II-1. Pathophysiology

Increased Brain Tissue Oxygenation During Arteriovenous Malformation Resection

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Abstract

The purpose of this study was to determine if baseline oxygen pressure (PO2), carbon dioxide pressure (PCO2), and pH in brain tissue adjacent to an arteriovenous malformation (AVM) is different from measures in control patients. In addition, PO2, PCO2, and pH changes were measured during the course of AVM resection. Two groups were studied. Group 1 (n=8) were non-ischemic patients scheduled for cerebral aneurysm clipping. Group 2 (n=13) were patients undergoing neurosurgery for AVM resection. Following craniotomy, the dura was retracted and a PO2, PCO2, pH sensor inserted into non-ischemic brain tissue in Group 1. In Group 2, the sensor was inserted into tissue adjacent to the AVM. Following equilibration, tissue gases and pH were measured during steady state anesthetic conditions in Group 1 and during AVM resection in Group 2. The results show that under baseline conditions before the start of surgery, tissue PO2 was decreased in AVM compared to control patients but PCO2 and pH were not changed. During AVM resection, PO2 increased, PCO2 decreased, and pH increased compared to baseline measures. These parameters did not change in control patients over a similar time period. The results suggest that chronic cerebrovascular adaptation occur in AVM patients with decreased tissue perfusion pressure as an adjustment for decreased oxygen delivery. During AVM resection, this adaptation produces a hyperemic environment with relative tissue hyperoxia, hypocapnia, and alkalosis which is not corrected by the end of surgery.

Key words: arteriovenous malformation, brain oxygen, CO2, pH, ischemia, hyperemia

Introduction

Arteriovenous malformations (AVMs) may decrease tissue perfusion pressure and produce vasomotor paralysis and ischemia.6,13) During surgical resection of the AVM, restoration of normal tissue perfusion increases cerebral blood flow (CBF)20,21) and may produce hyperperfusion complications due to perfusion pressure breakthrough.2,10) However, baseline CBF is not different in AVM patients compared to surgical controls and cerebrovascular carbon dioxide (CO2) reactivity and autoregulation are intact.20,21) This suggests that cerebrovascular regulation is present before and after AVM surgery and does not support a vasoparalysis mechanism mediating the pathological events which occur after AVM resection.

Although CBF may not be significantly altered by decreases in arterial feeding pressure, local perfusion may be affected. Increased capillary exchange may occur in order to optimize tissue oxygenation, CO2 clearance, and tissue pH.7,14) After AVM resection, these adaptive changes may produce tissue hyperperfusion and relative hyperoxia when perfusion pressure is normalized at a time when CBF is not markedly increased and autoregulation is intact. This is consistent with a report that jugular bulb oxygen saturation may be elevated after AVM resection and the risk of hyperemic complications increased when saturation was above 80%.10) The purpose of this study was to determine whether brain tissue oxygen pressure (PO2), CO2 pressure (PCO2), and pH measures before and after AVM resection are consistent with hypoperfusion and hyperperfusion, respectively.

Materials and Methods

These studies were approved by the University of Illinois Institutional Review Board for Clinical Research and informed consent was received. Two groups were tested. Patients in Group 1 (n=8) served as controls for the study. A craniotomy and neurosurgery were performed in these patients for cerebral aneurysm clipping. Before surgery, none of these patients bled, had clinical symptoms of ische-
All patients were anesthetized with 3–5 mg/kg thiopental and 10–15 µg/kg fentanyl. Tracheal intubation was facilitated with 0.1 mg/kg vecuronium and the lungs were ventilated with 0.5–1.5% isoflurane and oxygen in room air (fractional inspired oxygen = 0.4). Esophageal temperature was measured and allowed to decrease to approximately 35°C. Arterial PCO₂ was maintained between 30 and 35 mmHg. Monitoring included mean radial arterial pressure (MAP) measured by a Marquette Electronics Tramscope (Milwaukee, Wisc., U.S.A.), and end tidal isoflurane and PCO₂ measured by a Datex Ultima (Helsinki, Finland).

**Tissue PO₂, PCO₂, and pH:** Following the craniotomy, the anesthetic regimen was maintained constant for the remainder of the study. In patients in Group 1, recording was terminated if the steady state anesthetic conditions were altered or temporary brain artery clipping was produced. In patients in Group 2, data were recorded throughout the surgical procedure. In all patients, after the dura was retracted, a Paratrend 7 PO₂, PCO₂, pH, and temperature probe (Biomedical Sensor, Malvern, Penn., U.S.A.) was inserted vertically into a gyrus of cortex tissue 2–3 cm from the AVM in a region with a common vascular supply to the AVM. The probe is designed for intravascular blood gas monitoring. It is supplied as a sterile, disposable device comprised of two modified optical fibers for the measurements of PCO₂ and pH, a miniaturized Clark electrode for PO₂ measurement and a thermocouple for the determination of temperature. The outer surface of the sensor has a covalently bonded heparin coating. The sensing elements are located within the final 4 cm of the probe, which is 0.5 mm in diameter. The void between the sensors is filled with acrylamide gel containing phenol red. Changes in hydrogen ion concentration produce color changes in phenol red, which can be detected by the pH fiber optic element. The CO₂ sensor includes an ion impermeable barrier which excludes the movement of hydrogen ions but allows the movement of CO₂. Inside the barrier, CO₂ alters the local pH, producing a color change in phenol red which is detected by the CO₂ fiber optic elements. The Clark electrode maintains a constant voltage and measures the current produced by the reduction of oxygen at the cathode. The length of the anode (1 cm) and cathode (3 mm) allows an average measurement of PO₂ over a 1 cm length of tissue. The PO₂, PCO₂, and pH measures were corrected for local temperature to 37°C.

The sensor was packaged with a tonometer containing buffer solution which serves as a calibrating medium. The sensor was calibrated with three precision gases supplied with the monitor before insertion into the patient. The gases are: 1 = 2% CO₂, 15% O₂, balance N₂; 2 = 5% CO₂, 15% O₂, balance N₂; 3 = 10% CO₂, 15% O₂, balance N₂. Each gas is bubbled into the calibrating solution for 10 minutes. The oxygen calibration curve (0 to 120 mmHg) is constructed using an electrical zero and the 15% O₂ gas, assuming linear properties of the electrode. The CO₂ and pH calibration curves are constructed within the range of 10–80 mmHg and 6.80–7.80, respectively using the three CO₂ gas concentrations, 2% = 14 mmHg (pH = 7.83), 5% = 36 mmHg (pH = 7.43), 10% = 71 mmHg (pH = 7.13). The range and 95% confidence limits for each sensor have been determined in vitro testing: O₂, range 0–120 mmHg, 95% confidence limits = +1 mmHg; CO₂, range = 10–80 mmHg, 95% confidence limits = +3 mmHg; pH, range = 6.80–7.80, 95% confidence limits = +0.03. The 0% to 90% response time for each sensor is: O₂ = 70 sec, CO₂ = 143 sec, pH = 78 sec.

For insertion, the outer non-sterile introducer system was covered with a sterile sheath. The sterile sensor was then extended from the end of the system and visually inserted into cortex tissue of interest during the surgery. In AVM patients, the tissue sensor was inserted into tissue adjacent to the AVM. In control patients, sensor measurements were in non-ischemic tissue. The Paratrend sensor was inserted 4 cm into cortex tissue in order to ensure that all sensing elements were in brain tissue. The tissue area was covered by a sterile towel to avoid light contamination of the fiber optic elements. An RS-232 connection in the back of the monitor supplied PO₂, PCO₂, pH, and temperature measures continuously. All monitored data, including MAP, anesthetic gases, tissue gases, and blood flow were collected continuously and averaged every 10 sec.

**CBF:** In one patient, an AVM with a single draining vein was identified. In this patient we measured AVM blood flow continuously during surgery using a Transonics flow probe (Transonics Systems, Ithaca, N.Y., U.S.A.). The flow probe was placed around the vein following its surgical isolation. A Paratrend 7 sensor was inserted adjacent to the AVM and a Vasamedics laser Doppler flow probe (St Paul, Minn., U.S.A.) was placed on the cortex surface in.
the vicinity of the Paratrend sensor. The Doppler measures blood flow within 1–2 mm of the cortex surface by combining the measurement of blood cell volume and velocity within that region. The perfusion units have been proposed to be of ml·100 g⁻¹·min⁻¹. AVM and tissue blood flow were measured continuously with tissue PO₂, PCO₂, and pH during resection of the AVM.

Statistics: Differences in mean values between the two groups were analyzed by unpaired t-test. Differences from the start to the end of surgery were analyzed using paired t-tests. If the data distribution failed the underlying assumptions for normality, equal variance, and outlying and influential points for parametric testing, then non-parametric analyses using Kruskal Wallis or Wilcoxon tests were performed.

Results

The changes in physiological variables from the start to the end of the procedures were also monitored. MAP, brain temperature, and arterial blood gases were not different between control and AVM patients and these variables did not change over the experimental period. In patients undergoing AVM resection, tissue PO₂ was significantly lower under baseline conditions compared to control patients but PCO₂ and pH were not different (Fig. 1). At the end of AVM resection, tissue PO₂ was significantly increased, PCO₂ decreased, and pH increased compared to baseline levels. In control patients, tissue variables did not change during the steady state surgical period. An example of the changes in tissue PO₂, PCO₂, and pH during AVM resection is shown in Fig. 2. Twenty minutes after recording was initiated, there was a 140 mmHg increase in tissue PO₂. This was accompanied by a decrease in tissue PCO₂ and an increase in pH. During this interval, there was no change in MAP or ventilation.

In a second AVM patient a single vein was determined to be draining the entire AVM. A Transonics flow probe was placed on this vein and a laser Doppler probe placed on the cortex surface in the vicinity of the Paratrend sensor. AVM flow decreased steadily throughout the AVM resection (Fig. 3). Large increases in tissue blood flow were seen during the course of AVM resection. These increases appeared to be related to increases in tissue PO₂, particularly in the beginning of AVM resection. At the end of surgery, AVM flow had decreased to zero, tissue blood flow had increased 500%, and PO₂ increased 350%.

Discussion

These results show that under baseline anesthetic conditions, brain tissue PO₂ decreased in the regional adjacent to the AVM. This is consistent with reports that low resistance flow through the AVM produces a lower arterial feeding pressure in surrounding tissue which can produce hypoxia. At the same time, we did not observe a significant difference in baseline tissue PCO₂ or pH between control and AVM patients. This suggests that tissue CO₂ clearance was normal and metabolic acidosis was not present. In contrast, ischemic patients have tissue hypoxia, hypercapnia, and acidosis. We suggest that the baseline measures made in AVM patients here represents an increase in capillary exchange during chronically reduced tissue perfusion.
Fig. 2 Tissue oxygen pressure (PO₂), carbon dioxide pressure (PCO₂), and pH during arteriovenous malformation resection. Approximately 20 minutes after the start of surgery there was a marked increase in PO₂ which was related in time to a decrease in PCO₂ and an increase in pH.

Under baseline conditions, we observed a PO₂ of 32 mmHg in brain tissue of non-ischemic aneurysm patients. This is generally consistent with other reports. Using a Paratrend sensor, Zauner et al. reported a normal PO₂ in cat cortex of 42 mmHg and Hoffman et al. reported non-ischemic tissue PO₂ of 37 mmHg in patients. Using a multiwire surface PO₂ electrode on rabbit cortex, Murr et al. reported a range of median PO₂ range of 32-39 mmHg during fentanyl anesthesia. Using a similar system in patients, Assad et al. reported median PO₂ in the range of 33-36 mmHg in normal tissue. Meixenberg et al. used a Clark electrode to measure PO₂ on the cortex surface in patients and found an average value of 48 mmHg. Measuring interstitial PO₂ in head-injured patients using a Clark type electrode, van Santbrink et al. reported average values of 16 mmHg after trauma, which increased to 35 mmHg 24 hours later. These data are consistent with theoretical determinations that PO₂ values <20 mmHg may be indicative of inadequate tissue oxygenation. Similarly, tissue PCO₂ >60 mmHg and pH <7.0 is seen in ischemic patients.

Hyperemic complications have been reported after AVM resection, including brain swelling and hemorrhage. It is hypothesized that chronic reduction of cerebral perfusion pressure may induce a state of vasomotor paralysis which attenuates the ability to constrict to a suddenly increase in perfusion pressure. Consistent with this, studies measuring CBF before and after AVM resection have consistently shown a small but significant increase in tissue flow following surgery. However, baseline
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CBF was not different from controls and vascular CO₂ reactivity and pressure autoregulation were normal. In addition, the incidence of normal perfusion pressure breakthrough is apparently infrequent. This does not support the theory that perfusion pressure breakthrough produces marked hyperemia after AVM resection.

It is possible that the cerebral vascular tissue associated with an AVM maintains the ability to autoregulate during a decrease in perfusion pressure by decreasing pre-capillary resistance and enhancing capillary perfusion. This would enhance the viability of tissue in a low perfusion environment, allowing maximum oxygenation and CO₂ clearance. This is consistent with positron emission tomography studies in AVM patients which show that cerebral blood volume is increased, suggesting local dilation. When perfusion pressure is suddenly returned to normal, an enhanced blood-tissue interface could produce hyperoxia, hypocapnia, and alkalosis. This would be consistent with symptoms of occlusive hyperemia following AVM resection and reports that apparent hyperemic complications are most apparent when jugular bulb oxygen saturation is elevated above 80%. However, there is little evidence that capillary recruitment occurs under normal physiological conditions. Changes in brain tissue blood flow usually occur by an increase in velocity rather than an increase in capillary perfusion.

There are potential problems with the methods used here which need to be evaluated. The Paratrend 7 sensor has been validated for measurement of arterial blood gases and the principles of measurement should be valid for tissue extracellular fluid. However, the sensor (4 cm long, 0.5 mm in diameter) will produce some local tissue injury by its insertion which may affect baseline measurements. In control patients without ischemia we found that tissue PO₂, PCO₂, and pH measurements equilibrate within 30 minutes of probe insertion and remain stable for 2 hours during steady state surgical conditions. This is consistent with other reports and suggests that the baseline measurements of PO₂, PCO₂, and pH are valid and stable throughout the course of this study. The PO₂, PCO₂, and pH sensors are located along the final 4 cm of the Paratrend probe and would therefore be measuring each parameter from a different region. However, the construction of the Clark electrode provides an average PO₂ measurement over approximately 1 cm of the probe. Also, the ease of diffusion of CO₂ provides a small CO₂ gradient throughout brain tissue. This suggests that the measurement of each sensor should not be markedly disassociated with respect to the region being measured. This is consistent with our finding that PO₂, PCO₂, and pH changes occur simultaneously during the AVM resection.

The fact that the sensing elements of the Paratrend 7 are distributed along the final 4 cm of this probe suggest that our local tissue measurements may be measuring different tissue regions. This may be a problem if local tissue perfusion changes occur independently of surrounding tissue. However, AVM associated decreases in tissue perfusion pressure affects a clinically significant amount of tissue surrounding the AVM. This agrees with our finding that PO₂ was consistently decreased in all AVM patients. In addition, AVM resection produced changes in PO₂, PCO₂, and pH which were temporally related and consistent with an increase in tissue perfusion. This supports the conclusion that the measures of tissue PO₂, PCO₂, and pH reflect a relatively homogeneous tissue.

The majority of the patients tested here received 1-2 embolization procedures with these measurements. It is possible that embolization affected the results of our study by attenuating AVM blood flow. However, since the AVM still provided a high flow shunt of CBF in all cases, we assume that the hemodynamic characteristics of the AVM were intact. The changes in tissue PO₂, PCO₂, and pH during AVM resection would be consistent with this hypothesis.

In conclusion, under baseline conditions, PO₂ is decreased while PCO₂ and pH are normal in tissue adjacent to an AVM. During AVM resection, PO₂ and pH increased above control levels while PCO₂ decreased and the increases in PO₂ are associated with transient increases in laser Doppler flow.

References

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