Differences in Cerebral Blood Flow with Pulsatile and Nonpulsatile Flow in Normal and Ischemic Brain

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Abstract

The effect of pulsatile versus nonpulsatile perfusion on regional cerebral blood flow (CBF) was tested in a canine model with and without focal ischemia. Nine dogs were placed on total cardiopulmonary bypass with a flow rate of 100 cc/kg/min. at normothermia. Control cerebral blood flow measurements were made in both cerebral hemispheres using the hydrogen clearance technique during pulsatile and nonpulsatile perfusion. The cerebral blood flow measurements were repeated after lateralized ischemia was induced by occluding one middle cerebral artery and the ipsilateral carotid artery. Ischemia was confirmed by cerebral blood flow measurements and electroencephalograph changes in these anesthetized animals.

In non-ischemic brain, pulsatile perfusion increased cerebral blood flow 19% over that measured during nonpulsatile perfusion. The reduced flow seen with nonpulsatile perfusion never fell into ischemic ranges (i.e., below 25 cc/100 g/min.) in normal brain tissue. However, in brain rendered ischemic by occlusion of conductance vessels, pulsatile perfusion increased cerebral blood flow 55% over nonpulsatile perfusion, presumably by recruiting collaterals more effectively.

This study suggests important physiologic benefits from pulsatile perfusion, especially to patients on cardiopulmonary bypass with cerebrovascular insufficiency.

Introduction

The significance of the pulse has been debated for many years. It was not until William Harvey discovered the pulmonary and systemic circulation that the nature of the pulse was more clearly understood. With the introduction of cardiopulmonary bypass in the early 1950s, there has been a renewed interest in the importance of pulsatile blood flow. Despite many studies that have looked at the effect of nonpulsatile and pulsatile blood flow on the vital organs, the controversy continues. The brain is one of the vital organs of interest to those studying nonpulsatile and pulsatile blood flows. The effect of pulsatile flow on cerebral metabolism is not clearly understood, but evidence suggests that some pulsation of the blood is necessary for optimal cerebral protection. The purpose of this study was to examine the effect of pulsatile blood flow on regional cerebral blood flow in the ischemic and non-ischemic brain.

Materials and Methods

Nine dogs weighing 15 to 22 kilograms were anesthetized with Pentobarbital (20 mg/kg), paralyzed with pancuronium (0.1 mg/kg) and then intubated and ventilated with 100% O2. The scalp and temporalis muscles were stripped from the skull, electroencephalograph electrodes were implanted into the exposed skull according to a 12-lead pediatric electroencephalograph (EEG) montage, and four 90% platinum/10% iridium electrodes were implanted into the cerebral cortex for cerebral blood flow (CBF) measurements. An arterial pressure monitoring catheter was introduced into the femoral artery to record blood pressure. Cardiopulmonary bypass (right atrial-femoral artery) was initiated at 100 cc/kg/min. flow (Figure 1). Local cerebral blood flow, by the hydrogen clearance technique was performed during nonpulsatile and pulsatile perfusion. Mean arterial blood pressure (MABP), cardiopulmonary bypass (CBP) blood flow, and heart rate (HR) were kept constant. Hematocrit was followed closely, and arterial pH, pCO2 and PO2 were maintained normal at 37°C.

The right hemisphere was made ischemic by applying aneurysm clips to the right middle cerebral artery (MCA) and the right internal carotid artery (ICA) through a subtemporal approach.

Regions of the brain were classified as ischemic or non-ischemic according to the decrease in local cerebral blood flow measurements following middle cerebral artery-internal carotid artery occlusion. Ischemic
regions were defined as those areas in which the post-occlusion local cerebral blood flow was less than 50% of the pre-occlusion values. Local cerebral blood flow values were determined from the hydrogen clearance curve using the standard clearance blood flow technique.

EEG monitoring (12-lead montage) following the occlusion of the middle cerebral artery and the internal carotid artery provided further evidence of cerebral ischemia. Using computerized mapping of EEG, a shift from fast frequency alpha to slow frequency delta was seen following vessel occlusion.

Surgical Procedures: Cardiopulmonary Bypass

Following induction of anesthesia, a right thoracotomy was performed between the fifth and sixth ribs. The superior vena cava (SVC) and the inferior vena cava (IVC) were isolated and encircled with umbilical tapes. The azygos vein was also isolated. The animal was heparinized with 300 units/kg, and the CPB circuit was primed with heparinized canine blood.

A 34 F cannula was placed in the inferior vena cava through a right atrial incision and a second 34 F cannula was passed into the superior vena cava through an incision in the azygos vein. The cannulae were secured in place with umbilical tapes. The femoral artery was cannulated with a 14 F cannula. The aorta was then cross-clamped, excluding the coronary and pulmonary circulation. A Cobe Stockert roller pump and a Cobe Optiflow 11 were used to provide CPB at 100 cc/kg/min. flow. The oxygenator was supplied with 100% O₂, and 10% H₂ gas was added to the oxygenator for cerebral blood flow measurements.

Maximum pulsation was achieved using the Cobe Stockert pulsatile roller pump and the pulse pressure was recorded from the arterial pressure line. Nonpulsatile flow required some system modification, because of a 10 mm Hg pulse pressure persisting in the continuous flow mode of the roller pump. Three partially air-filled arterial filters were placed in series proximal to the femoral inflow. These structures acted as capacitors dampening the pulse oscillation to less than 3 mm Hg.

Production of Focal Ischemia

Acute cerebral ischemia was produced by occlusion of both the right middle cerebral artery and the intracranial portion of the right internal carotid artery with aneurysm clips. This classic model of hemispheric ischemia in the canine model requires resection of the temporalis muscle and a craniectomy through the alisphenoid. The frontal lobe was gently elevated under microscopic control, exposing the vessels of interest. The aneurysm clips were placed on the proximal middle cerebral artery and on the internal carotid artery distal to the posterior communicating artery. Vessel occlusion was confirmed visually as well as by the predicted drops in the cerebral blood flow of the middle cerebral artery distributions.

Results

Once the animal was placed on normothermic CPB at 100 cc/kg/min., the animal was alternatively perfused with nonpulsatile and pulsatile flows, during which cerebral blood flow determinations were made. Using the arterial filters partially filled with air, the blood pressure tracings had a pulse pressure of less than 3 mm of mercury (nonpulsatile). Pulsatile flow was produced so that the ejection phase was 40% of the cardiac cycle. Beats per minute were constant at 100/minute, producing a mean pulse pressure of 39 ± 11 mm Hg during perfusion in the non-ischemic animal and 36 ± 7 mm Hg in the ischemic animal.

The hemodynamic changes during pulsatile and nonpulsatile perfusion before middle cerebral artery and internal carotid artery occlusions are listed in Table 1. The mean arterial blood pressure increased only slightly during changes from nonpulsatile to pulsatile perfusion; 71 ± 16 to 72 ± 16 mm Hg in the non-ischemic dogs and 76 ± 16 to 77 ± 14 mm Hg in the ischemic dogs. CPB blood flow decreased insignificantly from 1.7 ± .3 l/min. during nonpulsatile perfusion to 1.6 ± .3 l/min. during pulsatile perfusion in the non-ischemic dog, and from 1.6 ± .3 to 1.5 ± .3 l/min. in the ischemic dog. Hematocrit, arterial blood gas parameters, and pulse rate did not change significantly during changes from nonpulsatile to pulsatile perfusion.
Effect of Nonpulsatile and Pulsatile Flow on Local Cerebral Blood Flow

Ischemic areas of the brain were defined as those areas of the brain demonstrating a 50% decrease in local cerebral blood flow following middle cerebral artery-internal carotid artery occlusion. In the non-ischemic model, there was a significant difference in local cerebral blood flow between nonpulsatile and pulsatile perfusion. When the perfusion changed from nonpulsatile (pulse pressure less than 3 mm Hg) to pulsatile flow (pulse pressure 39 ± 11 mm Hg), local cerebral blood flow increased 16%, from 32 ± 10 to 38 ± 11 cc/100 gm/min. (p < 0.01). In the ischemic areas of the brain, a more profound effect was seen. Local cerebral blood flow increased 55% from 11 ± 15 cc/100 gm/min. to 17 ± 7 cc/100 gm/min. (p < 0.01) during pulsatile perfusion (Figure 2).

Discussion

The importance of delivering pulsatile flow, rather than continuous flow during extracorporeal circulation has not been completely established. However, the evidence suggests that pulsatile flow in the aorta and large arteries generates a more appropriate blood flow through most organs than does a nonpulsatile wave form, and that better organ function results. In the kidneys, pulsatile perfusion better preserved renal function, and decreased blood pooling. In cardiac studies pulsatile perfusion better preserved subendocardial coronary flow and myocardial metabolism in the fibrillating heart during CPB. Effects of pulsatile perfusion have also been demonstrated in a small number of cerebral studies. Sanderson reported dif-

### Table 1
Mean values for the hemodynamic parameters of dogs during pulsatile and nonpulsatile perfusion

<table>
<thead>
<tr>
<th></th>
<th>Nonischemic Dogs</th>
<th>Ischemic Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Maximum Pulsatile Perfusion</td>
<td>Nonpulsatile Perfusion</td>
</tr>
<tr>
<td>Mean Art. Pressure (mm Hg)</td>
<td>71±/-16</td>
<td>72±/-16</td>
</tr>
<tr>
<td>Pulse Rate</td>
<td>99±/-11</td>
<td>96±/-9</td>
</tr>
<tr>
<td>Bypass Output (L/min)</td>
<td>1.7±/-0.3</td>
<td>1.6±/-0.3</td>
</tr>
<tr>
<td>Pulse Pressure (mm Hg)</td>
<td>39±/-11</td>
<td>&lt;4</td>
</tr>
<tr>
<td>Arterial pCO₂ (mm Hg)</td>
<td>28±/-9</td>
<td>29±/-7</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>30±/-5</td>
<td>30±/-6</td>
</tr>
</tbody>
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Figure 2: Mean cerebral blood flow in dogs during nonpulsatile and pulsatile perfusion in the non-ischemic and ischemic models.
fuse early ischemic changes in the brains of dogs undergoing nonpulsatile CPB. These changes were not present in animals undergoing pulsatile perfusion. Matsumoto found evidence that blood flow in the cerebral microcirculation was better (less capillary collapse and sludging) in animals undergoing pulsatile perfusion than in a group of animals undergoing nonpulsatile perfusion.

In this study using a canine stroke model, local cerebral blood flow increased 16% (p < 0.01) in the non-ischemic brain and increased 55% (p < 0.01) in the ischemic brain when perfusion changed from nonpulsatile to pulsatile flow. This data shows the effect of pulsatile flow was more pronounced in the ischemic brain.

Although the difference between nonpulsatile and pulsatile perfusion may not be critically important for short periods of time in patients with normal cerebral circulation, it may be crucial to those patients with compromised cerebral blood flow during cardiopulmonary bypass for any length of time. It has been well established that there is a high incidence of carotid disease in cardiac patients. Therefore, in these patients undergoing cardiopulmonary bypass, pulsatile perfusion may prove to be very important.

Questions from the Audience

Question—Brad Smith: Do you have p values for that. Were they statistically significant differences, and what were the levels?

Answer: It was less than 0.01.

Question—Tom Frasier: I wonder if you could just elaborate for us exactly how you determine cerebral blood flow. You said something about hydrogen clearance. I'm not familiar with that.

Answer: It was just using the hydrogen clearance technique, which is a “wash out.” Just a hydrogen “wash out.”