Hyperoxia

To THE EDITOR: We read with great interest the article by Diringer and colleagues (Diringer MN, Aiyagari V, Zazulia AR, Videen TO, Powe WJ: Effect of hyperoxia on cerebral metabolic rate for oxygen using positron emission tomography in patients with acute severe head injury. J Neurosurg 106:526–529, April, 2007).

Abstract

Object. Recent observations indicate that traumatic brain injury (TBI) may be associated with mitochondrial dysfunction. This, along with growing use of brain tissue PO2 monitors, has led to considerable interest in the potential use of ventilation with 100% oxygen to treat patients who have suffered a TBI. To date, the impact of normobaric hyperoxia has only been evaluated using indirect measures of its impact on brain metabolism. To determine if normobaric hyperoxia improves brain oxygen metabolism following acute TBI, the authors directly measured the cerebral metabolic rate for oxygen (CMRO2) with positron emission tomography before and after ventilation with 100% oxygen.

Methods. Baseline measurements of arterial and jugular venous blood gases, mean arterial blood pressure, intracranial pressure, cerebral blood flow (CBF), cerebral blood volume, oxygen extraction fraction, and CMRO2 were made at baseline while the patients underwent ventilation with a fraction of inspired oxygen (FiO2) of 0.3 to 0.5. The FiO2 was then increased to 1.0, and 1 hour later all measurements were repeated.

Five patients were studied a mean of 17.9 ± 5.8 hours (range 12–23 hours) after trauma. The median admission Glasgow Coma Scale score was 7 (range 3–9). During ventilation with 100% oxygen, there was a marked rise in PaO2 (from 117 ± 31 to 371 ± 99 mm Hg, p < 0.0001) and a small rise in arterial oxygen content (12.7 ± 4.0 to 13.3 ± 4.6 vol %, p = 0.03). There were no significant changes in systemic hemodynamic or other blood gas measurements. At the baseline evaluation, bimemispheric CBF was 39 ± 12 ml/100 g/min and bimemispheric CMRO2 was 1.9 ± 0.6 ml/100 g/min. During hyperoxia there was no significant change in either of these measurements. (Values are given as the mean ± standard deviation throughout.)

Conclusions. Normobaric hyperoxia did not improve brain oxygen metabolism. In the absence of outcome data from clinical trials, these preliminary data do not support the use of 100% oxygen in patients with acute TBI, although larger confirmatory studies are needed.

Diringer and colleagues have used sophisticated 15O-labeled oxygen positron emission tomography (PET) to assess the metabolic effect of 1 hour of an inspired concentration of 100% O2 at normobaric conditions on severe TBI. The results in the five patients studied showed no improvement in brain oxygen metabolism.

We would like to make several comments and observations regarding this paper and the ongoing dialogue as to the role of hyperoxia in the treatment of patients with severe TBI. First, the authors are to be commended for performing this relatively difficult but very sophisticated multimodality 15O PET imaging study of oxidative metabolism. This type of imaging has the advantage of providing a comprehensive metabolic “picture” of the whole brain as well as of regional areas.

In our view, there needs to be a clear distinction between the potential of hyperbaric hyperoxia compared with normobaric hyperoxia in the treatment of severe TBI. In the introduction, the authors state, “In one series in which the impact of hyperbaric hyperoxia (100% oxygen at 1.5 atm) on cerebral metabolism was studied, investigators found that in the 15% of patients with reduced CBF, there was a modest improvement in global CMRO2 1 and 6 hours after hyperbaric oxygenation.” A closer reading of our paper, however, shows that patients with “normal” CBF also consistently showed improved CMRO2 1 hour after hyperbaric oxygenation (HBO) treatment. Thus, 62% of all patients studied showed an improvement in CMRO2 1 hour after HBO treatment. Only those patients with “raised” CBF did not show significant improvement in CMRO2 after 1 hour. It should be noted that all patient groups showed significant reductions in cerebrospinal fluid lactate levels 1- and 6-hours post-HBO treatment.

The timing of the posttreatment PET imaging is somewhat problematic. For example, in a lateral fluid-percussion injury in rats, mitochondrial function remained depressed immediately after 1 hour of HBO treatment at 1.5 atm. At 3 hours post-HBO treatment, however, during which time the animal received 100% O2 at normobaric pressures, mitochondrial function had recovered to a level similar to that of sham-injured animals. It is also clear from our own work, as well as that of Menzel and colleagues, that brain tissue PO2 increases in a progressive fashion over the first several hours of treatment with normobaric hyperoxia. If the hypothesis is that hyperoxia improves the subsequent ability to use delivered O2, then it may be that the optimal metabolic effect occurs posttreatment.

Our own ongoing prospective clinical trial comparing the effect of hyperbaric hyperoxia to normobaric hyperoxia, as well as work in injured animals, strongly suggests that HBO treatment has a greater beneficial effect. Using the rat model of lateral fluid-percussion injury, Daughtery and associates have documented that HBO produces brain tissue PO2 levels 10 times greater than those induced by normobaric 30% oxygen (30 mm Hg compared with 300 mm Hg, respectively) and three times greater than those generated by normobaric 100% O2 (100 mm Hg compared with 300 mm Hg, respectively). We have demonstrated the same differential brain tissue PO2 levels in humans. It is important to note that HBO at 1.5 atm increases the amount of dissolved O2 in the plasma from 0.3 ml/dl (in air) to 3.2 ml/dl, which is on the order of 10 times more.

Given the fact that there are diffusion barriers to oxygen delivery to brain tissue, the brain tissue PO2 levels achieved may be critical to mitochondrial function. Hyperbaric O2 greatly increases the oxygen diffusion gradient from the lungs to blood to brain tissue. Nonhemoglobin O2 transport may be more significant than previously believed. If, as it appears, the presence of O2 induces the mitochondria to begin to function, brain tissue PO2 levels may be critical. This finding could explain the more robust effect of HBO in the model of lateral fluid-percussion injury to the brain compared with normobaric 100% O2.
Suprapetrosal Craniotomy


Abstract

**Object.** The primary aim of this study was to establish standard sites for bur holes that maintain constant anatomical relationships with the skull base and neural structures and can serve as the basal aspect of supratentorial temporocerebral craniotomies.

**Methods.** To determine cranial–cerebral relationships, the authors created bur holes in 16 adult cadaveric skulls. Three bur holes were made on each side of the skulls (32 cerebral hemispheres). The authors then introduced plastic catheters through the bur holes to evaluate pertinent cranial and neural landmarks.

The first bur hole, located anterior to the auricle of the ear, appeared to have a particular anatomical relationship with the anterior aspect of the petrous portion of the temporal bone and the most anterior aspect of the midbrain. The second bur hole, whose base was located 1 cm above the interface of the parietomastoid and squamous sutures, had a particular relationship with the posterior border of the petrous portion of the temporal bone and with the posterior aspect of the midbrain. The third bur hole, whose base was located 1 cm above the asterion, was mostly supratentorial and particularly related to the preoccipital notch.

**Conclusions.** The preauricular bur hole and the bur hole whose base was located 1 cm above the interface of the parietomastoid and squamous sutures delimit anteriorly and posteriorly the external projection of the petrous bone and the midbrain. The middle fossa floor is located anterior to the site of the preauricular bur hole, and the superior surface of the tentorium is posterior to the bur hole located above the parietomastoid–squamous suture interface. Together with the bur hole whose base is located above the asterion, these bur holes can be considered standards for temporocerebral craniotomies.

I wish to bring to the reader’s attention the strikingly similar work that my colleagues and I published about a decade ago that was unfortunately overlooked in the authors’ bibliography.1,2

In our work, the focus was to reliably locate the underlying transverse sinus, transverse–sigmoid junction, posterior fossa dura, and supratentorial dura above the transverse sinus, based on external landmarks as a guide to postero-lateral skull base approaches. We reliably determined the level of the distal transverse sinus to be located beneath a line of projection between the root of the zygomatic process and the inion. As Ribas and Rodrigues also found,
the junction of the squamosal and parietomastoid sutures marks the anterior border of the upper curve of the sigmoid sinus and therefore serves as a useful landmark for opening over the supratentorial dura above the sinuses.

Ribas and Rodrigues reconfirmed the generally unreliable position of the asterion with respect to the underlying transverse sinus. We performed our study on 100 skulls and found that the asterion was found directly over the transverse or sigmoid sinuses in more than 60% of specimens. Ribas and Rodrigues found that placing their bur hole 1 cm above the asterion resulted in 43% of the bur holes lying over or partially over the transverse sinus. The results of our study would have predicted this finding because the asterion was located within 1 cm below the transverse sinus in 32% of skulls on the right and 25% on the left in our specimens.

The relationship between external landmarks and underlying structures is an important issue that should be particularly emphasized during the training phase of neurosurgery. I commend the authors on expanding this type of work to apply to other approaches.

J. DIAZ DAY, M.D.
The University of Texas Health Science Center at San Antonio
San Antonio, Texas

References


RESPONSE: We thank Dr. Diaz Day for his comments about our recent article and about his own contributions to the same subject, and for the opportunity to express regret for not citing his previous studies in our paper.

In 1985, during a short fellowship with Prof. Rhoton, I studied the anatomical relationships between the cranial sutures and the transverse and sigmoid sinuses with the aim of establishing starting points and limits for different posterior fossa approaches, using the asterion and the parietomastoid suture/squamous suture meeting point as the main landmarks. This study was subsequently completed at the University of São Paulo Medical School where it was presented as my doctoral thesis in 1991, initially and partially published as a book chapter in Prof. Samii’s book in 1994, and in 2005 was more completely published in the journal Neurosurgical Focus, which noted your 1996 publication. Regarding the results of both studies, it is noteworthy and gratifying that our findings pertinent to the topography, particularly of the asterion and the junction of the transverse and sigmoid sinuses, were very similar to yours. Our recent article about the suprapetrosal craniotomy published in the journal Neurosurgery was complementary to our previously noted work, and the data in this paper were obtained in a more extensive investigation that also included the study of sulcal key points in cranial–cerebral relationships.

Please excuse us for the omission of these two important papers published in such a significant journal, which would definitely have enriched the discussion of our article. (DOI: 10.3171/JNS-07/10/0899)

GUILLERME CARVALHAL RIBAS, M.D.
University of São Paulo Medical School
São Paulo, Brazil

Platelets and Stents


Abstract

Object. The aim of this study was to report 1-year angiographic follow-up results and midterm clinical outcomes in patients with symptomatic intracranial atherosclerotic lesions treated with stent placement.

Methods. Ten patients with ischemic symptoms referable to stenotic intracranial atherosclerotic arteries, with greater than 60% stenosis, underwent elective surgery in which a primary stent was placed. All patients underwent pretreatment (≥ 1 week) combination oral antiplatelet (clopidogrel and aspirin) therapy and long-term (6-month) combination oral antiplatelet (clopidogrel and aspirin) therapy after stents were placed. The procedure involved selecting stents of the same size as the diameter of the target vessel and slowly inflating the balloon to its nominal pressure. One-year angiographic and midterm clinical follow-up data were obtained.

The stents were successfully placed in all patients without any perioperative complication. The mean preoperative stenosis rate of 81% decreased to 4% after the stent was placed. Nine patients who underwent follow-up angiography (one patient refused) at a mean of 12.3 months (range 10–19 months) had no changes in luminal diameter compared with the immediate postoperative luminal diameter. Luminal narrowing increased, from 15 to 38%, in one case in which there was comparatively greater residual stenosis (15%). No patient suffered new ischemic symptoms during a mean clinical follow-up period of 21 months (range 12–36 months).

Conclusions. Elective stent surgery can provide good angio-
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graphic and clinical midterm outcomes in patients with symptomatic intracranial atherosclerotic stenosis, and the procedure is associated with a high degree of technical success. Reassessment of these promising results is needed in a larger population and in a randomized prospective comparison study.

In this study, all patients underwent pretreatment (≥ 1 week) with combination oral antiplatelet (clopidogrel and aspirin) therapy and long-term (6-month) combination oral antiplatelet (clopidogrel and aspirin) therapy after stents were placed. The use of dual antiplatelet therapy in neurosurgical patients is clearly of increasing interest to neurosurgeons.

In February 2007, the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, and American College of Surgeons issued new recommendations regarding the optimal duration of dual antiplatelet therapy in patients with coronary artery stents. The guidelines also discussed the increased risk of early discontinuation of dual antiplatelet therapy. Although at first glance, these new guidelines may appear to have little direct effect on the perioperative course of patients presenting for neurosurgical procedures, a closer inspection reveals broader implications.

The new guidelines specifically recommend postponing elective surgery for 1 year in patients with a new drug-eluting stent (DES), and if surgery cannot be deferred, strongly considering the continuation of aspirin during the perioperative period. Before we discuss the possible ramifications of these new guidelines, it is relevant to briefly review how they came into place.

Whereas simple balloon angioplasty was an important advance in medical technology that allowed for the reversal of coronary artery occlusion in patients with coronary artery disease, long-term patency rates were low secondary to neointimal hyperplasia and vessel restenosis. Coronary stents, which hold the inner wall of the artery in its newly compressed position, prevent elastic recoil; in addition, the vessel’s extracellular matrix is protected from exposure and the incidence of restenosis is reduced. The first coronary stents employed clinically were bare metal stents (BMS). Although the use of BMS improved long-term patency compared with balloon angioplasty, a significant number of patients continued to develop neointimal hyperplasia and restenosis. Restenosis rates approached 30% in certain high-risk groups such as patients with diabetes mellitus and those with extended coronary artery lesions or small coronary vessels that required treatment. In 2002, the Food and Drug Administration approved the use of DESs in the US. These new stents slowly release antineoplastic agents, paclitaxel or sirolimus, which reduce the proliferation of smooth muscles cells and the incidence of restenosis. A potential side effect of the use of the antineoplastic agents used in DES is a delay in the endothelialization of the stent.

Until a stent undergoes endothelialization, there is a significant risk of stent thrombosis, which is associated with a catastrophic myocardial infarction. The incidence of stent thrombosis and early vessel closure after coronary stent implantation was markedly reduced by the adoption of clopidogrel antiplatelet therapy and improved techniques for stent deployment. The widespread adoption of dual antiplatelet therapy (aspirin and clopidogrel) has further reduced the risk of subacute thrombosis after BMS implantation to the range of 0.5 to 1.9%. As the antineoplastic agents in DES likely delay endothelialization, a longer time course of antiplatelet therapy is required to prevent stent thrombosis.

The BASKET-LATE (Basil Stent Kosten-Effektivitats Trial–Late Thrombotic Events) examined the incidence of clinical events after cessation of clopidogrel therapy. The authors observed that clopidogrel discontinuation (between 7 and 18 months) was associated with increases in the incidence of cardiac death or myocardial infarction at 18 months (4.9% after DES compared with 1.3% after BMS implantation).1 More recently, Eisenstein and associates reported that clopidogrel use predicted lower rates of death at 6, 12, and perhaps up to 24 months after DES placement but not after BMS placement, suggesting endothelialization after DES may take longer than initially proposed. The results of these trials and others have initiated the formation of these new guidelines.

The risk of discontinuing dual antiplatelet therapy for surgery has also been associated with an unacceptably high incidence of perioperative cardiac morbidity and death. Vicenzi and coworkers enrolled 103 patients in a prospective, observational multicenter study using predefined heparin therapy and antiplatelet medication in patients undergoing noncardiac procedures after placement of a coronary artery stent. All patients received coronary artery stents within 1 year before noncardiac surgery. Clopidogrel and aspirin drug therapy was not, or only briefly, interrupted and heparin was administered to all patients to prevent thrombosis. Despite appropriate care, 44.7% of the patients suffered perioperative complications, and 4.9% died. All but two adverse events were cardiac in nature. The risk of suffering an event was 2.11-fold greater in patients with recent stents (<35 days before surgery) as compared with percutaneous cardiac intervention more than 90 days before surgery. The results of this study strongly suggested that, if possible, surgery should be avoided in any patient who has recently undergone coronary artery stent placement and that the risks of cardiac complications and thrombosis exceed the risks of bleeding.

Obviously, excessive bleeding of any kind can have disastrous ramifications for neurosurgical patients. Thus, these new guidelines may have much greater impact in neurosurgery than in perhaps any other surgical subspecialty. Although it may be very easy to delay surgery for more than 1 year after coronary artery stent placement in some patients undergoing completely elective procedures and the decision to prematurely discontinue dual antiplatelet therapy in a truly urgent or emergent situation is simple, many clinical situations in neurosurgery are more complex and will require careful consideration. If a patient with a coronary artery stent is asked to discontinue dual antiplatelet therapy within 1 year of stent placement, we must be certain that the risks of bleeding and not delaying surgery exceed the very real risk of a major adverse cardiac event. This is an important issue and raises many additional questions, such as: if clopidogrel is discontinued, can a patient be safely maintained on aspirin in the perioperative period, as the guidelines encourage? How soon after surgery can antiplatelet therapy be restarted? Should the answers to these questions change when considering cranial compared with spinal procedures?

Unfortunately, there is little direct evidence to guide decision making in this matter. Coordination between cardi-
ologists, neurosurgeons, and neuroanesthesiologists will be required to optimize the perioperative care of every patient. There is no doubt that it would be beneficial to neurosurgical organizations and members to educate their constituent surgeons regarding these important concerns about our patients with coronary artery disease undergoing surgical procedures and to address them in a proactive fashion.

EDWARD C. NEMERGUT, M.D.
MARK E. SHAFFREY, M.D.
University of Virginia Health System
Charlottesville, Virginia

References


RESPONSE: We appreciate the thoughtful and rewarding comments by Drs. Nemergut and Shaffrey. With recent advances in stent technology, placement of an intracranial stent is increasingly being used for the treatment of intracranial atherosclerotic arterial stenosis in the neurosurgical field, despite the lack of a unique stent designed for use in the tortuous intracranial vasculature. Scant data are available and few large studies have been conducted on intracranial stent placement, however, because of the short history of this procedure, compared with coronary angiographic studies. Unfortunately, on this account, there is a paucity of reports regarding how to treat a patient after placement of an intracranial arterial stent. Additionally, we cannot draw any definitive conclusion about optimal periprocedural antiplatelet management from our study, which was not a large randomized clinical trial and was not designed to answer this question. The issue Drs. Nemergut and Shaffrey raise is a subject clinicians working in the neuroendovascular field need to address. As they point out, bleeding of any kind in patients undergoing brain surgery can cause greater catastrophic consequences than in any other surgical subspecialty. Thus, neurosurgeons, as well as neuroendovascular surgeons, will be required to make great efforts to define the optimal duration of dual antiplatelet therapy in patients treated using intracranial stents by conducting large randomized clinical trials, as they have been conducted in coronary angiographic studies. We are grateful to Drs. Nemergut and Shaffrey for highlighting this important issue and look forward to further discussion on this matter. (DOI: 10.3171/JNS-07/10/0900)

CHANG-YOUNG LEE, M.D.
MAN-BIN YIM, M.D., PH.D.
Keimyung University School of Medicine
Daegu, South Korea