. No significant differences in postmortem M. longissimus pH or color resulted from administration of the α or β receptor cell blocking agents.

Introduction

Anoxia conditions in the pig are associated with rapid increases of lactic acid in the circulatory system, and these metabolic changes can result in the development of pale, watery musculature postmortem (Forrest et al., 1968; Lister et al., 1970). This acidosis condition could result from an abnormal regulation of the microcirculatory system causing extreme constriction or dilation of the capillaries resulting in reduced blood flow in the tissues and anoxia conditions (Topel, 1968).

Serotonin (5-hydroxytryptamine) has been implicated in the control of vascular tone and hemostatic action (Page, 1954; Erspamer, 1954). It has been suggested (Bowman, Rand and West, 1969) that serotonin appears to constrict the venules relatively more than the arterioles, thus causing a pooling of blood in the capillaries under some physiological conditions.

Block, Pierce and Lillehei (1966) stated that prolonged restriction of microcirculatory inflow and outflow renders the capillary bed ischemic, with resultant local acidosis. Dietzman, Block and Lillehei (1966) reported that reduction of vasoconstriction could be accomplished by reducing the effects of sympathetic nerve stimulation by administering an α—blocking agent such as phenoxybenzamine. Hardaway (1970) stated that in addition to the effect of phenoxybenzamine on adrenergic receptors, it also has antiserotonin properties.

These studies offer the justification for further investigation on the effects of α and β receptor blocking agents on development of blood acidosis and postmortem development of pale, watery pork.

Another object of the study was to determine the relationship between blood serotonin levels and plasma cortisol since Mandell and Spooner (1968) observed that a rise in the level of circulating corticoids produced a demonstrable shift in tryptophan metabolism. Adrenal corticoid levels also have been associated with the abnormal condition of stress susceptibility and development of pale, watery musculature postmortem (Topel et al. 1968; Judge et al. 1968; Sebranek, Marple and Cassens, 1971).

Materials and Methods

Eighteen market-weight barrows (92 to 95 kg) of crossbred Yorkshire and Hampshire breeding were randomly assigned to one of three equal sized experimental groups. The pigs represented the high U.S.D.A. 1 grade and were obtained from the Iowa State University Swine Breeding Farm. The pigs were obtained from the stress-susceptible swine herd developed at the Animal Breeding Farm.
The pigs were catheterized via the anterior vena cava to facilitate collection of rested blood samples. Blood samples were collected once in the morning and once in the afternoon for 2 consecutive days. Two hours prior to the administered exercise period, six of the pigs were given an alpha receptor-cell blocking agent (50 mg phenoxybenzamine hydrochloride) via the anterior vena cava. Six pigs were given a beta receptor-cell blocking agent (1.5 mg propranolol) via the anterior vena cava 1 hr. before the exercise period. The remaining six pigs were used as controls. The animals were physically exercised for 5 min. and blood samples were collected for blood pH, serotonin and plasma cortisol levels.

Blood pH was determined at each sampling time. The analysis involved the use of a Corning Model 12 blood pH meter with temperature of the samples stabilized at 37 C. Plasma cortisol levels were determined by the protein binding method reported by Wipp and Lyon, 1970. Blood serotonin was determined by a procedure reported by Waalkes (1959).

The animals were slaughtered and processed at the Iowa State University Meat Laboratory. The carcasses were chilled for 24 hr. at 2 C and then the pH of the longissimus muscle was determined by direct contact with a single electrode from a Beckman Zeromatic pH Meter. Muscle color was determined with a Photovolt 610 Photoelectric Reflection Meter standardized against reflectance of a magnesium oxide standard. The data were analyzed according to the least squares methods described by Snedecor and Cochran (1967).

Results and Discussion

The levels of blood serotonin reported in table 1 are in the range reported by Erspamer (1954), who found the average values for the pig to be 0.26 µg/ml and for the mature human the average range was 0.1 to 0.2 µg/ml (Green, Paasonen and Gairman, 1957). The serotonin values obtained from pigs before they were stressed showed considerable variation between the animals represented in each treatment group. Correlation coefficients among the blood characteristics studied before infusion of phenoxybenzamine and propranolol are presented in table 2. A significant (P<.01) and negative correlation (r=−.44) was obtained between blood serotonin levels and plasma cortisol. This negative relationship may be expected, based on the work of Labrie and Korner (1968). They determined that basal levels of tryptophan pyrrolase activity are not altered by hypophysectomy, but hypophysectomized rats responded to injected hydrocortisone with a greater stimulation of tryptophan pyrrolase activity than did intact rats. Tryptophan pyrrolase catalyzes the conversion of tryptophan to formyl kynurenine rather than to serotonin (5-hydroxytryptamine). These results suggest an inverse relationship in the metabolic pathways for cortisol and serotonin.

A negative and significant (P<.01) correlation was found between blood serotonin and blood pH from samples collected before the administered stress period. The blood sampling method used in this study subjected the pig to a minimum amount of stress during the collection procedure. Some excitement usually occurred, however, and the sample, therefore, cannot be considered as a completely rested sample. From the present data it can be observed that in the blood samples collected before a stress, a lower blood pH is associated with an increase in serotonin levels. This follows the theory of Bowman et al. (1969) that serotonin is associated with the development of acid content in the blood by altering the normal regulation of the capillaries. Alteration in the level of serotonin in the nervous system also is associated with changes in behavior and EKG patterns. Drugs that mimic or block the actions of serotonin on peripheral tissues produce changes in behavior or mood, suggesting that drugs of this kind interfere with the actions of serotonin in the brain (Bowman et al., 1969). The influence of serotonin on altering behavior or mood may be related to a litter response observed in

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Serotonin µg/ml</th>
<th>Cortisol µg/100 ml</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.200</td>
<td>3.70</td>
<td>7.481</td>
</tr>
<tr>
<td>Phenoxybenzamine</td>
<td>0.225</td>
<td>4.02</td>
<td>7.457</td>
</tr>
<tr>
<td>Propranolol</td>
<td>0.201</td>
<td>2.70</td>
<td>7.466</td>
</tr>
<tr>
<td>SE</td>
<td>0.127</td>
<td>0.45</td>
<td>0.033</td>
</tr>
</tbody>
</table>

* Means are not significantly different (P>.05).
the pigs used in this study. A litter of eight pigs, divided into the three treatment groups, had a mean blood serotonin level of 0.302 μg/ml from the samples collected before treatment or administered stress. The mean value for the other pigs in the study, when collected under the same conditions was 0.122 μg/ml. All the pigs from the litter with 0.302 μg/ml serotonin, showed signs of the Porcine Stress Syndrome (Topel et al., 1968) during the stress period and would be classified as "stress-susceptible" pigs. The other pigs in the study didn't show the characteristic signs of the Porcine Stress Syndrome when subjected to five minutes of physical exercise. These data suggest a relationship between serotonin metabolism and stress adaptation in the pig.

Blood serotonin levels decreased during the 5-min. stress period, and plasma cortisol increased in all three groups (table 1 and 3). Nonsignificant differences were observed for the effects of phenoxybenzamine or propranolol treatment on blood serotonin or plasma cortisol levels. Phenoxybenzamine had a greater response in reducing blood serotonin levels after stress than did propranolol, but the differences was not significant. The administered levels for propranolol and phenoxybenzamine were selected to give a partial and not a complete blockage. These data therefore, partly substantiate the postulation of Hardaway (1970) that phenoxybenzamine has the effect of inhibiting serotonin production.

Pigs treated with phenoxybenzamine had a significantly lower blood pH after the 5-min. stress period when compared to the other two groups. According to the theory that excessive lactic acid accumulation in the periphery is the result of the pooling of blood due to extreme vasodilation, one could postulate the significant decrease in blood pH was associated with phenoxybenzamine blockage of the receptors. This would result in extreme vasodilation with resultant pooling of blood in the capillaries.

Table 4 describes the effects of treatment on M. longissimus pH and color 24 hr. postmortem. M. longissimus pH and color characteristics were not significantly altered by the treatments used in this study. Considerable variation existed between individual carcasses in each group for M. longissimus pH and color. Porcine muscle pH and color characteristics 24 hr. postmortem are highly influenced by the degree of ante mortem stress (Briskey et al., 1959) and the pig's ability to adapt to the stress condition (Topel et al., 1971). Pigs showing signs of the Porcine Stress Syndrome can have pale, watery musculature, normal or dark colored muscle in their carcass depending on the degree of stress susceptibility and the intensity and duration of stress prior to slaughter (Topel et al., 1971). The pigs used in this study received a uniform stress but their ability to adapt to stress conditions varied considerably when individuals in each treatment group were compared. The levels of phenoxybenzamine and propranolol used in this study to cause a partial blockage of the α and β receptors did not result in any uniform response on M. longissimus pH and color characteristics. It appears that the pigs ability to adapt to the administered stress was a major factor in altering M. longissimus pH and color traits for the animals used in each treatment. This resulted in considerable variation for color and pH values between individual animals.

Literature Cited


TABLE 3. LEAST SQUARES MEANS FOR BLOOD SEROTONIN, CORTISOL AND pH FROM SAMPLES COLLECTED AFTER STRESS FROM CONTROL PIGS AND THOSE GIVEN PHENOXYBENZAMINE AND PROPRANOLOL

<table>
<thead>
<tr>
<th>Treatment groups</th>
<th>Serotonin μg/ml</th>
<th>Cortisol μg/100 ml</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.161</td>
<td>7.15</td>
<td>7.184*</td>
</tr>
<tr>
<td>Phenoxybenzamine</td>
<td>0.140</td>
<td>7.52</td>
<td>7.055b</td>
</tr>
<tr>
<td>Propranolol</td>
<td>0.165</td>
<td>6.13</td>
<td>7.190a</td>
</tr>
<tr>
<td>SE</td>
<td>0.085</td>
<td>0.80</td>
<td>0.041</td>
</tr>
</tbody>
</table>

* Means with different superscripts within the same trait are significantly different at the P<.05 level.


