Alteration in Cardiovascular Function of Piglets during the Growth Process

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ABSTRACT. The changes with growth in the intrinsic cardiovascular functions of piglets between the ages of 2 and 12 weeks were investigated by recording simultaneously the heart rate, femoral arterial pressure, right and left intraventricular pressure, left intraventricular dP/dt, aortic flow and stroke volume before and after autonomic blockade under anesthesia with halothane. The values in cardiovascular function increased with body weight through the growing stage examined in this study, regardless of autonomic blockade. The intrinsic cardiovascular function of piglets during the growth process was regulated sympathetically in all the parameters except for stroke volume, which might be regulated autonomically through the Frank-Starling mechanism rather than autonomic nervous system.—KEY WORDS: autonomic blockade, cardiovascular function, piglet.


Swine is a valuable model for biomedical research and often used as an experimental animal for cardiovascular research [9]. Therefore, recently, several reports on swine cardiovascular function and its regulation mechanism have been accumulated [1, 2, 3, 6, 7, 8, 13, 14, 18, 19], but little is known on the development of intrinsic cardiovascular function through the growing stage.

In previous studies, we have suggested that the heart rate of piglets at rest may be regulated more sympathetically than that of rats through the growing stage [12]. It is presumed, therefore, that the intrinsic cardiovascular function of piglets may be usually enhanced by the autonomic nervous system.

The present study aimed to elucidate the changes in intrinsic cardiovascular function of piglets during the growth process, indicating the heart rate, femoral arterial pressure, right and left intraventricular pressure, left intraventricular dP/dt, aortic flow and stroke volume after autonomic blockade.

MATERIALS AND METHODS

A total of 12 domestic piglets (crossbred of Duroc, Landrace and Hampshire) aged 2 to 12 weeks, many of which were litter-mates, were used for evaluating the intrinsic cardiovascular function. All animals were intubated and the tracheal tube was connected to a respirator for inhalation with a mixture of oxygen and halothane (Japan Hoechst). The inhalation rate was at 12/ min, and the rectal temperature of the animals was kept between 35°C and 37°C throughout the experimental period.

The hemodynamic parameters adopted were the right and left intraventricular pressure (RVSP, LVSP), left intraventricular dP/dt (Max LVdP/dt), femoral arterial pressure (FAP), aortic flow (AF), stroke volume (SV) and heart rate (HR). A single 7F catheter (Cordis) was inserted into the right ventricle via the left external jugular vein. The lumen was used for RVSP measurements by connecting it to a pressure transducer (Toyo Boldwin MPU-0.5—290-0-III). A catheter with a tip transducer (Tokai
Rika Denki TPC 2RN136F30) was inserted into the left ventricle via the left carotid artery for recording LVSP. A 7F thermodilution catheter was placed into the aortic arch via the left femoral artery for the determination of AF [4]. The thermodilution curve was integrated by a signal processor (NEC Sanei, 7T08). AF was calculated from the following equation.

$$Q = \frac{60 \times V_i \times S_i \times C_i \times (T_b - T_i)}{S_b \times C_b \times A}$$

where $V_i$ = volume of injection in ml; $A$ = area of the thermodilution curve; $T_b$, $T_i$, $S_b$, $S_i$, $C_b$, $C_i$ = temperature (T), specific gravity (S), and specific heat (C) of blood (b) and indicator (i), respectively; and the value of $S_i \times C_i / S_b \times C_b$ is 1.08 when physiological salt solution is used as an indicator.

SV was calculated dividing AF by HR. Max LVdP/dt as an index of myocardial contractility was obtained by feeding LVSP into a differential amplifier (NEC Sanei, 1309). The electrocardiogram in lead II was recorded with a biophysiograph (NEC Sanei, 1206). HR was calculated from the RR interval of the electrocardiogram. All tracings were recorded simultaneously on a pen-writing recorder (NEC Sanei, RECTI-HORIZ-8K).

Autonomic blockade was carried out after control recordings for cardiovascular function had been obtained. At first, either a single dose of atropine (Tokyo Kasei, 0.1 mg/kg) or propranolol (Sigma, 1.0 mg/kg) was injected through an ear vein. Secondly, the remaining drug was given 10 min later. The measurements obtained 10 min after the second injection were considered to be representative of a condition where autonomic nervous function had been blocked completely. The dose of propranolol was determined as the minimum dose that was able to block the increase in heart rate induced by a single intravenous injection of 1.25 μg/kg of isoproterenol (Nikken Kaga-

ku), while that of atropine was determined as the minimum dose that was able to block the decrease in heart rate induced by a single intravenous injection of 200 μg/kg of acetylcholine (Daichi Seiyaku).

The measurements obtained before and after autonomic blockade were analyzed by Student's paired t-test and the linear regression analysis. The results were considered to be statistically significant when the P value was less than 0.01 or 0.05.

RESULTS

Figure 1 shows the original records obtained before and after autonomic blockade in a piglet at 8 weeks of age. After autonomic blockade, HR decreased and other hemodynamic parameters were also reduced. Furthermore, it was apparent that AF had diminished, because the slope of the aortic thermodilution curve became gentle.

As shown in Fig. 2, a significant correla-

BEFORE

AFTER

ECG 1 mV |
RVP (mmHg) 50 [ |
LVP (mmHg) 100 |
LVdP/dt (mmHg/sec) -2000 |
FAP (mmHg) 150 |
37.0 |
ATC (°C) 36.6 |

Fig. 1. Original records before and after autonomic blockade in a pig at 8 weeks of age. ECG: electrocardiogram in limb lead II RVP: right intraventricular pressure LVP: left intraventricular pressure LVdP/dt: differential value of left intraventricular pressure FAP: femoral arterial pressure ATC: aortic thermodilution curve
tion was recognized between age and body weight \( (p<0.01) \). Therefore, when the respective body weight was arranged in abscissa instead of age, HR, before and after autonomic blockade in each animal were presented as shown in Fig. 3. The values obtained from this experimental period were not dependent on body weight regardless of autonomic blockade. The magnitude of HR responses to autonomic blockade differed according to the individual, but a significant decrease in HR was observed after autonomic blockade \( (p<0.01) \).

Figure 4 shows the alteration with body weight in the other hemodynamic measurements (RVSP, LVSP, Max LV dP/dt, FAP, AF, SV) before and after autonomic blockade. Linear regression analysis revealed a significant positive correlation between body weight and all of the parameters \( (p<0.01 \text{ or } 0.05) \). Furthermore, the values for all parameters except for SV were significantly reduced after autonomic blockade \( (p<0.01 \text{ or } 0.05) \). The regression line between body weight and SV was approximately consistent before and after autonomic blockade.

**DISCUSSION**

The cardiovascular system is regulated by autonomic nervous system, one of the body’s major regulating mechanisms. Therefore, if it is possible to achieve specific denervation, we should be able to estimate the intrinsic cardiovascular function. It has been reported that simultaneous administration of adrenergic and muscarinic receptor blockers enables intrinsic cardiovascular function to be estimated easily \[10\]. In this experiment, therefore, pharmacological denervation using propranolol and atropine was performed. We determined these dosages from our previous examination \[12\] and by reference to previous reports \[8, 14\].

In this study, halothane was used for animal anesthesia. Although halothane causes slight hypotension, it does not change HR, nor does it increase the concentration of catecholamines in the blood. Moreover, it is said to be the most desirable anesthetic for pigs, since both induction and control can be easily done during maintenance of anesthesia \[5, 17\].

The hemodynamic measurements shown in this study were lower than those obtained
in previous studies [2, 3, 15, 16], most of which used sodium pentobarbital as an anesthetic. This was probably due to the depression of sympathetic nervous function and/or the elevation of parasympathetic nervous function with halothane anesthesia [11].

The control measurements for all hemodynamic parameters except for HR increased with advancing age, moreover, the values in these parameters after autonomic blockade also increased age-dependently. However, all of these values except for SV were diminished significantly after autonomic blockade. The fact means that the net autonomic nervous tone, which is expressed as a sum of the sympathetic and parasympathetic nervous functions, has been shifted to the parasympathetic condition after autonomic blockade, regardless of age, since the cardiovascular system of the piglet may be regulated sympathetically during the experimental period [12].

On the other hand, although HR before and after autonomic blockade in this experiment were independent of age, it has been
known that control heart rate and intrinsic heart rate (defined as the HR after autonomic blockade) decreased with advancing age in unanesthetized piglet [12]. The values before and after autonomic blockade in hemodynamic parameters established a significant positive correlation between body weight through this experimental period, although the magnitude of the responses differed according to the individual and the parameters. The pre-existing autonomic activity in each animal might have subtle difference in the cause of factors such as trauma, depth of anesthesia, acid-base state etc.

SV alone was the less influenced parameter to autonomic blockade. SV is not only affected by the mechanical factors such as end-diastolic volume, left ventricle contraction and ejection pressure which are regulated directly or indirectly by the autonomic nervous system, but is regulated autonomically through Frank-Starling mechanism which seems to be age dependent in the pig [19]. In the present study, SV was not changed markedly, despite the fact that both the left ventricle contraction and the ejection pressure were diminished after autonomic blockade. It seems that Frank-Starling mechanism responded to end-diastolic volume, so that SV was maintained at the value before autonomic blockade. As HR decreased after autonomic blockade, it is thought that AF significantly decreased after autonomic blockade, in spite of unchanged SV.

From the results obtained in this study, it was presumed that the intrinsic cardiovascular function of piglets increased with body weight through the growing stage, and was regulated sympathetically in all the parameters except for SV, which might be regulated autonomically through the Frank-Starling mechanism rather than autonomic nervous system.

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要 約

育成期にあるブタの心血管系機能の推移：滋賀正貴・広瀬 稔・菅野 茂（東京大学農学部家畜環境生理学教室）——2-12週齢の三元交雑種育成豚における心血管系機能の推移を明らかにする目的で、ハローセン麻酔下、プロプラノロールおよびアトロビン投与前後の心拍数、大腿動脈圧、左心室内圧、左心室内圧微分波、大動脈血流および1回心拍出量の測定を行った。その結果、心拍数を除くすべての測定値が自律神経遮断の有無にかかわらず、体重の増加にともなって増加すること、また、1回心拍出量を除く他の測定値は自律神経遮断後、いずれも有意に減少することがわかった。これらのことから、育成期にあるブタの心血管系機能は交感神経が優位な状態で調節されているけれども、1回心拍出量のみは自律神経性調節よりむしろ、Frank-Starlingの法則にもとづく心臓自体の制御機構により調節されていることが示唆された。