Introduction

Olfactory disorders may be characterized as conductive or sensorineural in nature. Conductive impairments arise from interference with the access of odors to olfactory receptors and are commonly observed in patients with obstructive nasal or sinus disease. Sensorineural disorders arise from damage to the olfactory receptors or to the olfactory pathways and may occur as the result of many causes including upper respiratory infections, head trauma, brain surgery and cerebrovascular accidents. Whereas conductive impairments may improve with treatment of their underlying cause, there is little that can be done to cure or treat sensorineural losses effectively. In particular, recovery from head trauma can take many months or even years, and is often incomplete, even after apparent physical recovery.

The olfactory nerve's axons must traverse small perforations in the cribriform plate of the ethmoid bone prior to dissemination on the surface of the olfactory bulb. They are therefore vulnerable to tearing or severing as a result of coup contra coup forces that may be associated with head injury. Retraction of the brain occurring during neurosurgical procedures may similarly injure olfactory nerves where they

Citation


Abstract

Objectives: To determine the effect of transorbital craniotomy through a suprabrow approach on olfaction and thereby develop a human model to evaluate the efficacy of medical therapy in the treatment of sensorineural anosmia.

Methods: Retrospective chart review of all patients undergoing transorbital craniotomy through a suprabrow approach at a major medical center from April, 1997 through June, 2000. The effect of surgery on olfactory function was investigated via a phone questionnaire that assessed the sense of smell prior to and following craniotomy. Objective evaluation of olfactory function was evaluated via forced-choice threshold to phenylethyl alcohol and/or odor identification testing.

Results: 28 patients completed retrospective phone interviews. Subjectively, 18 patients noted no change in their sense of smell postoperatively, 7 noted a decreased sense of smell and 3 noted improvement. 18 of 28 patients underwent objective testing, which did not agree with patient self-assessment in 4 of 18 instances. 8 of 18 patients tested anosmic and one of 18 tested unilaterally anosmic. No recovery of function was noted at follow-up of at least 8 months after surgery. Postoperative anosmia was more likely in midline or bilateral lesions (p= 0.050).

Conclusions: Currently, no human model for the evaluation of therapeutic interventions in the treatment of sensorineural olfactory loss exists. Hyposmia and anosmia are common sequelae of transorbital craniotomy through a suprabrow approach. Such surgical procedures present opportunities for randomized, placebo-controlled human subjects trials studying the effect of medical therapy on the recovery of olfactory function.

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INTRODUCTION

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The olfactory nerve's axons must traverse small perforations in the cribriform plate of the ethmoid bone prior to dissemination on the surface of the olfactory bulb. They are therefore vulnerable to tearing or severing as a result of coup contra coup forces that may be associated with head injury. Retraction of the brain occurring during neurosurgical procedures may similarly injure olfactory nerves where they...
traverse the cribriform plate. In an analogous model, complete transection of the olfactory nerves in mice results in a transient, total loss of smell. Recovery sufficient to carry out a simple buried food-finding task occurs within about three weeks following the nerve transection procedure in mice. However, mice given a single dose of supplemental Vitamin A (all-trans retinoic acid) 24 hours post-operatively accomplish this food finding task within one week following the nerve transection. This finding suggests that further study into the therapeutic administration of Vitamin A for treatment of olfactory dysfunction due to physical trauma is warranted.

Unfortunately, no human model for the evaluation of therapeutic interventions in the treatment of sensorineural olfactory loss currently exists. Recruitment of human subjects with viral and trauma-induced anosmia poses logistical difficulties in the timing of treatment and the documentation of pre-morbid olfactory function. Although brain retraction is minimized during transorbital craniotomy through a suprabrow approach, many patients undergoing these procedures complain of smell loss on either one or both sides of their nose. The present study is undertaken to investigate the potential for transorbital craniotomy procedures to serve as opportunities for randomized, placebo-controlled human subjects trials studying the effect of medical therapy on the recovery of olfactory function.

MATERIALS AND METHODS

After institutional review board approval was obtained, the medical records of 28 patients who underwent transorbital craniotomy through a suprabrow approach at the Neurosensory Institute of Wills Eye Hospital and the Thomas Jefferson University from April, 1997 through June, 2000 were retrospectively reviewed. No medical records were excluded from review. Technical details of this surgical technique have been previously described.

Patients were contacted by phone and asked to respond to a questionnaire (Figure 1). Following completion of the questionnaire, patients were asked to come to the Monell-Jefferson Taste & Smell Clinic [MJC] for olfactory testing or to complete the University of Pennsylvania Smell Identification Test [UPSIT] at home.

The psychophysical methods used to assess olfactory function at MJC have been described in detail previously. Olfactory thresholds are obtained for phenylethyl alcohol [PEA], an odor stimulus that elicits little or no nasal trigeminal response at any concentration. Additionally, a 40-item, 4 alternative forced choice odor identification task is performed. Patients who were unable to travel to MJC for testing, completed an UPSIT at home. The UPSIT is a 40-item 4-alternative, forced choice identification test using microencapsulated odors and is commercially available (Sensonics, Inc., Haddonfield, NJ). Patients were instructed to occlude one side of the nose and perform 20 items. They then occluded the other side of the nose and completed the remaining twenty items. The UPSIT and its 20 item fragment have been shown to have very high internal consistency reliability. Patients unable to smell PEA and/or exhibiting random performance (less than 10 correct unilateral responses or less than 20 combined responses) on odor identification testing were judged to be anosmic.

RESULTS

28 patients including 11 males and 17 females underwent transorbital craniotomy via a suprabrow approach. Age ranged from 35 to 78 (mean=57). Seventeen patients underwent surgery for meningiomas, (9 frontal lobe, 5 sphenoid wing, 2 parasellar, 1 olfactory groove). Other diagnoses included craniopharyngioma (4), pituitary adenoma (3), schwannoma (2), cavernous sinus hemangioma (1), and foreign body (1). Tumors were judged to be bilateral, midline or unilateral based upon preoperative magnetic resonance imaging and intraoperative findings.

Each patient's subjective assessment of his or her ability to smell before and after surgery is plotted in Figure Two. Cumulative data for each patient's perceived change in the sense of smell is shown in Figure Three. Follow-up ranged from 8 to 65 months (mean=25 months) No patients reported anosmia preoperatively. Three patients noted improvement in their sense of smell postoperatively. Of these patients, the patient who felt his smell improved from very good to excellent underwent objective testing indicating intact olfactory function. The patients who felt their sense of smell improved from poor to excellent and from average to excellent did not wish to undergo objective testing.

Eighteen patients noted no change in their sense of smell following their surgery. Of the two patients who felt their average sense of smell remained average, one underwent testing which revealed anosmia. Of the 11 patients who felt their very good sense of smell remained very good, nine underwent objective testing. Seven patients evidenced intact smell function, one tested anosmic and the remaining patient tested unilaterally anosmic. Of the 5 patients who felt their
excellent sense of smell remained excellent postoperatively, one returned for olfactory testing and was found to be anosmic.

Seven patients noted a decrease in their sense of smell postoperatively. One patient with a poor preoperative sense of smell and three patients with a very good preoperative sense of smell underwent testing which confirmed their impression of postoperative anosmia. 2 of 3 patients who felt their excellent sense of smell disappeared postoperatively underwent testing, which revealed anosmia. One patient declined testing.

Overall, six patients reported postoperative anosmia of which 5 tested anosmic and 1 declined testing. Three reported an average sense of smell of which 1 tested normal, 1 tested anosmic and 1 declined testing. 11 reported a very good sense of smell of which 7 tested normal, 1 tested anosmic, 1 tested unilaterally anosmic and 2 declined testing. Finally, eight patients reported an excellent postoperative sense of smell of which 1 tested normal, one of whom tested normal, one of whom tested anosmic and 6 of whom declined testing.

In view of the variability between objective and subjective test results, data analysis was carried out primarily on the 18 patients undergoing objective testing (Table I). 8 of 18 tested anosmic. 1 of 18 tested unilaterally anosmic. Postoperative anosmia was more likely in patients with midline lesions such as craniopharyngioma or pituitary adenoma. Preservation of smell was more likely in cases of unilateral lesions (p=0.050, Fisher exact test, two-tail). The patient's sex did not influence outcome (p=0.131, Fisher exact test (two-tail).

DISCUSSION

Patients undergoing transorbital craniotomy via the suprabrow approach typically have benign lesions such as meningiomas, craniopharyngiomas and pituitary adenomas (Table I). In our series, all of the patients undergoing surgery were able to participate in olfactory testing, although some patients declined testing. Unfortunately, because this study was performed retrospectively, objective pre-operative olfactory testing was not performed. Patients' subjective impressions of their olfactory function did not always agree with objective testing. Patient 15, who exhibited short-term memory loss, believed her postoperative sense of smell to be excellent, yet she could not smell PEA and failed odor identification testing. Patients 11 and 18 also tested anosmic despite believing their sense of smell to be intact. Finally, patient 10 was unaware of her unilateral anosmia. Future studies must include pre and post operative objective assessments of olfactory function.

The pathophysiologic explanations for anosmia and hyposmia occurring after neurosurgical procedures have not been completely delineated. Loss of olfaction may result from frontal lobe retraction with shearing of the olfactory axons as they traverse the cribriform plate, direct mechanical injury (i.e. retraction, compression or excision) to the olfactory axons or olfactory bulb, compromise of the vascular supply to the olfactory system or injury to the central olfactory pathways... Localized frontal subcranial approaches to the skullbase have been described which minimize frontal lobe retraction and conserve olfaction on the uninvolved side... The common factor in these patients appears to be unilateral disease at the anterior skull base permitting only partial resection of the ipsilateral olfactory nerves without compromise of the surgical result. Indeed, review of operative records in this series revealed olfactory loss to be more likely in cases involving bilateral or midline retraction of the brain (Table I: p=0.050).

The passage of time following surgery did not appear to improve the initial outcome. Only one patient, who declined testing, noted an improvement from an average sense of smell immediately after surgery to an excellent sense of smell at the time of his phone interview. On the other hand, patients 12 and 13 noted progressive postoperative deterioration in their olfactory function, and both tested anosmic. All remaining patients noted no difference in their sense of smell with the passage of time following surgery with follow-ups ranging from 8 to 65 months (mean=25 months).

CONCLUSION

Currently, no human model for the evaluation of therapeutic interventions in the treatment of sensorineural olfactory loss exists. Recruitment of human subjects with viral and trauma-induced anosmia poses logistical difficulties in the timing of treatment and the documentation of pre-morbid olfactory function. Patients undergoing transorbital craniotomy through a suprabrow approach typically have benign lesions and are able to participate in olfactory testing. Within this group of patients, those with bilateral or midline lesions...
commonly sustain perioperative insults resulting in anosmia. This type of surgery may therefore serve as a human model for the evaluation of therapeutic interventions in the treatment of sensorineural olfactory loss. Consequently, we have begun an IRB-approved randomized, placebo-controlled trial studying the effect of vitamin A on the recovery of olfactory function in patients undergoing trans orbital craniotomy through a suprabrow approach.

Figure 1
Figure 1: Olfaction Questionnaire

1. Prior to your neurosurgery; how would you have described your overall ability to smell?
   - None
   - Poor
   - Average
   - Very Good
   - Excellent

2. Was there a change in your ability to smell following your surgery?
   - No change
   - Diminished smell (Time Frame: 0 Immediate 0 Days 0 Weeks)
   - Right side only
   - Left side only
   - Both sides
   - Complete loss of smell (Time Frame: 0 Immediate 0 Days 0 Weeks)
   - Right side only
   - Left side only
   - Both sides
   - Distinctions in odor quality (Time Frame: 0 Immediate 0 Days 0 Weeks)
   - Right side only
   - Left side only
   - Both sides

3. Has there been any further change in your ability to smell since your surgery?
   - No change
   - Smell has improved but is not back to normal
   - Right side only
   - Left side only
   - Both sides
   - (Time Frame: 0 Immediate 0 Days 0 Weeks)
   - Smell has completely recovered
   - Right side only
   - Left side only
   - Both sides
   - Smell has gotten worse
   - Right side only
   - Left side only
   - Both sides
   - (Time Frame: 0 Immediate 0 Days 0 Weeks)

4. How would you currently describe your overall ability to smell?
   - None
   - Poor
   - Average
   - Very Good
   - Excellent

Figure 2
Figure 2: Patient's subjective assessment of his or her sense of smell (1 = anosmia, 5 = excellent sense of smell) preoperatively and at the time of their telephone interview postoperatively. N=28

Figure 3
Figure 3: Subjective Assessment of Change in Olfactory Function Following Transorbital Craniotomy

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