

Impact of Intraoperative Ventilation with High Oxygen Content to Reduce the Incidence and Extent of Postoperative Pneumocephalus in Patients Undergoing Craniotomies

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Introduction and Background

Pneumocephalus, defined as an accumulation of intracranial air, is a common finding after neurosurgical procedures. However, pneumocephalus is not associated with any symptoms in the vast majority of cases [1,2]. Nevertheless, concomitant symptoms including, but not limited to, cephalalgia, nausea and vomiting, and changes in neurological status, may be present [2]. If untreated, increased intracranial pressure (ICP) as a result of pneumocephalus could become a life-threatening clinical situation.

In addition to neurosurgery, other possible causes of pneumocephalus include craniofacial trauma, infections, and skull base lesions. Although infrequent, spontaneous pneumocephalus has been described as well [2].

By Reasoner et al. 66% of CT scans performed after intracranial surgery showed that 5-10% of the volume was occupied by intracranial air entrapped during intervention and identifiable in all the postoperative scans [2]. Commonly, the re-absorption process of this air will take between 2 and 3 weeks. Perioperative factors associated with the onset of pneumocephalus may be classified as surgery related (e.g. positioning of the head, length of the surgery), anesthesia-related (e.g. use of N₂O, mannitol, hyperventilation, neuraxial anesthesia), and patient-related (e.g. hydrocephalus or lumbar drainage of cerebrospinal fluid) [1].

Several approaches have been attempted to prevent postoperative pneumocephalus. These measures include modification in surgical technique, irrigation with saline at the stage of dura closure, among others.

Beppu et al. (2006) conducted a prospective study enrolling 40 patients undergoing intraventricular neurosurgical procedures, and analyzed the efficacy of intradural continuous insufflation of CO₂ (2 liters/min) during the surgery. The volume of entrapped intracranial air evaluated by a postoperative CT was significantly lower in patients treated with CO₂ insufflation [1]. The authors considered that the effectiveness of the therapy was due to the differences between CO₂ gravity and absorption rate in comparison with room air. Therefore, the study concluded that replacing intracranial air using intraoperative CO₂ insufflation, may improve postoperative outcomes by shortening the time needed for air re-absorption.

Gore et al. (2008) studied the effects of mask inhalation with 100% oxygen on the extent of post craniotomy pneumocephalus on a series

of 11 patients [3]. After postoperative day 1, pneumocephalus was reduced in 65% in the interventional group in contrast to 31% in the control group. Similarly to the results showed by Beppu et al., the authors concluded that the time required for postoperative intracranial air re-absorption was significantly decreased in the interventional group (p=0.009) [3].

Aoki N and Sakai T (1993) published a prospective trial carried out in 36 patients with diagnosis of subdural hematoma. Through a percutaneous tapping procedure, 23 hematomas were treated by replacing the hematoma area with oxygen (O₂) [4]. Additionally, patients underwent postoperative CT scans in order to assess and compare the procedure outcomes with a control group. The authors reported a favorable outcome with a fast absorption of oxygen; the preservation of the inner hematoma membrane allowed no leak into the subdural space and subarachnoid space [4].

Branger et al. noticed a faster bubble absorption by using different concentrations of oxygen in hyperbaric simulation models (at 2.8 atmosphere absolute ATA) [5]. Therefore, the reduction of time required for bubble absorption is proportional to the concentration of oxygen in the air mixture [5]. Additionally, decreasing N₂ concentration at a specified pressure will also promote similar results [5]. Maximal acceleration of the bubble diffusion is obtained when the inert gas concentration in the air mixture is zero [5].

Theoretically, similar processes regulate air bubble absorption and residual post craniotomy entrapped air. The aforementioned studies concluded that air replacement with a gas characterized by superior absorptive properties (CO₂ or O₂), should be considered an effective method for treating the postoperative pneumocephalus. While CO₂ may be used during surgery to insufflate the operative field, inhalation of oxygen is an easy and simple method applied for treatment and prevention of postoperative pneumocephalus.

Normo and hyperbaric oxygen use have been described for pneumocephalus and air embolism therapy; However there are no published reports indicating oxygen administration as a preventive measure for these conditions. [3,5].

Hypothesis

Intraoperative ventilation with pure O₂ instead of the commonly used ratio 1:1 will have a positive prophylactic effect on occurrence and extent of postoperative pneumocephalus in neurosurgical patients.

Objectives

Primary Objective

To compare the rate of occurrence and volume of postoperative pneumocephalus in patients undergoing surgical procedures to treat hemispheric or posterior cranial fossa tumors receiving intraoperative ventilation with pure oxygen during the last stage of surgery (hemostasis and wound closure) versus a conventional 1:1 oxygen/air mixture.

Secondary Objectives

To compare the incidence and volume of postoperative pneumocephalus in patients undergoing surgery in sitting and supine positions.

To compare postoperative neurological outcomes and intensive care unit length of stay among patients with posterior cranial fossa tumors, supratentorial tumors, and patients undergoing transsphenoidal/endoscopic procedures.

The secondary aim assessments will be descriptive only, and there will be no intent to recruit sufficient number of patients to reach high power of the study. Such descriptive data will help us to better understand the role of various factors in development of pneumocephalus and to design more targeted prospective trials in the future.

Material and Methods

Study design

A prospective, randomized, single-blinded study intending to compare the rate of occurrence and volume of postoperative pneumocephalus in patients receiving intraoperative ventilation with pure oxygen during the last stage of surgery (hemostasis and wound closure) versus a conventional 1:1 oxygen/air mixture.

Study population

Adult patients (>18 years) at Ohio State University Wexner Medical Center, with an American Society of Anesthesiologists (ASA) physical status of II-IV. Furthermore, the study will be conducted in the following patient populations:

Adult patients with supra and infratentorial tumors (astrocytomas and glioblastoma multiforme, etc.) undergoing open procedures in the sitting, prone, lateral, park bench, and other positions.

Adult patients undergoing endoscopic tumor resection in the sitting, prone, lateral, park bench and other positions. This group will include patients undergoing intradural transnasal transsphenoidal approach to sellar and parasellar structures.

Sample size and statistical analysis

After obtaining written informed consent from patients who met the inclusion criteria without any exclusion criteria, a hundred sixty (160) subjects will be randomized for the study.

Appropriate statistical tests will be applied to assess the extent and incidence of postoperative pneumocephalus for the intervention group when compared to the control group. The sample size is determined based on the data variance reported in existing publications on the topic with similar design.

With a sample size of 80 patients per group, we expect to have 80% power to detect a 20% decrease in volume in the intervention group at an alpha of 0.05 assuming the mean pneumocephalus volume in the control group is 87 ml with a standard deviation of 40.

The study is designed as a prospective single-blinded trial. The intervention required per study protocol consists of 100% oxygen administration during the last period of anesthesia. This short intervention is considered harmless and, in fact, is being applied as a routine measure in some cases. No procedure related adverse events are expected to be reported during the study.

Inclusion and exclusion criteria

Inclusion criteria

Neurosurgical patients >18 years, males and females, undergoing hemispheric or posterior cranial fossa tumor resections, and consenting to the study

American Society of Anesthesiologists (ASA) physical status of II-IV

Exclusion criteria

Severe cardio-respiratory disorders

Bleeding disorders

History of previous brain and skull surgery requiring cranial bone reconstruction

History of severe traumatic brain injury (TBI)

Significant preoperative cerebral edema causing decrease in consciousness

Randomization

The study will be planned and conducted according to all the required institutional and state regulations related to clinical research. One hundred and sixty patients will be randomly distributed (random table) into 2 groups: control and interventional.

Control Group (A): Will receive controlled ventilation throughout the surgery with a conventional 1:1 oxygen/air gas mixture.

Interventional Group (B): Will receive controlled ventilation with a conventional 1:1 oxygen/air gas mixture from the beginning of the surgery and during the tumor removal phase. However, patients in group B will be switched to controlled ventilation with 100% oxygen once the tumor resection is completed and hemostasis started. They will inhale 100% oxygen until extubation.

Study procedures

As a standard of care, during the early postoperative period, both groups will receive supplemental oxygen via nasal cannula. The patients will undergo postoperative CT within 1-6 hours post-surgery as part of standard care. CT scans will be assessed and interpreted by a blinded radiologist in order to diagnose the frequency and the extent of postoperative pneumocephalus (quantification).

TeraRecon Intuition software version 4.4.11.265.8092 will be used, retrieving the CT scan data from the system and loading it into the software program. All CT data will maintain a 1 mm slice increment. The air in the skull will be identified and circled using a region of interest (ROI) tool. The area defined for measurements to be applied in

this study is within the skull in any space occupied by brain. This would exclude any air trapped between the bone from graft placement or between the skin and the skull. Once all the visually identified areas of “air” are circled and then selected within the skull, a Hounsfield unit (HU) threshold tool will be used to remove any excluded tissue. The setting of 150 HU or less will be applied, and the selected areas will be presented in 2D and 3D. Only the areas identified within the ROI will account for the 3D image. The volume will be calculated in cm³ using the software presented by clicking the “volume” measurement tool.

Considering similarity of the groups and randomization, it is expected that the duration of the last part of surgery and the lapsing time from the end of surgery to postoperative CT acquisition will be the same for the control and treatment groups. The following data will be considered for intergroup analysis and selection bias exclusion: demographics (age, sex, weight, BMI), oxygen inhalation time, the period between end of surgery and the CT scan completion. The occurrence of adverse events and neurological status will be assessed before the CT scan.

Also, we intend to perform subgroup analysis of patients undergoing conventional craniotomy versus minimally invasive techniques, as well as patients with posterior cranial fossa tumors versus middle and anterior cranial fossa pathology. As mentioned before, these appraisals will be descriptive only, and no attempts will be made to reach statistical significance and high power of the study.

The early postoperative adverse events and neurological status will be assessed in the recovery room. For each patient, the clinical neurological status will be compared with the baseline evaluation.

Adverse Events and Safety Assessments

Based on our standard procedures (SOP), the existence of adverse events (AE) and serious adverse events (SAE) will be recorded during

the 72-hour post-operative period. The relationship to the study intervention and the severity of an adverse event will be determined by the Principal Investigator and recorded accordingly.

Withdrawal Criteria from the Study

The study participants have the right to withdraw from the clinical trial at any time for any reason. The principal investigator also has the right to remove a subject from the study because of an adverse event, protocol violation or unreliable behavior (The Declaration of Helsinki).

References

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