Effect of Phlebotomy on Coronary Blood Flow in Calves with Brisket Disease[1] (37066)

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(Introduced by G. E. Cartwright)

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Brisket disease (BD) or pulmonary hypertensive heart disease of cattle provides an opportunity to study the effects of ventricular hypertrophy, dilatation and failure on coronary hemodynamics in the absence of coronary or valvular heart disease (1). In a previous study, we demonstrated that left and right ventricular function in BD could be improved by phlebotomy during the acute phase of the disease (2). The purpose of this study was twofold: (a) to measure CBF by the ^{133}Xenon technique in BD calves during the acute phase of the disease and (b) to determine the effects of phlebotomy in BD calves on coronary hemodynamics.

Methods. Eleven studies were performed in 11 unanesthetized calves (average wt. 130 kg) with brisket disease breathing spontaneously. All studies were performed with the animals restrained lying on their left side.

Under local lidocaine, infiltration anesthesia surgical cutdowns were made over a branch of the left femoral artery (FA), the right external jugular vein, and right carotid artery. A #18 Jelco plastic needle 10 cm in length was inserted into the branch of the left FA and advanced proximally. Two #8 Lehman catheters were introduced into the external jugular vein. One was advanced under fluoroscopic guidance to the coronary sinus (CS) while the other was advanced to the pulmonary artery. A #8 Lehman catheter was introduced into the right carotid artery and advanced to the left ventricle. A #7 Sones catheter was also introduced into the right carotid and positioned in the left coronary artery. Correct placement of the latter was determined angiographically. The FA cannula and all catheters were connected to P23Db pressure transducers.

Measurement of CBF by the ^{133}Xenon technique was performed by injecting ^{133}Xenon into the left coronary artery. The ^{133}Xenon (supplied by the Oak Ridge National Laboratory, Oak Ridge, Tennessee) was dissolved in sterile saline to give a concentration of 0.2–0.8 mCi/cc. Myocardial isotope washout curves were obtained with a collimated scintillation detector (1 in. thallium activated sodium iodide crystal) which was placed against the sternum and aimed at the heart. The curves were recorded on an oscillographic recorder (Minneapolis Honeywell Model 1612, Denver, Colorado) at a paper speed of 1 mm/sec. The $T_{½}$ (time required for radioactivity to decrease by half) was obtained by plotting the radioactivity from each washout curve on semilogarithmic paper. CBF was calculated according to the formula:

$$\text{CBF (ml/min/100 g)} = \frac{.69 \times .72 \times 100}{T_{½}\ \text{(min)}/1.05},$$

where 0.69 = log to the base e of 2, 0.72 = partition coefficient for ^{133}Xenon, 1.05 = specific gravity of the myocardium. For the measurement of myocardial oxygen consumption (MV_{O_2}) samples of blood were obtained simultaneously from the CS and FA and analyzed for O_2 content using the Van Slyke method. MV_{O_2} was calculated according to

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the formula:

$$M\dot{V}_{O_2}\ (ml/min/100\ g) = CBF \times \text{myocardial AV difference of } O_2\ (C\bar{A}VO_2).$$

Each arterial sample was also analyzed for CO_2 tension (P_{ACO_2}) and pH using the Astrup apparatus. Each CS sample was also analyzed for O_2 tension (P_{CSO_2}).

Cardiac output (CO) was measured using the indicator dilution technique injecting 5 to 10 mg of indocyanine green dye into the pulmonary artery while sampling blood from the femoral artery through a Gilson densitometer (Gilson Medical Electronics, Middleton, Wis.) at a rate of 30 ml/min. The indicator–dilution curves, pressures and the electrocardiogram were also recorded on the oscilloscope recorder.

Left ventricular stroke work (LVSW) was calculated in gram meters (gM) according to the formula:

$$LVSW\ (gM) = \frac{SV \times (SAP - LVEDP) \times 13.6 \times 1.055}{1000},$$

where SV = stroke volume, SAP = systemic arterial pressure (mm Hg), LVEDP = left ventricular end diastolic pressure (mm Hg), 13.6 = factor for converting mm Hg to mm H_2O, and 1.055 = specific gravity of blood.

Right ventricular stroke work (RVSW) was calculated according to the formula:

$$RVSW\ (gM) = \frac{SV \times (\overline{PAP} - \overline{CSP}) \times 13.6 \times 1.055}{1000},$$

where $\overline{PAP}$ = mean pulmonary arterial pressure (mm Hg), $\overline{CSP}$ = mean coronary sinus pressure (mm Hg).

Coronary perfusion pressure (CPP) was calculated as the difference between SAP and CSP. Coronary vascular resistance (CVR) was calculated according to the formula:

$$CVR\ (mm\ Hg/ml/min) = \frac{CPP}{CBF}$$

In the control period before phlebotomy, pressures and CO were measured twice, CBF five times and $M\dot{V}_{O_2}$ once. For statistical analysis the average of the above determinations for each variable was used. Venesections ranging from 500 to 2500 ml (average 1700) were performed to obtain significant lowering of right atrial pressure. Fifteen minutes following completion of the phlebotomy hemodynamic variables were again measured. Similar to the control period, pressures and CO were measured twice, CBF five times and $M\dot{V}_{O_2}$ once. Following completion of the study the blood was returned to the animal.

Results. Mean values for each hemodynamic variable before and after phlebotomy are listed in Table I. In the control period CO was low whereas PAP, LVEDP, and CSP were markedly elevated. Following phlebotomy heart rate, CO, RVSW, and CPP increased significantly whereas there was a significant fall in CSP, $C_{A\bar{V}O_2}$, volume of packed red cells (VPRC), LVEDP, and SAP. There was no significant change in PAP and LVSW. Arterial oxyhemoglobin saturation (S_{AO_2}) was low in the control period and did not change after phlebotomy. CBF and CS oxyhemoglobin saturation (S_{CSO_2}) increased and $C_{A\bar{V}O_2}$ decreased following phlebotomy whereas there was no significant change in $M\dot{V}_{O_2}$ and CVR. CBF/$M\dot{V}O_2$ ratio increased significantly following phlebotomy.

There was no significant relationship between CBF and CPP, CO, S_{AO_2}, heart rate, LVSW, RVSW or total right and left ventricular work. Also, a significant relationship was not found between $M\dot{V}_{O_2}$ and CO, LV SW, RVSW, total ventricular work, CPP, S_{CSO_2}, $C_{A\bar{V}O_2}$, or S_{AO_2}.

Discussion. There are several factors present in BD that might be expected to reduce total CBF: low CO, decreased CPP and, for the right ventricular flow, increased right ventricular wall tension consequent upon severe right ventricular dilatation and hypertension. The purpose of phlebotomy was to determine whether improvement in overall cardiovascular function achieved by that means is accompanied by significant alteration in coronary hemodynamics (2). Following phlebotomy the increase in CBF could be related to

TABLE I. Comparison of Hemodynamics before and after Phlebotomy in 11 Calves.

	Control	After phlebotomy	Difference	*P* values
Heart rate, beats/min	103 ± 6.4	112 ± 6.9	−8.8 ± 2.8	<.02
CO, ml/min/kg	57 ± 9.2	80 ± 7.9	−22.9 ± 4.5	<.01
SAP, mm Hg	116 ± 6.0	111 ± 5.3	+5.4 ± 2.3	<.05
PAP, mm Hg	87 ± 8.0	85 ± 7.9	+1.7 ± 4.7	NS
LVEDP, mm Hg	15 ± 3.3	9 ± 2.2	+5.4 ± 2.3	<.05
CSP, mm Hg	32 ± 4.0	17 ± 2.8	+14.6 ± 2.1	<.01
CPP, mm Hg	84 ± 7.9	94 ± 5.6	−9.3 ± 3.3	<.02
CBF, ml/min/100g	62 ± 4.9	86 ± 8.2	−23.4 ± 7.5	<.02
CVR, mm Hg/ml/min/100g	1.36 ± 0.8	1.19 ± .13	+.17 ± .11	NS
RVSW, g*M*	63 ± 17.4	83 ± 12.3	−20.3 ± 2.5	<.05
LVSW, g*M*	124 ± 25.1	148 ± 25.0	−23.9 ± 10.9	NS
MV_{O_2}, ml/min/100g	8.0 ± 0.7	9.2 ± 1.0	−0.5 ± 0.9	NS
CBF/MV_{O_2}	7.7 ± 0.40	9.5 ± 0.6	−2.1 ± 0.5	<.01
C_{AVO_2}, ml/100 ml	13.21 ± 0.6	10.95 ± 0.7	+2.69 ± .51	<.01
C_{CSO_2}, ml/100 ml	2.02 ± 0.33	2.62 ± .48	−.61 ± .37	NS
S_{CSO_2}, %	10.1 ± 1.8	14.1 ± 2.3	−3.6 ± 1.2	<.02
P_{CSO_2}, mm Hg	17.4 ± 1.9	16.8 ± 2.1	+0.4 ± 0.8	NS
S_{AO_2}, %	78.5 ± 2.7	79.4 ± 3.3	−1.5 ± 2.20	NS
P_{ACO_2}, mm Hg	35.3 ± 2.0	35.4 ± 1.8	−.6 ± 1.1	NS
pH	7.40 ± .01	7.40 ± .03	−.02 ± .01	<.02
VPRC	43.8 ± 1.1	37 ± 1.4	+7.1 ± 4.3	<.01
P_{AO_2}, mm Hg	48.8 ± 2.7	49.7 ± 3.4	−.5 ± 2.6	NS

CO = cardiac output; SAP = mean systemic arterial pressure; PAP = mean pulmonary artery pressure; LVEDP = left ventricular end diastolic pressure; CSP = coronary sinus pressure; CPP = coronary perfusion pressure; RVSW = right ventricular stroke work; LVSW = left ventricular stroke work; CBF = coronary blood flow; CVR = coronary vascular resistance; MV_{O_2} = myocardial oxygen consumption; C_{AVO_2} = myocardial arteriovenous oxygen difference; S_{CSO_2} = oxyhemoglobin saturation of coronary sinus blood; P_{CSO_2} = oxygen tension of coronary sinus blood; S_{AO_2} = arterial oxyhemoglobin saturation; C_{CSO_2} = coronary sinus O_2 content; VPRC = volume of packed red cells; P_{ACO_2} = arterial CO_2 tension; P_{AO_2} = arterial O_2 tension; NS = not significant. Each value indicates mean ± standard error the mean (SEM). Difference column indicates value in "Control" column minus value in "After phlebotomy" column.

increase in CO and CPP. Additional factors that cannot be discounted include the slight increase in heart rate and the slight reduction in arterial O_2 content owing to hemodilution.

Absence of a rise in $M\dot{V}_{O_2}$ acutely following phlebotomy in the BD calves despite a rise in CBF can be explained only by decreased extraction. The fact that $M\dot{V}_{O_2}$ is similar during severe heart failure and following phlebotomy in the BD calves may be related to a balance of factors that determine $M\dot{V}_{O_2}$—myocardial tension, the contractile force of the myocardium and to a lesser extent external cardiac work (3). The reduced contractile state of the two ventricles during heart failure would favor a decreased $M\dot{V}_{O_2}$ whereas right ventricular dilatation and hypertension would tend to augment myocardial tension and increase $M\dot{V}_{O_2}$. In the left ventricle, the myocardial tension developed would be a balance of the decrease in left ventricular systolic pressure and degree of dilatation of the left ventricle. Following phlebotomy contractile state of the two ventricles presumably improves and myocardial tension decreases.

The results of this study must be interpreted in view of the limitations of the ^{133}Xenon method for measuring CBF (4, 5). In this study all ^{133}Xenon injections were made into the left coronary artery. The

^{133}Xenon method measures the flow per weight of myocardium perfused by the injected ^{133}Xenon. How much of the right ventricular myocardium in the calf is perfused by the left coronary artery is not clear. Secondly, how much right ventricular flow is altered during brisket disease is not known. Selective measurement of left and right coronary flow in normal and BD calves would be helpful.

Summary. The effect of phlebotomy (average volume 1700 ml) on coronary hemodynamics was evaluated in 11 calves with BD or pulmonary hypertensive heart disease of cattle. CBF was measured by the ^{133}Xenon technique. In the control period the characteristic findings of BD were present: low CO, severe pulmonary hypertension, marked elevation of right ventricular diastolic and moderate elevation of left ventricular diastolic pressures. Following phlebotomy there was a significant increase in CBF, heart rate, CO, RVSW, and CPP accompanied by a significant decrease in CSP, $C_{A\bar{V}O_2}$, LVEDP and SAP. There was no significant change in $M\dot{V}_{O_2}$. The rise in CBF can be explained by the increase in myocardial perfusion pressure whereas the absence of significant change in $M\dot{V}_{O_2}$ may be related to a balance of the determinants of $M\dot{V}_{O_2}$. The changes in CBF and $M\dot{V}_{O_2}$ must be interpreted by our inability to separate these variables into the contribution from each ventricle.

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