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Early Diagnosis Of Postoperative Delirium in Patients Who Underwent General Surgery

Genel Cerrahi Hastalarında Postoperatif Deliryum Erken Tanısı

ABSTRACT

Objective:

Postoperative delirium (POD) is a common postoperative complication. This study aimed to diagnose POD early primarily in patients who underwent General Surgery.

Material and Methods:

Data of 303 patients at the age of 18 and above who were operated by General Surgery Clinic between March 2018 and May 2018, who received general anesthesia were included in the study. Patients' demographic data, occupation, educational status, income level, additional diseases, ASA (American Society of Anesthesia) score, previous surgeries, history of a psychiatric or neurological disease, history of alcohol, cigarette, or drug use, and memory problems were recorded. Mini Mental State Examination (MMSE) was used to identify preoperative mental levels of the patients.

Diagnosis of the patient, name, duration and features of the surgery to be performed, whether the surgery was urgent or elective, drugs used, type of catheterization were recorded. The diagnosis of POD in patients was evaluated with Confusion Assessment Method (CAM).

Results:

POD developed in 2-6% (8 patients) of the patients. Results showed that the risk of delirium decreased as the education levels of the patients increased. A significant relationship was recorded between delirium and only midazolam among anesthetic agents used.

Conclusion:

Diagnosing POD with CAM in an early postoperative period was advantageous. The treatment planning of the patients for POD could be done in the early period. By doing this, increase in mortality, morbidity and cost as a result of missing the diagnosis of POD was prevented.

Key Words:

Postoperative Delirium, General Surgery, Cognitive Disorders

ÖZ

Amaç:

Postoperatif deliryum (POD) sık görülen bir postoperatif komplikasyondur. Bu çalışmada öncelikle Genel Cerrahi uygulanan hastalarda POD tanısının erken konulması amaçlanmıştır.

Gereç ve Yöntemler:

Mart 2018-Mayıs 2018 tarihleri arasında Genel Cerrahi Kliniği tarafından ameliyat edilen ve genel anestezi uygulanan 18 yaş ve üzeri 303 hastanın verileri çalışmaya dahil edildi.

Hastaların demografik verileri, mesleği, eğitim durumu, gelir düzeyi, ek hastalıkları, ASA (Amerikan Anestezi Derneği) skoru, geçirilmiş ameliyatları, psikiyatrik veya nörolojik hastalık öyküsü, alkol, sigara veya uyuşturucu madde kullanım öyküsü ve hafıza sorunları sorgulandı. kaydedildi. Hastaların ameliyat öncesi mental düzeylerini belirlemek için Mini Mental Durum Muayenesi (MMSE) kullanıldı.

Hastanın teşhisi, adı, yapılacak ameliyatın süresi ve özellikleri, ameliyatın acil veya elektif olup olmadığı, kullanılan ilaçlar, kateterizasyon tipi kaydedilir. Hastalarda POD tanısı Konfüzyon Değerlendirme Yöntemi (CAM) ile değerlendirildi. Bulgular: Hastaların %2-6'sında (8 hasta) POD gelişti. Sonuçlar, hastaların eğitim düzeyi arttıkça deliryum riskinin azaldığını gösterdi. Kullanılan anestezi ajanları arasında deliryum ile sadece midazolam arasında anlamlı ilişki saptanmıştır.

Sonuç:

Postoperatif erken dönemde CAM ile POD tanısı koymak avantajlıydı. POD hastalarının tedavi planlaması erken dönemde yapılabilmektedir. Bu sayede POD tanısının atlanması sonucu mortalite, morbidite ve maliyet artışının önüne geçilmiştir.

Anahtar Kelimeler:

Postoperatif Deliryum, Genel Cerrahi, Bilişsel Bozukluklar

INTRODUCTION

Delirium is a clinical syndrome that rapidly and suddenly starts, that develops due to disruption of cerebral homeostasis for a temporary period, and that is also accompanied by changes in consciousness, perception, thought, and sleep/wake cycle (1). It is a common and crucial medical condition that is accompanied by acute changes in consciousness, attention deficit and impaired cognitive functions mostly in patients with ongoing hospitalization (2).

“Postoperative Delirium” in patients who undergo a surgery is characterized by acute impairments in consciousness and cognitive thoughts. There is a significant disorientation. It has a sudden onset and the symptoms differ. Moreover, the symptoms become more severe at nights. That is why it is also called “Sundown Syndrome”. If the patient is examined at his or her normal times, course of the delirium and accordingly its diagnosis may easily be missed out. POD is a syndrome that prolongs the recovery period and that increases morbidity and mortality as well as the duration of hospital stay (3).

It is important to evaluate preoperative mental status of the patients in order to diagnose POD. Therefore, standardized Mini Mental State Examination (MMSE) is the most commonly used test for this purpose (4).

CAM used in the diagnosis of POD is a test compliant with DSM-IV criteria. It is a delirium evaluation test most commonly used by people who are not psychiatrists. It can easily be

applied. Its utility has been revealed in important clinical studies (5,6).

While the prevalence of POD is 1-2% in general population it rises to 14% especially in patients at the age of 85 and above (7). Although its incidence and effects are more significant in old patient group it can be seen in all age groups. As the delirium which is preoperatively present and delirium which postoperatively develops can be distinguished, factors inducing this clinical condition can be detected and required interventions to prevent this can be done (8).

In the studies, predisposing factors apart from age were as follows: male gender, cognitive impairment or dementia, weak functional capacity, drug and alcohol addiction, primary neurological diseases, shock, hypoxia, electrolyte imbalances, chronic disease, chronic renal failure, dehydration, malnutrition and visual/auditory impairment. Both hypoxia and hypercarbia may be the responsible factors for the development of delirium (9). POD is seen 2-5 times more in patients with dementia than in patients without dementia.

Delirium in hospitalized patients is associated with increase in morbidity and mortality, extension in the duration of hospital stay, loss of physical function, delay in rehabilitation, increase in the costs at hospital, and increase in the need to be placed into nursing homes (10).

If the patient cannot be treated after being diagnosed with POD, the mortality and morbidity of the patient increase (11,12). The first step in the treatment is treating the factor that initiates delirium. Providing sufficient hydration, fixing electrolyte imbalance and preventing probable hypoxia are the most common interventions (13).

This article was produced from the specialization thesis of Doctor Fatih OLUS, in the Department of Anesthesiology and Reanimation under the supervision of Professor Doctor Ayşe Gulbin ARICI.

MATERIAL and METHODS

Our study included the data of 303 patients who were operated by General Surgery Clinic between March 2018 and May 2018, who were preoperatively, intraoperatively and postoperatively followed up by the Department of Anesthesiology and Reanimation, who were at the age of 18 and above, and who received general anesthesia.

This research complies with all the relevant national regulations, institutional policies and in accordance with the tenets of the Helsinki Declaration, and has been approved by the Akdeniz University Medical Faculty Ethical Committee (approval number: 21.02.2018/136)

Preoperative cognitive status of the patients who accepted to participate in the study were evaluated with MMSE (Mini Mental State Examination) test. The test was performed by the same person. Patients were divided into three groups according to their MMSE scores (≤ 17 : Severe Cognitive Impairment, 18-24: Moderate Cognitive Impairment, and ≥ 25 : Normal Cognitive Value).

Diagnosis of the patients, the surgery to be performed and its duration, whether the surgery was emergent or elective, the drugs used, the types of catheterization (arterial, central, Foley or nasogastric catheter), and patients with intraoperative Hb

value of <8 mg/dL were collected from anesthesia records and recorded. In addition, intraoperative vital findings (blood pressure, mean arterial pressure, peripheral oxygen saturation and end-tidal CO₂) of the patients were obtained from anesthesia records at 30 minute intervals and recorded. A decrease in mean arterial pressure more than 20% from baseline value was evaluated as hypotension.

The criteria of CAM that was performed by the same person in 24th, 48th and 72nd hours in the first 3 postoperative days and the effects of anesthesia and surgery on the level of consciousness were evaluated and it was aimed to diagnose POD early. Postoperative analgesia was administered to the patients by General Surgery Clinic within the scope of routine postoperative analgesia protocol (dexketoprofen: at a dose of 12.5 mg every 4-6 hours and tramadol: at a dose of 100 mg 2-3 times a day) of General Surgery Clinic.

Statistical Evaluation

Data were analysed with IBM SPSS Statistics 18© Copyright SPSS Inc. 2009 software. Whether continuous variables followed normal distribution was evaluated. Variables that followed parametric distribution were evaluated with Student's T-test and nonparametric continuous variables with Mann Whitney U test. Nonparametric/discrete variables were analysed with Chi-Square test. Statistical significance level was accepted as 0.05 in the study.

RESULTS

Mean age of the patients was 52.5±14.3 years. The youngest age was 18 and the oldest was 86 (Table I).

Table I. Demographic characteristics of the subjects

Demographic characteristics (n=303)	Sample (n)	%
Gender		
Female	165	54.5
Male	138	45.5
Level of Education		
Literate	18	5.9
Primary school graduate	85	28.1
Secondary school graduate	86	28.4
High school graduate	79	26.1
Graduated from a University	35	11.6

POD developed in 8 (2.6%) out of 303 patients included in the study. All of the PODs in these patients were in hyperactive form which is the most common and mostly diagnosed type. POD was seen in 4 (2.4%) out of 165 female patients and in 4 (2.9%) out of 138 male patients. The difference is not statistically significant (p: 0.798).

While mean age of the patients with POD was 70.2 mean age of the patients without POD was 52.0. The difference is statistically significant (p:0.0001).

When evaluated in terms of the level of education, POD was

seen in 2 (11.1%) out of 18 patients who were literate, in 5 (5.9%) out of 85 patients who were primary school graduates, and in 1 (1.1%) out of 86 patients who were secondary school graduates while POD was not seen in any of the patients who were high school and university graduates. The difference is statistically significant (p: 0.015).

MMSE scores were identified and divided into three groups (≤ 17 : Severe Cognitive Impairment, 18-24: Moderate Cognitive Impairment, and ≥ 25 : Normal Cognitive Value) (172). While POD was seen in none of the patients in the group with Severe Cognitive Impairment (≤ 17), it was seen in 3 (3.8%) out of 78 patients in the group with Moderate Cognitive Impairment (18-24) and in 5 (2.3%) out of 222 patients in the group with Normal Cognitive Value (≥ 25). The difference is not statistically significant (p:0.722).

Three (37.5%) out of 8 patients in whom POD developed had Hypertension(HT), 2 (25%) had Diabetes Mellitus (DM) and 3 (37.5%) had Chronic Artery Disease (CAD) (Table II).

Table II. POD incidence according to additional diseases

	Patient 1.	Patient 2.	Patient 3.	Patient 4.	Patient 5.	Patient 6.	Patient 7.	Patient 8.
Hypertension	-	+	+	+	-	-	-	-
Diabetes Mellitus	+	-	-	+	-	-	-	-
Chronic Artery Disease	-	+	-	-	+	-	+	-

While POD developed in 2 out of 138 patients in the category of ASA 1, it developed in 2 (1.8%) out of 112 patients in the category of ASA 2, and in 4 (7.5%) out of 53 patients in the category of ASA 3. The difference is statistically significant (p: 0.049).

POD was seen in 6 (4.7%) out of 125 patients in whom Midazolam added to Thiopental was used during induction, 1 (6.6%) out of 15 patients in whom only Midazolam was used during induction and 1 (0.9%) out of 116 patients in whom only Thiopental was used during induction. POD was not seen in any of 46 patients in whom only Propofol was used during induction (Table III).

Table III. POD incidence according to the drugs used.

Medicines used	POD (+)		POD (-)	
	(n)	(%)*	(n)	(%)*
Midazolam&Thiopental	6	%4.7	119	%95.3
Midazolam	1	%6.6	14	%93.4
Thiopental	1	%0.9	115	%99.1
Propofol	0	%0.0	46	%100
Sevoflurane	6	%3.7	158	%96.3
Desflurane	2	%1.5	134	%98.5
Fentanyl	2	%1.3	150	%98.7
Remifentanyl	0	%0.0	1	%100
Fentanyl&Remifentanyl	6	%4.0	142	%96
Opioid unused	0	%0.0	2	%100

While POD was seen in 4 (5.9%) out of 68 patients who underwent gastrointestinal surgery it was seen in 3 (3.7%) out of 82 patients who underwent hepatobiliary surgery and 1 (1.9%) out of 52 patients who underwent endocrine surgery. POD was not seen in any of 101 patients endocrine underwent breast surgery, proctology or other operational types. While POD was seen in 1 (14.3%) out of 7 patients with intraoperative hemoglobin results of Hb<8 mg/dL it was seen in 7 (2.4%) out of 296 patients with Hb ≥8 mg/dL (p: 0.052). While POD developed in 7 (2.3%) out of 300 patients with End-tidal CO₂ <45 mmHg, it developed in 1 (33.3%) out of 3 patients with End-tidal CO₂ ≥45 mmHg (p: 0.001)(Table IV).

Table IV: POD incidence according to intraoperative data

	POD (+)		POD (-)		Chi-squ/p
	(n)	Y(%)*	(n)	(%)*	
Hypotension (+)	3	%3.6	81	%96.4	0.392/0.531
Hypotension (-)	5	%2.3	214	%97.7	
Hemoglobin <8 mg/dl	1	%14.3	6	%85.7	3.780/0.052
Hemoglobin ≥8 mg/dl	7	%2.4	289	%97.6	
EtCO ₂ ≥45 mmHg	1	%33.3	2	%66.7	11.104/0.001
EtCO ₂ <45 mmHg	7	%2.3	293	%97.7	

While POD was not seen in any of the 199 patients who were awakened in the operation room after the surgery it was seen in 1 (1.6%) out of 61 patients who were awakened in PACU (Post-Anesthesia Care Unit) and 7 (16.3%) out of 43 patients who were awakened in intensive care units (ICU). The difference is statistically significant (p:0.000).

While POD was seen in 7 (6.4%) out of 109 patients in whom nasogastric (NG) tube was used it was seen in 1 (0.5%) out of 194 patients in whom NG tube was not used (p:0.002).

While the mean duration of surgery was 175.0 minutes in patients with POD it was 100.1 minutes in patients without POD. The difference between them is statistically significant (p:0.0001). While mean postoperative discharge time was 12.37 days in patients with POD it was 2.34 days in patients without POD. The difference is statistically significant (p:0.000). While the shortest discharge time was 1 day the longest discharge time was 31 days.

DISCUSSION

This study aimed to investigate the early diagnosis of POD in patients for whom a surgery was planned by General Surgery clinic, characteristics of the patients in whom POD developed and who were diagnosed early, features of the surgery and anesthesia, risk factors and conditions affecting morbidity/mortality. POD developed in 8 (2.6%) out of 303 patients who were included in the study.

In our study, mean age of the patients in whom POD developed was 70.2 years and mean age of the patients in whom POD did not develop was 52 years. There was a POD rate that increased to 13.2% in patients at the age of 65 and above. This increase may be associated with low level of cognitive reserve and high number of concurrent diseases in old patients. The relationship between age and POD rate in patients whom we diagnosed early is in compliance with literature (7).

It was reported in the study of Kyzirids et al. that the incidence of POD was higher in men and that male gender was a risk factor for POD. In our study, the rate of POD was 2.4% in women and 2.9% in men. No statistically significant difference was found between two genders in terms of POD development (14).

Sprung et al. reported in their study that the incidence of POD decreased by the increase in educational level (15). In our study, none of the patients who were high school and university graduate had POD. The incidence of POD decreases as the literacy rate increases, which is consistent with the study of Sprung et al. In the study of Raats et al., an increase was observed in the frequency of POD development with additional diseases and increase in ASA score (16). In our study, we recorded a significant relationship between the increase in ASA score and POD development. In addition, a significant relationship between POD development and HT, DM and CAD in patients who were transferred to ICU after a major surgery was recorded in the study of Abelha et al (17). ASA score and the rate of presence of additional disease were higher in patients who were diagnosed with POD at an early period in our study, which is consistent with literature.

No other agent but midazolam, one of intravenous or volatile anesthetic drugs that were preoperatively used, was reported to be responsible for the development of POD (18). POD did not develop in any of 46 patients in whom only propofol was used during induction. In the meta-analysis performed by Wang Peng et al., midazolam used for sedation was compared with other drugs (dexmedetomidine and propofol) and the rates of POD were higher in midazolam groups (19). In our study, the riskiest drug in terms of POD was midazolam and POD was not seen in any of the patients for whom propofol was used, which is clinically very significant. In addition, the use of midazolam and other drugs together could not be evaluated in our study. This is because we did not create separate groups for drug combinations in our study which was designed as an observational study. It is necessary to perform randomized controlled studies in order to obtain statistically precise and strong results. Evaluating midazolam as the riskiest drug in patients diagnosed with POD at an early period was consistent with literature and our knowledge. Therefore, patient selection should be considered in terms of the development of POD during the use of midazolam.

A significant relationship between invasive catheterization used for patients and the development of POD was reported in literature (20). In our study, a significant increase in the incidence rate of POD was recorded among patients in whom arterial cannulation, central venous catheterization, Foley catheter and nasogastric tube were used. Higher incidence of POD may be because arterial and CVP catheterizations are generally used in

patient groups with high risk for POD development and in long-duration surgeries.

In the study of Nazemi et al., hypercarbia was effective in the development of POD (21). In our study, while POD developed in patients with End-tidal CO₂ <45 mmHg at a rate of 2.3% it developed in patients with End-tidal CO₂ ≥45 mmHg at a rate of 33.3%. The incidence rate of POD was significantly higher in patients with End-tidal CO₂ ≥45 mmHg than in patients with End-tidal CO₂ <45 mmHg, which is consistent with literature. Hypotension and hypoperfusion alone are among the risk factors for POD. In our study, a decrease in mean arterial pressure more than 20% from baseline value was evaluated as hypotension. According to this definition, while POD was seen in 3.6% of the patients in whom hypotension developed it was seen in 2.3% of the patients in whom hypotension did not develop. No statistically significant difference was recorded (p:0.531). In our study which was designed as an observational study, it is not correct to comment on the rates of POD because the patients are intervened in the direction of routine protocols of our clinic and hypotension therapy is initiated in case hypotension develops. However, a higher rate of POD was recorded for patients with hypotension (6).

In the study of Raats et al., a significant relationship between preoperative anemia (Hb <7.6 mmol/L for women and <8.2 mmol/L for men) and POD was recorded (16). In our study, although the threshold value for Hb was different the incidence of POD in patients with Hb <8 mg/dL in intraoperative blood gases or hemogram results was higher, which is consistent with the study of Raats et al.

Regarding the places where the patients were awakened, POD developed in patients admitted to ICU at a rate of 16.3% and in patients admitted to PACU at a rate of 1.6%. These rates were statistically significant. However, POD was not seen in any of the patients who were awakened in the operating room. A long-lasting immobilization that changes the sleep/wake cycle, high number of catheterizations, and ICU hospitalization in addition to admission to ICU after a risky and major surgery are separately risk factors for POD (18). The results in our study are consistent with literature. Apart from induction, midazolam is frequently used for sedation in patients who will be transferred to ICU or PACU after the surgery. Patients who has a history of ICU and PACU are already at risk due to both their additional diseases and the risky and major surgeries they underwent. All these can increase the incidence rate of POD.

Like in literature, longer “durations of hospital stays” in patients in whom POD developed were found in our study (22). It is obvious that the development of POD extends the “duration of hospital stay”. However, it is also possible to conclude that “duration of hospital stay” in patients with a risk factor for POD may be extended as well and accordingly the risk of POD increases.

In literature, POD was diagnosed within the first seven days or in a longer period (23,24). In our study, there were 8 patients (2.6%) who were diagnosed early (the first 3 postoperative days). This rate is consistent with the reported rates of patients who were diagnosed with POD in literature (25). Moreover, the data obtained from the risk factors we investigated and the risk factors due to patients, surgery or anesthesia were consistent

with literature. Diagnosing POD with CAM in the first 3 postoperative days in patients who underwent general surgery was highly beneficial. Thanks to this, it was possible to perform the treatment planning of the patients and start the treatment at an early period.

CONCLUSION

It is important to detect a disorder in patients in risk groups, especially in old patients, with cognitive tests while preoperatively evaluating the patients in detail. It is highly important to preoperatively receive geriatric or psychiatric help and provide necessary information and training about the surgery and postoperative period for old patients. The anesthetist and surgeon should share the risky situation with family for patients in high-risk group. In case of the necessity of the surgery, it is recommended to minimize the duration of surgery and anesthesia and avoid benzodiazepines or other drugs that may cause the development of POD.

With the developments in medical science and improvements in living conditions worldwide, an increase in the surgical need of older patient group is predicted. Therefore, it is believed that POD is an important health problem that should be focused on more in the future as it may result in increase in mortality, morbidity and costs and it is highly possible to often miss its diagnosis.

Ethics Committee Approval:

This research complies with all the relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration, and has been approved by the Akdeniz University Medical Faculty Ethical Committee, (approval number: 21.02.2018/136).

Informed Consent:

All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions:

Concept – F.O., G.A.; Design – F.O., G.A., E.G.; Supervision – F.O., G.A., E.G.; Resources – F.O., G.A.; Materials – G.A., E.G.; Data Collection and/or Processing – F.O., G.A., E.G.; Analysis and/ or Interpretation -F.O., G.A. -; Literature Search - G.A., E.G.; Writing Manuscript - F.O., G.A., E.G; Critical Review - F.O., G.A., E.G

Conflict of Interest:

The authors have no conflict of interest to declare.

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