EDITORIAL VIEWS

Winnie the Pooh Revisited, or, The More Recent Adventures of Piglet

INITIAL STUDIES of the effects of anesthesia and surgery on the heart with ischemic heart disease used animal models with total interruption of blood flow through a coronary artery.[1-4] More recently, investigators have turned to models in which a coronary artery is experimentally narrowed but blood flow persists,[5-8] in order to more closely mimic the clinical situation. A major objective of such studies is to learn if one anesthetic regimen is more likely than another to avoid the development of myocardial ischemia in the presence of coronary artery stenosis.

In an article in this issue of ANESTHESIOLOGY, Merin et al.[9] present carefully gathered data describing the effect of reducing coronary blood flow in piglets anesthetized with either halothane or fentanyl. Fentanyl anesthesia was associated with greater coronary blood flow and myocardial oxygen consumption consistent with the higher systemic arterial pressure when compared to halothane. After hemodynamic measurements became stable, the investigators constricted the left anterior descending coronary artery until its blood flow was reduced by 60 per cent. Following constriction, the major hemodynamic variables during either anesthetic remained fairly constant although still quite different. In the presence of either anesthetic, the reduction of coronary blood flow was accompanied by metabolic evidence of myocardial ischemia.

Waters et al. previously demonstrated in anesthetized dogs that reduction of coronary blood flow to 48 ± 4 per cent of control values results in metabolic and mechanical evidence of ischemia.[10] The data of Merin et al. indicate that when piglets are anesthetized with either fentanyl or halothane, even though the two anesthetics are associated with markedly different hemodynamic variables and myocardial oxygen requirements, a 60 per cent re-

duction of coronary blood flow produces ischemia. Thus, this information extends and confirms the observations of Waters et al. Both of these laboratory studies imposed a coronary stenosis upon a preexisting stable anesthetic state. This contrasts with the clinical problem of anesthetizing the patient who already has severe narrowing of one or more coronary arteries. That patient must be anesthetized in such a manner that coronary blood flow is never reduced below the critical value at which ischemia occurs.

Unlike the model of Merin et al. in which a coronary artery is narrowed to an extent which invariably produces ischemia, an anesthetic produces ischemia in the heart with preexisting stenosis only when the tenuous balance between oxygen supply and demand is disturbed. Oxygen supply is determined by factors regulating blood flow through the stenosis and the myocardium.

Blood flow through the coronary bed is determined by the resistance (R) and the pressure gradient ($P_I - P_O$) across the bed. We have diagrammatically depicted these for the coronary circulation in figure 1. Total resistance is the sum of the resistances of both the large extramyocardial vessels and the small intramyocardial vessels. If coronary perfusion pressure falls, blood flow is maintained by a decrease in resistance. When the vessels are dilated fully, the vascular resistance can no longer fall and the flow decreases with pressure. In the normal coronary unit, the inflow pressure at the entrance to the small vessels (P_{I_s}) is virtually the same as aortic pressure since the pressure drop across the large vessels is negligible. In contrast, in patients and experimental models where there is a constriction of a large coronary vessel, there may be a considerable pressure drop across the stenosis. Therefore, P_{I_s} no longer equals the aortic pressure. If the constriction is severe but insufficient to cause myocardial ischemia at rest, the small vessels will have reached the limits of vasodilation, and their "autoregu-
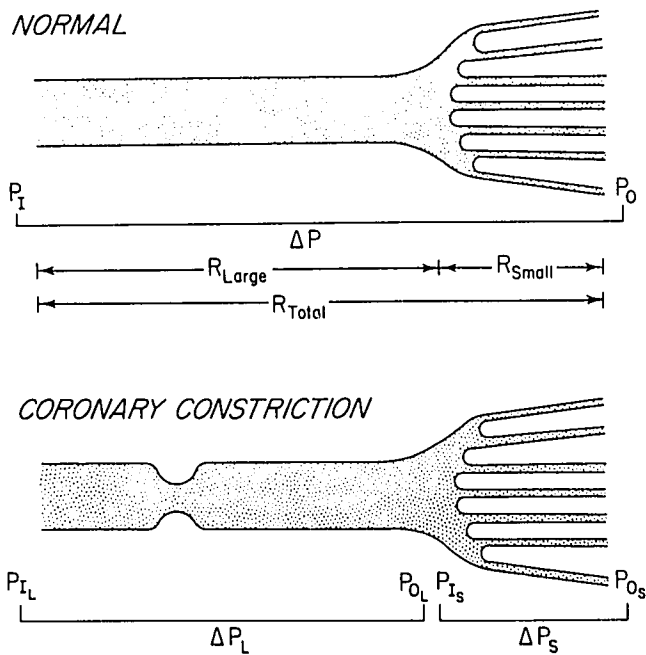
NORMAL

CORONARY CONSTRICTION

FIG. 1. Diagram of a normal coronary vascular unit and one supplied by a constricted coronary artery. Total resistance (R) is the sum of the resistances of the large extramyocardial and small intramyocardial blood vessels. In the normal unit, autroegulation is important in determining blood flow. The pressure (ΔP) is the difference between the inflow pressure (P_I) and outflow pressure (P_O). In the presence of a severe coronary constriction, there may be a pressure gradient across the narrowing ($P_{I_L} - P_{O_L}$). Therefore, the small vessel bed is not exposed to P_{I_L}, and P_{O_L} represents the inflow pressure to the small vessel bed (P_{I_s}). When the small vessel bed is dilated completely, as when the myocardium is ischemic, the pressure-flow characteristics of the constriction limit the blood flow available to the small vessel bed. See text for details.

latory reserve" is exhausted. At that time, blood flow is determined by the pressure gradient across the constriction ($P_{I_L} - P_{O_L}$) and physical laws determining flow through a narrowed tube, rather than by physiologic mechanisms regulating blood flow to the myocardium.

With this discussion as background, we can now address the clinical question of which of two anesthetic agents associated with different hemodynamic effects and myocardial oxygen requirements is the more likely to lead to ischemia in the presence of a fixed narrowing in a coronary artery. In order to examine this question with the presently available data we must estimate for each anesthetic 1) the minimal requirement for blood flow compatible with adequate myocardial oxygenation, and 2) the maximum flow through the stenosis. We have estimated these values using data from three sources: Waters et al.[10] and Merin et al.[9] for flow requirement, Merin et al.[9] for arterial pressure, and Verrier et al.[6] for the minimal pressure required to perfuse the myocardium with the critical flow. Our calculations are included in an appendix. Briefly, we will accept the contention

of Waters et al. that 50 per cent of the blood flow in the absence of constriction is the smallest quantity compatible with satisfactory myocardial oxygenation. For the left anterior descending (LAD) coronary artery of the piglets in the study by Merin et al., these minimum values are 13.2 ml/min for halothane and 20.1 ml/min for fentanyl. Our calculations indicate that a constriction of the cross-sectional area permitting 13.2 ml/min LAD flow during halothane anesthesia will permit a flow of 17.8 ml/min during fentanyl anesthesia. This is obviously less than the necessary 20.1 ml/min required for fentanyl anesthesia. The implication is that with this particular narrowing and the experimentally reported hemodynamic state and oxygen demand, a "low demand-low pressure" anesthetic will be tolerated without ischemia, whereas a "high demand-high pressure" anesthetic is associated with a myocardial oxygen deficit.

The major reason for the seemingly surprising outcome of our calculations is that flow through a stenosis is proportional to the square root of the pressure difference. Thus, a fourfold drop in aortic pressure will only produce a twofold reduction in coronary blood flow. There may, however, be a concomitant and greater fall of oxygen demand, so that ischemia does not occur despite the decreased oxygen supply. The higher driving pressure during fentanyl anesthesia increased the myocardial oxygen requirement to a greater degree than the increase of blood flow across the stenosis.

This theoretical analysis was performed using data from three different studies in two species. Furthermore, we made a considerable number of assumptions, some of which may be invalid. Therefore, the theory requires experimental proof. However, the consistency of the critical coronary flows and the overall hemodynamic data reported in the three papers gives us confidence in the correctness of our approach.

This editorial is prompted by a wish to learn if measuring the effect of constricting a coronary vessel until ischemia develops in the anesthetized laboratory animal leads to erroneous conclusions regarding the optimum management of an animal or patient with a preexisting critical stenosis. In the animal model Merin et al. showed no difference in the degree of ischemia during fentanyl vs. halothane. In contrast, our calculations indicate that fentanyl and halothane can produce quite different degrees of ischemia in the presence of an identical degree of coronary constriction. The question of whether, in the presence of a high-grade coronary constriction, an anesthetic regimen which allows "high myocardial function" and increased myocardial oxygen demand is less likely to result in a positive myocardial oxygen balance than one which is associated with "low myocardial function" and lesser oxygen demand is sufficiently important to warrant further carefully planned research. Much has

been written regarding the factors governing myocardial oxygen supply and demand, but little attention has been paid to the major differences between the pressure-flow relationships of normal coronary vascular units and those supplied by a narrowed coronary artery. It is very encouraging to the clinician that such questions are being asked. Our patients will benefit when they are resolved.

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APPENDIX

Steady laminar flow across a constriction in a tube is governed by the formula[11]

$$\Delta P = \frac{\rho}{2}\left(\frac{1}{A_c^2} - \frac{1}{A_a^2}\right) Q^2$$

where:

ΔP = pressure gradient (mmHg),

ρ = viscosity of blood,

Q = flow,

A_c = cross-sectional area of the constriction, and

A_a = cross-sectional area of the artery.

Accepting the contention of Waters *et al.*[10] that 50 per cent of control coronary blood flow is the minimum required to avoid ischemia, we can estimate that in the piglets study by Merin *et al.*,[9] 50 per cent of the control LAD flow of 26.5 ml/min, or 13.2 ml/min LAD blood flow should be just adequate for positive myocardial oxygen balance. Since any further flow reduction leads to ischemia, the vessels must be dilated fully. The minimum pressure corresponding to this flow is equivalent to the autoregulatory breakpoint.

Merin *et al.* did not report the mean diastolic arterial pressure, so we shall use the mean arterial pressure as inflow pressure to the coronary artery (P_{II}). We obtained the point of intersection from figure 3 of Verrier *et al.*[6] as the minimum allowable pressure P_{Is}, which in turn would equal P_{OI}. For halothane the values are 80 mmHg and 26 mmHg respectively. Thus, we can afford to have driving pressure reduced up to 54 mmHg across the constriction. Therefore,

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$$\frac{\Delta P}{Q^2} = \frac{\rho}{2}\left(\frac{1}{A_c^2} - \frac{1}{A_a^2}\right) = \frac{54}{(13.2)^2} = 0.31 \ (\text{mmHg} \cdot \text{ml}^{-1} \cdot \text{min}^{-1})^2$$

Thus, $\frac{\rho}{2}\left(\frac{1}{A_c^2} - \frac{1}{A_a^2}\right)$ is a "constriction constant" for the stenosis that just failed to produce ischemia under halothane anesthesia. This constant can be used to calculate the maximum possible flow through that stenosis for any value of pressure gradient.

The mean arterial pressure during fentanyl anesthesia was reported by Merin *et al.* as 138 mmHg and the LAD blood flow as 40.2 ml/min. Therefore, the minimal acceptable LAD flow is 20.1 ml/min. We used the point of intersection of Verrier *et al.* of 40 mmHg during N_2O anesthesia as P_{Is} fentanyl since the values for the arterial pressure and LVEDP during fentanyl anesthesia *vs.* nitrous oxide were similar in both studies. Therefore, the minimum allowable pressure drop across the constriction is 138–40 or 98 mmHg. Substituting 98 for ΔP

$$\frac{\Delta P}{Q^2} = \frac{98}{Q^2} = 0.31$$

we obtain a flow of 17.8 ml/min. If we were to use the same autoregulatory intersection point as for halothane, a similar calculation would yield a value of 19.0 ml/min, still less than the 20.1 ml/min required for fentanyl anesthesia.

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