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Prevalence and risk factors of hemodynamic instability during endoscopic transsphenoidal pituitary surgery: a retrospective analysis

Endoskopik transsfenoidal hipofiz cerrahisi sırasında hemodinamik instabilite prevalansı ve risk faktörleri: retrospektif bir analiz

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ABSTRACT

Background: Intraoperative hemodynamic instability in patients undergoing endoscopic transsphenoidal pituitary surgery (ETSS) for pituitary adenoma may lead to significant complications. We aimed to investigate the prevalence of hemodynamic instability and its associated risk factors in these patients.

Material and Method: This retrospective study included patients who underwent ETSS at Ankara Numune Training and Research Hospital between 14 January 2010 and 20 March 2014. Intraoperatively occurring episodes of bradycardia, hypotension, and hypertension were recorded. Distribution of hemodynamic instability was determined based on age groups, ASA class, tumor type, and anesthesia method.

Results: A total of 323 patients met the study criteria. Mean age of the patients was 46.88 ± 13.91 years and 54.5% were female. Intraoperative bradycardia was detected in 137 patients (42.41%), hypotension in 57 patients (17.65%), and hypertension in five patients (1.55%). Hemodynamic instability occurred in all of the patients over the age of 51. Patients classified as ASA III were more likely to have hemodynamic instability than patients with ASA I and ASA II ($P<0.05$). All 18 patients who were transferred to intensive care unit were in the age group of 61 years and over. The rate of hemodynamic instability was higher in patients with non-functioning tumor compared to that in patients with functioning tumors.

Conclusion: The rate of hemodynamic instability during ETSS is higher in the elderly, ASA III class and non-functioning tumors. These patients need a carefully planned anesthetic management.

Keywords: Endoscopic transsphenoidal pituitary surgery, pituitary adenoma, anesthesia, hemodynamic instability

ÖZ

Amaç: Hipofiz adenomu için endoskopik transsfenoidal hipofiz cerrahisi geçiren hastalarda intraoperatif dönemde ortaya çıkan hemodinamik instabilite önemli komplikasyonlara yol açabilir. Bizim amacımız bu hastalarda hemodinamik instabilitenin prevalansını ve onunla ilişkili risk faktörlerini araştırmaktır.

Gereç ve Yöntem: Endoskopik transsfenoidal hipofiz cerrahisi geçiren hastalarda intraoperatif dönemde ortaya çıkan bradikardi, hipotansiyon ve hipertansiyon kaydedildi. Yaş grupları, ASA sınıfı, tümör tipi ve anestezi metoduna göre hemodinamik instabilite dağılımı belirlendi.

Bulgular: Toplam 323 hasta çalışma kriterlerini karşıladı. Ortalama yaş 46,88±13,91 ve %54,5'i kadın cinsiyette idi. Intraoperatif dönemde 137 hastada bradikardi (%42.41), 57 hastada hipotansiyon (%17,65) ve 5 hastada hipertansiyon (%1,55) tespit edildi, 51 yaşın üzerindeki hastaların tamamında hemodinamik instabilite görüldü. ASA III olarak sınıflandırılan hastalarda ASA I ve ASA II'ye göre daha fazla oranda hemodinamik instabilite görüldü ($p<0.05$). Postoperatif dönemde yoğun bakıma transport edilen 18 hastanın tamamı 61 yaş ve üzeri hasta grubunda idi. Non-functioning tümör olan hastalarda functioning tümöre sahip olanlara göre hemodinamik instabilite oranı daha yüksekti.

Sonuç: ETSS sırasında hemodinamik instabilite oranı yaşlılarda, ASA III sınıfında ve çalışmayan tümörlerde daha yüksektir. Bu hastalar dikkatle planlanmış bir anestezi yönetimine ihtiyaç duyar.

Anahtar Kelimeler: Endoskopik transsfenoidal hipofiz cerrahisi, hipofiz adenomu, anestezi, hemodinamik instabilite

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INTRODUCTION

Maintaining the heart rate and blood pressure within normal limits is very critical to provide an adequate tissue perfusion. Abnormal excursions of heart rate and blood pressure lead to the clinical condition called as hemodynamic instability. If perioperatively emerging hemodynamic instability is severe and long-lasting, it may cause significant complications such as myocardial ischemia, cerebrovascular events, and acute kidney injury (1-4). A number of factors trigger hemodynamic instability during ETSS performed for pituitary adenomas. Bradycardia and arterial blood pressure changes may occur via trigemino-cardiac reflex during transsphenoidal surgery. Trigemino-cardiac reflex results from stimulation of trigeminal nerve receptors in the nose, and trigeminal ganglion and its roots (5,6). This reflex was reported in 10% of patients undergoing transsphenoidal surgery for pituitary adenomas (7).

Patients scheduled for ETSS may have comorbidities such as diabetes mellitus, hypertension, coronary artery disease, cardiomyopathy, and hyperthyroidism, which contribute to perioperative hemodynamic instability. If a patient has a functioning pituitary adenoma, several symptoms exist due to hormone excess. For example, the prevalence of clinical hypertension is 50% in patients with acromegaly, and it resolves markedly after ETSS (8,9). Eighty percent of patients with Cushing's disease have hypertension. Thyrotropic adenoma may cause pituitary hyperthyroidism. Failure to normalize thyroid functions preoperative may lead to perioperative hemodynamic instability (10).

Advanced age may pose an important risk for perioperative hemodynamic instability. Elderly patients who underwent ETSS for nonfunctioning pituitary adenoma were reported to be more likely to have elevated blood pressure than that in their younger counterparts (11).

As performed in nasal region, ETSS elicits intense pain. Unless adequately deep anesthesia is established, severe pain leads to blood pressure elevation. Since it is very important to ensure and maintain an appropriate field of surgical vision, any blood pressure elevation that can increase bleeding should not be allowed. Nevertheless, a very deep anesthetic due to concern about the occurrence of pain and awareness causes bradycardia and hypotension. While the rate of tachycardia was high in patients who received sevoflurane through inhalation anesthesia, bradycardia was more common in patients who were administered propofol by total intravenous anesthesia (12). Another cause of hypotension in the perioperative period is hypovolemia (1).

There are limited number of large-scale clinical studies regarding hemodynamic alterations emerged during ETSS. This study aimed to investigate the prevalence of hemodynamic instability and its associated risk factors in patients who underwent ETSS for pituitary adenoma in a time-period of more than four years in a tertiary care hospital.

MATERIAL AND METHOD

The data of patients who underwent ETSS in our hospital were obtained from medical records. Their age, gender, ASA (American Society of Anesthesiologists class score), and accompanying diseases were recorded. Pituitary tumors were classified as functioning and nonfunctioning. Duration of the surgery, anesthesia methods, and muscle relaxants were recorded. Intraoperatively, bradycardia (heart rate<50 beat/min), hypotension (an episode of a mean arterial pressure of <50 mmHg) or hypertension (systolic pressure>160 mmHg) were identified (13,14). It was determined whether patients were transferred into the intensive care unit in the postoperative period.

All patients electively underwent a standard ETSS. The patients were in the supine position, and pituitary tumor was removed with a surgical microscope. Patients were fasted for at least 6 hours preoperatively per standard anesthesia protocol in our hospital. Premedication was performed with intramuscular midazolam. Intraoperative monitoring was performed through electrocardiogram, heart rate, pulse oximetry, end-tidal concentration of carbon dioxide, and continuous monitoring of arterial blood pressure with indwelling radial artery catheter. Anesthesia was induced with propofol (0.5-3 mg/kg) and fentanyl (1-2 μg/kg) followed by muscle relaxation with vecuronium (0.15 mg/kg) or rocuronium (0.6 mg/kg). After the trachea was intubated, mechanical ventilation was initiated with air and oxygen mixture (FiO2 of 0.3-0.5). Maintenance anesthesia was established with sevoflurane (1%-3%) and remifentanil (0.1 to 0.2 μg/kg/min) or with total intravenous anesthesia (TIVA) protocol (propofol 4-12 mg/kg/h and remifentanil 0.1-2 μg/kg/min). The choice of muscle relaxants and the agents used for maintaining anesthesia was in anesthesiologist's discretion. The patients who had clinical deterioration such as requiring continuous monitoring and respiratory or cardiovascular support, or neurologic deficits were transferred to the intensive care unit.

Statistical Analysis

Data analysis was made through SPSS v. 19.0 for Windows (SPSS, Inc., Chicago, IL, USA). statistical package software. The Kolmogorov-Smirnov test was used to determine the distribution of variables. Categorical comparisons were made using Pearson Chi-Square, Fisher Chi-Square, or Yates Chi-Square tests. Intergroup parametric variables were compared with Student's t-test. Non-parametric variables were compared with the U-test. An overall 5% Type-I error level was used to infer statistical significant difference.

Ethical Declaration

This study was planned as a retrospective cross-sectional study. It was approved by the local ethics committee (Approval Number is 20796219/ E-14-219) and conducted in accordance with the ethical principles described by the Declaration of Helsinki.

RESULTS

A total of 323 patients met the study criteria and included to the statistical analyses. **Table 1** shows patient characteristics. Mean age of the patients was 46.88 ± 13.91 years and 54.5% were female. Over half of patients (52.9%) were ASA class II, and 26.9% had systemic comorbidity. The rate of patients with non-functioning tumors was 53.3%. Intraoperative data are presented in **Table 2**.

Table 1. Patient characteristics

		n	%
Age			
	21-30	35	10.8
	31-40	89	27.6
	41-50	83	25.7
	51-60	70	21.7
	61 and over	46	14.2
Gender			
	Male	147	45.5
	Female	176	54.5
ASA			
	ASA I	89	27.6
	ASA II	171	52.9
	ASA III	63	19.5
	ASA IV	-	-
Comorbid disease			
	Cardiovascular	34	10.5
	Respiratory	43	13.3
	Endocrine	68	21.1
	Comorbid diseases related to multiple systems	87	26.9
Pituitary tumor			
	Functioning	151	46.7
	Non-functioning	172	53.3

Table 2. Distribution of patients by surgery time, anesthesia method, and muscle relaxant agent

		n	%
Surgery time			
	0-2 Saat	52	16.1
	2-3 Saat	197	61.0
	3-4 Saat	74	22.9
Anesthesia methods			
	Sevoflurane	127	39.3
	TIVA	196	60.7
Muscle relaxant agents			
	Vecuronium	78	24.1
	Rocuronium	245	75.9

The mean duration of anesthesia and surgery was 114.52 ± 23.03 min and 97.00 ± 23:49 min, respectively. Maintenance anesthesia was established with TIVA in 60.7% of patients and with sevoflurane in 39.3%. Rocuronium was administered as neuromuscular blocking agents in 75.9% of patients and vecuronium in 24.1% of patients. Functioning tumor was more likely to be detected ≥61-year-old age group than that in other age groups (**Table 3**).

Table 3. Distribution of tumortypes by age groups

	Functioning		Non-functioning		P value
Age group	**n**	**%**	**n**	**%**	
21-30 years	22	14.6	13	7.6	<0.001
31-40 years	48	31.8	41	23.8	
41-50 years	51	33.8	32	18.6	
51-60 years	19	12.6	51	29.7	
>60 years	11	7.3	35	20.3	

Statistically significant difference existed in the distribution of functioning and non-functioning tumors among different age groups ($p<0.001$). While 33% of patients with functioning tumors were in 41-51 years' age group, 29.7% of those with non-functioning tumors were in 52-62 years' age group. Comparison of tumor types between sexes showed a statistically significant difference ($p<0.05$). While 58.5% of women had functioning tumor, 67.3% of male patients were detected to have non-functioning tumor.

Intraoperative bradycardia was detected in 137 patients (42.41%), hypotension in 57 patients (17.65%), and hypertension in five patients (1.55%). The distribution of hemodynamic instability by age groups, ASA class, tumor type, and anesthetic method was shown in Table 4. Hemodynamic instability occurred in all of the patients over the age of 51. Bradycardia was detected in 60% and hypotension in 40% of patients who were in 51-60 years' age group. In patients who were in ≥61-years' age group, 63.1% had hypotension and 36.9% had bradycardia. Patients classified as ASA III were more likely to have hemodynamic instability than patients with ASA I and ASA II ($p<0.05$). In patients with functioning tumor, 39.7% had bradycardia, 7.2% had hypotension, and 3.3% had hypertension. On the other hand, 44.7% of patients with non-functioning tumor had bradycardia and 26.7% had hypotension. Patients with functioning and non-functioning tumors significantly differed in terms of hemodynamic instability ($p<0.05$). Bradycardia was observed in 51.1%, hypotension in 22.8%, and hypertension in 3.9% of the patients who were administered sevoflurane. On the other hand, bradycardia and hypotension occurred in respectively 36.7% and 14.2% of the patients who received TIVA. The rates of hemodynamic instability were significantly different between patients who received sevoflurane and TIVA ($p<0.05$), (**Table 4**).

Table 4. Distribution of hemodynamic instability by age groups, ASA class, tumor type, and anesthesia method

	Bradycardia		Hypotension		Hypertension	
	n	%	n	%	n	%
Age						
21-30years (n=35)	8	22.8	0	0	5	14.2
31-40years (n=89)	43	48.3	0	0	0	0
41-50 years (n=83)	27	32.5	0	0	0	0
51-60years (n=70)	42	60.0	28	40.0	0	0
>60 years (n=46)	17	36.9	29	63.1	0	0
ASA						
ASA I (n=89)	25	28.0	-	-	5	5.6
ASA II (n=171)	78	45.6	28	16.3	-	-
ASA III (n=63)	34	53.9	29	46.0	-	-
ASA IV (n=0)	-	-	-	-	-	-
Tumor type						
Functioning (n=151)	60	39.7	11	7.2	5	3.3
Non-functioning (n=172)	77	44.7	46	26.7	--	--
Anesthesia method						
Sevoflurane (n=127)	65	51.1	29	22.8	3.9	100,0
TIVA (n=196)	72	36.7	28	14.2	--	--

Eighteen patients were transferred to intensive care unit in the postoperative period. All these patients were in the age group of 61 years and over. No need for intensive care was determined in patients below the age of 61. Eleven patients (17.4%) in ASA III class and seven patients (7.8%) in ASA II class were transferred to the intensive care unit. Neither tumor type nor anesthetic method altered the need for intensive care. All patients were extubated in the operating room after the completion of surgery. None of the patients who were transported to the intensive care unit were intubated. Sedation was not required for patients in the postoperative period. None of the patients had clinical situations associated with hemodynamic instability such as myocardial infarction, cerebrovascular accident or acute renal failure.

DISCUSSION

The rate of bradycardia, hypotension, and hypertension during ETSS was 42.41%, 17.65%, and 1.55%, respectively among patients in our study. Hemodynamic instability developed more common in elderly than in young patients, and postoperative intensive care was only required in older patients. This study demonstrated the importance of anesthesia management for ETSS in elderly patients. Comorbid diseases and invasiveness of surgical procedure is associated with mortality in patients with advanced age (15). The potency of anesthetic drugs increases in the elderly. Minimum alveolar concentration value of volatile anesthetics decreases with increasing age and elicits hemodynamic effects at higher doses (16). Administration of propofol is more likely to cause hypotension in the elderly than in younger patients (17). Older people are more susceptible to opioids than young people (18). In our study, we thought that the higher intraoperative occurrence of hypotension and bradycardia in the elderly patients resulted from the fact that the elderly are more sensitive to anesthetics. Intraoperative hypotension, even for a short time, is associated with poor perioperative outcomes (19). Therefore, doses of anesthetics should be carefully adjusted in elderly patients. Elderly population was associated with increased risk of postoperative residual neuromuscular blockade due to administration of either vecuronium or rocuronium. Therefore, postoperative muscle weakness, airway obstruction, and hypoxemia are more common in the elderly than young patients (20).

Reich et al. showed that hypotension that occurred after induction of anesthesia was associated with ASA III-IV class, having the age over 50, and administration of higher doses of propofol and fentanyl. The authors reported the incidence of hypotension as 7.7% and 12.6% of patients with ASA I-II class and ASA III-IV class, respectively (21). Consistently, we also detected higher prevalance of hemodynamic instability in patients with ASA III class than that in patients with ASA I-II class.

Hypertension and ischemic heart disease are more common than normal population in patients who have pituitary tumor leading to Cushing's disease secondary to ACTH hypersecretion. In fact, these conditions constitute the major reason for perioperative mortality. Activation of renin-angiotensin-aldosterone system cause increased blood volume and hypertension in 80% of patients with Cushing's disease (22,23). We found a higher incidence of intraoperative hypertension in patients with functioning tumors. Non-functioning tumors, i.e. tumors that do not secrete hormones, often lead to panhypopituitarism due to mass effect. Thyroid hormone and glucocorticoid replacement might be necessary in these patients preoperatively. They also tend to intraoperative hypotension due to increased sensitivity to general anesthetic agents (22-25). In our study, intraoperative hypotension and bradycardia were more common in patients with non-functioning tumors.

Due to the long duration of neurological surgery, complications such as meningitis, extracranial infection and pulmonary embolism may occur. Korinek et al reported that the risk of meningitis was a 70% increase if the duration of neurological surgery was longer than 4 hours (26). In our study, no operation lasted longer than 4 hours.

The major limitation of our study is that retrospective design does not allow us to investigate the mechanisms that mainly trigger hemodynamic instability. In addition, data on prevalence of trigeminocardiac reflex, volume status, and doses of anesthetic agents were not collected. Further prospective studies should be warranted in this manner.

In conclusion, we found a higher prevalence of intraoperative hemodynamic instability in elderly patients who underwent ETSS. While older patients required intensive care postoperatively, no young patient needed intensive care. Also, to have non-functioning tumor and to be in ASA III class increased the risk of intraoperative hemodynamic instability. Specific anesthesia protocols should be developed to reduce the risk of hemodynamic instability in the patients scheduled for ETSS.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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