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ANAESTHESIA FOR ENDOSCOPIC ENDONASAL TRANSPHENOIDAL RESECTION OF PITUITARY ADENOMA: INITIAL EXPERIENCE OF A SINGLE NIGERIAN CENTER

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ABSTRACT

Introduction: **Endoscopic endonasal transsphenoidal surgery (EETSS) is an established technique for the resection of pituitary tumors and is well-domesticated in our center due to its numerous benefits. This study aimed to provide insights into the anaesthetic management of patients with pituitary tumors for EETSS, analyze the perioperative complications, and associations between demographic data, perioperative complications, intensive care unit (ICU) management, and outcomes.**

Methods: **This prospective descriptive study includes all patients who underwent EETSS for pituitary adenoma under general anaesthesia in a tertiary center. Data collected through a semi-structured proforma from patients and patient medical records included socio-demographic data, peri-operative complications, ICU management, and outcome.**

Results: **There was a total of 60 patients (Male: Female was 1:1), an age range between 18 to 76 years, and the mean age was 30.9 (± 12.8 years). Most patients (65%) presented with visual complaints. Hypertension (30%) was the most common intercurrent illness. The American Society of Anesthesiologists (ASA) physical status II and III were 56.7% and 43.3% respectively. Intraoperative complications were hypertension 30%, hypotension 5%, and bradycardia 15%. 30% (15) of the patients were admitted into the ICU and 13 (21.7%) of those admitted were ventilated. ICU length of stay was between 1-6 days. Overall mortality was 10%. Bivariate analysis revealed a significant association was observed between mortality and tumor size (p=0.046), ventilator use (p=0.05), and ICU admission (p=0.008).**

Conclusion: **The tumor size, postoperative complications that necessitated ICU admission, and ventilator use in the ICU significantly impact the overall perioperative outcome.**

Keywords: Transsphenoidal, Pituitary, Anaesthesia

INTRODUCTION

Pituitary adenomas are described as the third most common brain tumors constituting 10–15% of all intracranial tumours[1] They are classified as either clinically functioning pituitary adenomas such as prolactinomas, adrenocorticotropic hormone-secreting, growth hormone-secreting, or thyroid-stimulating hormone-secreting adenomas or clinically non-functioning pituitary adenomas causing pressure on adjacent structures, leading to vision field impairment, hypopituitarism and sometimes ophthalmoplegia.[2]

Surgical removal can be done endoscopically or by transcranial approach[3]. The endoscopic transsphenoidal approach for the resection of pituitary tumors dates to over 100 years ago and offers some advantages over the transcranial approach considering the direct approach to the pathology in the sellar/suprasellar region with no brain retraction under dynamic endoscopy, minimal blood loss, fewer complications, shorter hospital stays, better patient comfort and low mortality rate.[4]

However, endoscopic endonasal transsphenoidal (EETSS) pituitary surgery poses unique challenges for neuro-anesthetists in the peri-operative period. Preoperatively, airway management may be challenging in up to 4% of patients undergoing resection of the pituitary lesion, and retrospective data from the University of Virginia showed an increased risk of unexpectedly difficult airway in acromegalic patients at over 9%. They may have sleep apnea with an increased risk of perioperative airway compromise[5]. Medical diseases such as hypertension, diabetes, and

ischaemic heart disease a major causes of perioperative mortality.[6,7] Furthermore, the procedure causes intensive noxious stimuli at various stages of surgery which may result in difficulty maintaining intraoperative hemodynamic stability.[8]

Anaesthetic goals for EETSS include optimizing cerebral oxygenation, maintaining hemodynamic stability, providing conditions to facilitate surgical exposure, managing intraoperative complications, allowing for rapid smooth emergence, and assessing neurologic function.[9]

This study aimed to provide insights into the anaesthetic management of patients with pituitary tumors for EETSS in our environment, analyze the perioperative complications, and associations between demographic data, perioperative complications, intensive care unit (ICU) management, and outcomes.

MATERIALS & METHODS

This Retrospective cohort study was conducted at the University College Hospital, Ibadan, Nigeria, between January 2020 and December 2022. The study included all adults above 18 years of age who had endoscopic transsphenoidal pituitary surgery under general anaesthesia. Retrieved data contained the demographic characteristics of the patients as well as the clinical and anaesthetic data from the clinical notes and intra-operative anaesthesia charts. Data was collected with the aid of a semi-structured proforma drawing relevant information from the patient's medical records. Data collected were socio-demographic data, clinical parameters, perioperative complications, ICU admission, length of ICU stay, types of adenomas, and patient outcome. The outcome may be dead or alive.

Variables:

Age, sex, ASA, and intercurrent medical illness were the independent variables while the size of the tumor, complications, ICU admission, and outcome were the dependent variables.

Statistical Analysis:

Data was analyzed using IBM Statistical Package for Social Sciences for Windows version 23.0 (SPSS Inc. Chicago Illinois). Participants' socio-demographic and clinical characteristics were presented as frequencies and percentages, while categorical, discrete, and continuous variables were visually presented in tables as appropriate. The study's outcomes were considered as dependent variables while socio-demographic variables were considered as independent variables. Bivariate analysis using Chi-square was used to examine the association between each independent variable and clinical interventions and conditions. A p-value of <0.05 was considered statistically significant.

Anaesthesia technique

Preoperatively, the patients were reviewed by the consultant neuro- anaesthetist. History, physical examination, and review of investigations including laboratory, radiological (plain X-ray skull, CT scan of brain and MRI of brain), pituitary hormone analysis; preoperative visual field analysis and grouping and cross-matching of blood was done. The patients benefitted from multi-disciplinary team care, which included endocrinologists for full hormonal optimization and cardiologist review before the surgery. Thereafter, a detailed explanation of the surgical procedure, surgical approach, fitness to undergo surgery, airway assessment, and informed consent were taken. The need for nasal packs which may cause postoperative nasal obstruction necessitating mouth breathing postoperatively was also explained to the patients. Patients were fasted overnight as per anesthetic protocol in the hospital and premedicated with Tab Diazepam 5mg per oris at night and on the morning of the surgery.

On arrival into the neurosurgical operating suite, intravenous access was established for IV fluid (crystalloid) and drug administration; patients were premedicated with IV Dexamethasone $0.1mgkg^{-2}$ to reduce peri-lesional brain oedema, IV omeprazole 20mg and IV Ondansetrone $0.1mgkg^{-2}$ to reduce nausea and vomiting.

Routine monitoring included non-invasive arterial pressure, heart rate, respiratory rate, and oxygen saturation while some of our patients (28 patients) had invasive blood pressure monitoring. All patients had general anaesthesia with endotracheal intubation and were pre-oxygenated with 100% oxygen for 3 to 5 minutes, glycopyrrolate 0.1mg and IV fentanyl 100 micrograms were given in all cases before induction. Anaesthesia was induced with propofol 1-2mg/kg, and muscle relaxation for endotracheal intubation was facilitated with pancuronium 0.1mg/kg, on a few occasions that there was anticipated difficult intubation, suxamethonium was given, direct laryngoscopy with insertion of the appropriate size reinforced endotracheal tube was done afterward.

After confirmation of correct tube placement patients were mechanically ventilated; intermittent positive pressure ventilation with tidal volume 6-8ml/kg, respiratory rate adjusted to maintain an end-tidal carbon dioxide of 30-35mmHg. Anaesthesia was maintained with isoflurane 1% / 100% of oxygen/ pancuronium and morphine of 0.1mg/kg or total

intravenous anaesthesia of propofol at 150-200 mcg/kg/min plus 100% of oxygen/pancuronium depending on the intraoperative hemodynamics of the patients. After intubation, a pharyngeal pack was inserted under direct laryngoscopy to prevent the risk of aspiration and filling the stomach with blood and surgical site debris. Xylometazoline 0.05% nasal spray, topical lidocaine, and epinephrine mixture were sprayed into the mucosa surface of the nose to decongest the nasal mucosa to improve access and reduce bleeding.

Parameters monitored intraoperatively included blood pressure, heart rate, fluid intake, estimated blood loss, and anaesthetic agents used. Bradycardia is a heart rate < 50 beats/min, hypotension is an episode of a mean arterial blood pressure < 50mmHg, or hypertension is systolic > 160mmHg.

After the surgery, all anaesthetic agents were discontinued 100% of oxygen was administered and the residual neuromuscular blockade was reversed with IV atropine and neostigmine, the endotracheal tube was removed if patients were able to obey verbal commands and were breathing adequately they were transferred into the recovery room however if patients had clinical deterioration such as requiring continuous monitoring and respiratory or cardiovascular support or neurological deficit they were transferred to the intensive care unit.

Data analysis: Statistical analysis was conducted with IBM's Statistical Package for the Social Sciences (SPSS) version 23.

RESULTS

There were 60 patients. The male: female was 1:1 Other demographic characteristics as in Table 1. The main symptoms were headaches in 4 (6.7%) of patients and visual disturbances in 39(66.3%), while 17(28.3%) experienced both. Primary surgery was in 88.3% of patients, while 11.7% had redo surgery There was preoperative blood transfusion in 10% of patients, while 51% received transfusion intraoperatively. The

Table 1: Patient demographic data, clinical and post-operative characteristics

Demographic data	Frequency	Percentage (%)
Age group		
18-34	6	10.0
35-65	47	78.3
>65	7	11.7
Mean (SD) range years	30.9. ±12.8[24 to 76]	
Gender		
Male	30	50.0
Female	30	50.0
ASA Classification		
II	34	56.7
III	26	43.3
Intercurrent medical illness		
None	28	46.7
Hypertension	18	30.6
Hypertension/Diabetes	5	8.3
Diabetes	1	1.7
Hormonal imbalance	8	13.3
Size of pituitary tumor		
Macro	56	93.3
Micro	4	6.7
Preoperative blood transfusion	6	10
Intraoperative blood transfusion	31	52.7
Preoperative PCV Mean ± SD [range]	37.7±2.8 [31.2-45.0]	
EBL Mean ± SD [range]	706.6±428.8 [180.0 to 1900.0]	
Intra-operative complications		
Hypertension	18	30.6
Bradycardia	9	15.3
Hypotension	3	5.1
Tachycardia	1	1.7
Hypoglyceamia	1	1.7
ICU Admission	18	30
ICU admission (with ventilation)	5	8.5
ICU admission (without ventilation)	13	22.1
No ICU admission	42	71.4
Patient outcome		
Dead	6	10
Discharged	54	90.0

Table 2: Association of patient clinical characteristics and outcome

Sex	**Discharged N (%)**	**Dead N (%)**	**p-value**
Male	28(51.9)	2(33.3)	0.339
Female	26(48.1)	4(66.7)	
Size of tumor	**Discharged**	**Dead**	**p-value**
Micro	2(3.7)	2(33.3)	0.046
Macro	52(96.3)	4(66.7)	
Preoperative blood Transfused	**Discharged**	**Dead**	**p-value**
No	48(88.9)	6(100.0)	0.389
Yes	6(11.1)	0	
Intraoperative blood transfusion	**Discharged**	**Dead**	**p-value**
Transfused	28(51.9)	3(50.0)	0.931
Not transfused	26(48.1)	3(50.0)	
Intercurrent medical illness	**Discharged**	**Dead**	**p-value**
None	25(46.3)	3(50.0)	0.943
Hypertension	16(29.6)	2(33.3)	
Hypertension and diabetes	5(9.3)	0	
Diabetes	1(1.9)	0	
Others	7(13.0)	1(16.7)	
Intra complication	**Discharged**	**Dead**	**p-value**
presence	32(59.3)	3(50.0)	0.689
none	22(40.7)	3(50.0)	
Post complication	**Discharged**	**Dead**	**p-value**
None	33(61.1)	1(16.7)	0.037
Presence	21(38.9)	5(83.3)	
ICU admission	**Discharged**	**Dead**	
No	41(97.6)	1(2.4)	0.008
Yes	13(72.2)	5(27.8)	
Use of ventilation	**Discharged**	**Dead**	
No	52(94.5)	3(5.5)	0.005
Yes	2(40.0)	3(60.0)	
ASA			
2	34	3	
3	20	3	

intraoperative anesthesia complications were in 25 patients; About a third of the patients had Hypertension while only 1.7% had Tachycardia.

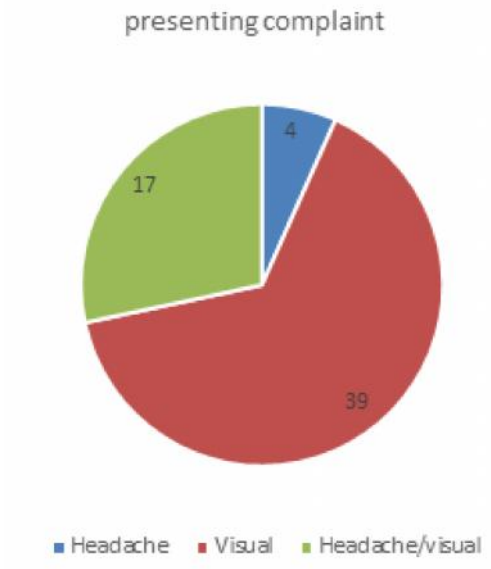

Figure 1: Presenting complaint.

The major postoperative complications were surgically related and included CSF leak (4 patients), headache (3 patients), meningitis (3 patients), personality changes (2 patients), pneumocephalus (2 patients), haematoma (2 patients), and diabetes insipidus (5 patients). However, 1 patient each had acute chest syndrome, Addison disease, seizures, and stroke.

Postoperatively, 30% of the patients were admitted into the ICU, of which 8.3% were ventilated. The length of ICU stay was between 1-6 days though, most of the patients spent only one day (38.9%). 90% of patients were discharged home postoperatively while 10% died. However, a significant association was observed between postoperative complications, and patients admitted into the ICU, ventilation, and patient outcomes.

Among patients with postoperative complications, 43.3% of deaths occurred. Additionally, ICU admission was correlated with outcomes, as 27.8% of ICU-admitted patients died. Among ventilated patients, 60%

resulted in mortality, indicating a significant correlation between ventilator use and outcomes.

Bivariate analysis revealed no significant associations between patient outcome and age, gender, PCV, surgery duration, anesthesia duration, estimated blood loss, gender, procedure type, blood transfusion, and intraoperative complications.

DISCUSSION

Endoscopic endonasal transsphenoidal surgery has progressively over time become the standard of care for the resection of both functioning and non-functioning pituitary adenomas of varying sizes due to the multiple advantages which include direct access to the tumor without brain retraction, minimal blood loss, shorter hospital stays, better patient comfort and low mortality rate.[4,6]

The endoscopic transsphenoidal pituitary tumor excision provides the anaesthetist with a multitude of unique challenges among those are the surgical approach, effects of hormone secreted by the pituitary gland, maintenance of hemodynamic stability to decrease bleeding, maintenance of a clear field by hypotensive anaesthesia and smooth emergence.

A thorough pre-anesthesia assessment is therefore mandatory as was done on all our patients. Hypertension, diabetes mellitus, hormonal derangement, and anaemia were some of the preoperative abnormalities noticed in our cohort of patients as in previous studies.[8,9] A multidisciplinary approach including inputs from the cardiologist and endocrinologist to optimize these abnormalities in the preoperative period is essential.

The mean age of patients in our study was 30.9 years with a male-to-female sex ratio of 1:1, these figures are lower compared with a higher mean age of 46.88±13.91 and 54.5% female preponderance in a study by Acar *et al.*[8]

The American Society of Anesthesiologists (ASA) grading score was used to assess the pre-operative risk and is believed to be an independent risk factor for perioperative mortality.[10] The majority of our patients were ASA 2, and although our study did not indicate any significant correlation between ASA score and outcome, likely because a those who had greater than ASA II essentially had comorbidities which predisposed them to a higher incidence of intraoperative complications, as reported also by Acar et al, but did not impact on the overall outcome.

Pre-operative anaemic is a recognized predictor of poor outcomes after surgery, and blood transfusion is more frequent among anaemic patients.[11] However, in our study, pre-operative blood transfusion was administered to a small fraction of our patients (10%), which may have impacted the overall favorable patient outcome. While it is true that no significant association was observed between the pre-operative blood transfusion and overall patient outcome, we cannot draw definite conclusions due to the limited representation of our sample size in the broader population. Additionally, perioperative transfusions have been associated with unfavorable impacts on surgical morbidity and mortality, potentially due to a combination of acute blood loss and adverse effects linked to transfusion products[11] in cancer surgeries generally However, our study's findings did not align with this narrative, as we did not identify a significant association between pre- or intraoperative blood transfusion and patient outcomes.

The anaesthetic technique used for the endoscopic transsphenoidal surgery in this study was general anaesthesia with endotracheal intubation. General anesthesia maintenance was with either total intravenous anaesthesia (TIVA) propofol or inhalational isoflurane.1 Although TIVA and inhalational anaesthetic have not been shown to greatly differ in the establishment of stable haemodynamic parameters, TIVA has been shown to significantly improve intraoperative visualization and decrease total blood loss in a study by Wormald *et al.*[12]

The rate of bradycardia, hypotension, and hypertension intraoperatively was 15%, 5%, and 30% respectively among patients in our study. Hypertension was noticed to be the most common intraoperative complication seen, although this did not have any significant correlation with mortality in this study. Cardiovascular responses in the form of hypertension and tachycardia are frequently encountered in many intracranial surgical procedures.[13] Hypertension in this study may be due to the severe nociceptive stimuli experienced by patients during submucosa adrenaline infiltration in the nose, nasal speculum insertion, and sphenoid and sellae dissection.[14] We treated this by increasing the depth of anaesthesia or increasing opioid administration, subsequently leading to hypotension and bradycardia. Controlled hypotension and bradycardia have been a standard for endoscopic sinus surgery to reduce bleeding and improve operative condition; bradycardia at 42.41%, hypotension at 17.64%, and bradycardia at 1.55% were recorded by Acar, *et al.*[8] though they attributed the high rate of hemodynamic instability during their study to the sensitivity of anaesthestic agents in the elderly.

Anesthesia and surgery durations both fell within the average range, with a mean score of 305.05 minutes and 352.23minutes respectively. Interestingly, despite that surgery and anesthesia duration, and the estimated blood loss, were slightly higher among the deceased patients, there was no clear indication of any significant correlation between these variables and mortality.

The postoperative care of transsphenoidal surgical patients is critical to good outcomes. The decision to transfer patients to ICU depends on the protocol of the hospital, operative pathology, medical condition of the patients, and the invasiveness of the procedure[15]. Our study showed that the majority of our patients were discharged to the post anaesthesia recovery room and a third of the patients were admitted into the intensive care unit where they spent between 1-6 days. Most patients were admitted into the ICU for intensive monitoring rather than intensive care, a study has advocated short stays in the recovery room or neurological ward or even same-day discharge in selected patients[15]. In our study, the patients were admitted into the ICU due to prolonged surgery, need for ventilation, and intraoperative events.

ICU admission and ventilation use significantly correlated with poor outcomes in this study. In the study by Chowdhury *et al.*[16], tracheal reintubation and prolonged ventilation resulted in pulmonary complications and attributed the indication for reintubation in neurosurgery to be due to neurological deterioration due to intracranial bleeding or haematoma which led to ventilatory support. In order of incidence Cerebrospinal fluid (CSF) leak, headache, hormonal problems, meningitis, seizures, fever, haematoma, and stroke are the postoperative complications observed in our study with an incidence rate of 43.3%.

The cerebrospinal fluid leak was the commonest complication in this study like the study by Chowdhury et al[16], they attributed this to patients with large tumor sizes requiring greater manipulation and a high incidence of CSF leak although another study by Shiney et al did not find any relationship between the size of the tumor and postoperative CSF leak[17].

Surgeries that last longer increase the risk of complications such as meningitis, extracranial infection, and pulmonary embolism during ETSS. In addition, Korinek et al[18]. observed a 70% increase in meningitis risk when neurological surgery lasted more than 4 hours, which is plausible given that in our study, the surgical duration among those with perioperative complications frequently exceeded this threshold.

CONCLUSION

The finding of this study underlines the safety of endoscopic transsphenoidal surgery in the management of pituitary adenomas in our environment. The shift towards this technique despite the large sizes of tumors has resulted in favorable outcomes for patients, with low postoperative complications and mortality. This study identified ICU admission and postoperative complications as factors influencing patient outcomes. However, it's important to consider that these outcomes are subject to multiple factors, including patient intercurrent illness, preoperative optimization, and surgical technique.

Limitation

A major limitation of our study is that we solely assessed patient outcomes in terms of mortality and survival, thus not capturing the complete scope of patient recovery, including aspects like visual acuity and other potential complications. This is however due to the scope of the paper which is mainly an emphasis on the anaesthesia technique, complications, and impact on mortality and survival. Our study is also constrained because it is a single-center study which can limit the generalizability of our findings, though there were multiple surgeons involved. Another limitation of this study was that there were missed data which accounted for the incompleteness of some information.

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