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Research article

Clinico-Statistical Study of Postoperative Delirium in Patients with Malignant Tumors in the Oral and Maxillofacial Region

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Abstract

Purpose: Delirium is a condition of brain dysfunction arising from physical and drug causes. We retrospectively investigated the status of postoperative delirium in patients with malignancies of the stomatognathic region. **Materials and Methods:** Two-hundred patients (115 men and 85 women) who underwent surgery under general anesthesia in our dental hospital between January and December 2015 were included. **Results:** Postoperative delirium occurred in 11 patients (8 men and 3 women), with an incidence of 5.5 %, and the incidence of postoperative delirium in head and neck surgery with free flap reconstruction was 16.9%. All patients had hyperactive delirium and onset within 3 days post-surgery. Tracheostomy, neck dissection, tumor resection, and free flap reconstruction were performed in all patients diagnosed with delirium. Statistical analysis showed that the risk factors for postoperative delirium included operation time, anesthesia time, blood loss, postoperative hypertension, low hemoglobin, C-reactive protein, albumin level < 3 g/dL SpO₂ < 90%, insomnia, and diarrhea. **Conclusion:** Pinpointing a single risk factor for postoperative delirium is difficult, and it is desirable to begin prophylactic intervention before surgery and prevent its progression. Therefore, it is beneficial to identify symptoms of postoperative delirium early and prevent its worsening, with close consultation with psychiatrists.

Keywords: Low sodium diet, urine sodium, arterial hypertension, lifestyle, educational program

Introduction

Delirium is an acute disorder affecting consciousness, attention, and perception due to physical or drug causes, and its symptoms vary. It is primarily diagnosed based on the Diagnostic and Statistical Manual (DSM-5) of the American Psychiatric Association [1]. Postoperative delirium is a major complication after extensive surgical procedures. The National Institute for Health and Care Excellence (NICE) guidelines regarding delirium describe the following risk factors: age >65 years, pre-existing cognitive impairment, and current hip fracture or serious illness [2]. Postoperative delirium is often associated with other complications, and early identification of symptoms and prompt response are crucial in preventing the symptoms from worsening. Patients who undergo major head and neck cancer surgeries are at high

risk for postoperative delirium because they have a high prevalence of several risk factors, including advanced age and a long duration of surgery (that may take more than 600 min), immediate reconstruction with free flap is performed [3-5]. The onset of delirium often occurs within 3 days after surgery, and almost all reports indicate that the onset of delirium is experienced under intensive care unit (ICU) management [6-10]. However, our dental hospital is adjacent to a medical school teaching hospital, and we have routinely been conducting postoperative management in close collaboration with psychiatrists, without using the ICU. The purpose of this study was to examine the factors that contribute to the development of postoperative delirium and to discuss its prevention.

Materials and Methods

A total of 200 patients (115 men and 85 women) who underwent surgery for malignant tumors of the oral and maxillofacial region between January and December 2015 at our hospital were enrolled in this study (Table 1).

Table 1. Operative characteristics of patients

	No.
TR	95
ND	22
TR + ND	14
Tracheotomy + TR	1
Tracheotomy + ND	1
Tracheotomy + TR + ND	2
TR + ND + R	15
Tracheotomy + TR + ND + R	50
Total	200

TR: tumor resection; ND: neck dissection; R: immediate reconstruction by free flap

We chose the year 2015 because this was the year in which we started to regularly request consultations with a psychiatrist for the patients. The primary surgical sites were the tongue (93 patients), mandibular gingiva (41 patients), buccal mucosa (26 patients), maxillary gingiva (25 patients), floor of the mouth (9 patients), palate (3 patients), submandibular gland (2 patients), sublingual gland (2 patients), and unknown primary site (1 patient with cancer of unknown origin). We examined the onset, duration, and subtype of the delirium.

To explore the risk factors for postoperative delirium, age, sex, smoking history, drinking history, drug history, and medical history focusing on cerebral, metabolic, cardiovascular, and psychiatric diseases were examined; the following potential aggravating factors were also investigated: operative method, prolonged duration of surgery, anesthetic time, blood loss, reduced hemoglobin level (Hb), lowered C-reactive protein (CRP), albumin (Alb) level lower than 3 g/dL, hypertension, SpO₂ reduction of 90% or less, fever of 38°C or higher temperature, insomnia, diarrhea, and constipation within 2 days postoperatively.

To evaluate hypertension, the criteria in the “Japanese Guidelines for the Treatment of Hypertension 2014” were used [11]. Diagnosis of delirium was made by a specialist psychiatrist based on DSM-5 diagnostic criteria.

All statistical analyses were performed using SPSS version 22.0 (Armonk, NY: IBM Corp). The Mann-Whitney U test was performed to analyse age, operation time, anesthetic time, blood loss, Hb, and CRP levels. To analyze sex, alcohol consumption, smoking history, history of administration, low Alb level, postoperative hypertension, SpO₂, fever, insomnia, diarrhea, and constipation, the Fisher’s exact test (two-tailed) was performed. Statistical significance was set at $p < 0.05$.

The study protocol was approved by the Research Ethical Review Board of the Faculty of Dentistry of Tokyo Medical and Dental University (D2020-029). The requirement for written informed consent from each patient was waived because of the

retrospective nature of the study.

Results

Postoperative delirium occurred in 11 patients (8 men and 3 women), with an incidence of 5.5% among all head and neck cancer surgeries. Among the subtypes of delirium, all patients showed hyperactive delirium. The onset of postoperative delirium was within 3 days for all patients; it was on the day of surgery for three patients, on the next day for six patients, and on the second day and the third day after surgery for one patient each. The duration of delirium was 1 d (one patient), 3 days (one patient), five days (one patient), six days (two patients), 7 days (one patient), nine days (one patient), 10 days (two patients), seventeen days (one patient), and 28 days (one patient), and a median of 7 days.

Table 2a shows the characteristics and preoperative data of patients with and without delirium. The median age of the delirium group was 74 years (50–82 years), and that of the group without delirium was 66 years (30–90 years); though the delirium group tended to be older, the difference was not significant. The past medical history showed that the delirium group had the highest incidence of hypertension, followed by diabetes mellitus, dyslipidemia, and hyperuricemia; however, only hypertension showed a statistically significant difference with the non-delirium group.

All patients in the delirium group underwent tracheostomy, neck dissection, tumor resection, and free flap transfer. The incidence of postoperative delirium when head and neck surgery was followed by free flap reconstruction was 16.9% (11/65). Statistically significant differences were observed in operative time, anesthetic time, blood loss, Hb, CRP, Alb (<3 g/dL), SpO₂ (<90%), insomnia, and diarrhea (Table 2b).

Discussion

Delirium is an acute disorder of consciousness, attention, and cognition, and is characterized by varying symptoms. The primary symptom of delirium is impaired attention, which is present in 97% of the patients with delirium [12]. Besides the symptoms, it is often accompanied by disturbances of the sleep-wake cycle, affective disorders, and psychomotor disorders. Based on the changes in psychomotor activity, delirium is classified into three subtypes: hyperactive (increased activity, restlessness, wandering), hypoactive (decreased activity, decreased speed, decreased rate and amount of speech, and reduced awareness of surroundings), and mixed types [1,13]. Postoperative delirium generally occurs in 10–50% of patients and contributes to a subsequent decline in cognitive function and increased risk of dementia [13]. The incidence of delirium in patients with cancer is high, with 25% of patients admitted to the hospital developing delirium [14]. Prognosis reportedly worsens with delirium [9,15], and cognitive function may not return to preoperative levels even after 6 months or 1 year in patients aged >60 years who develop postoperative delirium [16].

In this study, the incidence of postoperative delirium was low at 5.5%, and the incidence of delirium following head and neck surgery with free flap reconstruction was 16.9% (11/65). The incidence of postoperative delirium in the head and neck region ranged from 10.9–33.3%; among them, the incidence varied for reconstruction with free flap alone [17]. In this study, the time

Table 2a. Characteristics and preoperative data of patients with and without delirium

		With delirium (n=11)	Without delirium (n=189)	p-value
Age (y)	Median	74	66	p=0.0574 ^a
	Min-Max	50-82	30-90	
Sex	Male	8 (72.7%)	107 (56.6%)	p=0.3601 ^b
	Female	3 (27.3%)	82 (43.4%)	
Alcohol habit	Current+Past	6 (54.5%)	99 (52.4%)	p=1 ^b
	Never	5 (45.5%)	90 (47.6%)	
Smoking habit	Current+Past	6 (54.5%)	57 (30.2%)	p=0.1039 ^b
	Never	5 (45.5%)	132 (69.8%)	
Drug history	Benzodiazepines	3 (27.3%)	36 (19%)	p=0.4513 ^b
	H2-blocker	1 (9.1%)	9 (4.8%)	p=0.4397 ^b
Medical history	Stroke	0	7 (3.7%)	p=1 ^b
	Cerebral aneurysm	1 (9.1%)	1 (0.5%)	p=0.1072 ^b
	Hypertension	7 (63.6%)	53 (28.0%)	p=0.0186 ^b
	Deabetes mellitus	3 (27.3%)	22 (11.6%)	p=0.1445 ^b
	Dyslipidemia	2 (18.2%)	36 (19%)	p=1 ^b
	Hyperuricemia	2 (18.2%)	16 (8.5%)	p=0.2589 ^b
	Depression	0	5 (2.6%)	p=1 ^b
	Insomnia	3 (27.2%)	35 (18.5%)	p=0.4406 ^b
	Dementia	0	1 (0.5%)	p=1 ^b

^aMann-Whitney U test, ^bFisher's exact test

of onset of postoperative delirium was within 3 days after surgery for all patients. In previous reports, the onset of delirium was usually within the first week after surgery, and the duration of delirium has not been clearly described [5,17]. In the present study, all patients showed hyperactive subtype of delirium. Hypoactive delirium is known to be more common than hyperactive delirium, especially in the presence of severe physical illness [18]; however, hypoactive delirium is often mistaken for depression or dementia and is more difficult to recognize than hyperactive delirium. Studies that on the diagnosis of delirium among physicians and nurses suggest that they diagnose only 20–50% of cases [19-23]. Many screening tools have been validated for assessing delirium, and the confusion assessment method (CAM) is the most widely used instrument to identify delirium; however, specific training is needed for the evaluation [24]. Although our hospital does not manage patients in the ICU, nurses provide prompt postoperative care, and it is desirable to introduce assessment methods such as CAM to evaluate hypoactive delirium more accurately.

To prevent the development of postoperative delirium, it is necessary to identify and remove the risk factors. In this study, the risk factors for the development of postoperative delirium, including operation time, anesthetic time, blood loss, hypertension, Hb, CRP, Alb (< 3 g/dL), SpO₂ (< 90%), insomnia, diarrhea, and physical factors were evaluated. Zhu et al. performed

Table 2b. Intra operative and postoperative data of patients with and without delirium

		With delirium (n=11)	Without delirium (n=189)	p value
Length of operation (min)	Median	703	231	p<0.0001 ^a
	Min- Max	455-1082	31-954	
Length of general anesthesia (min)	Median	787	201	p<0.0001 ^a
	Min-Max	528-1164	75-1027	
Blood loss (ml)	Median	465	128	p<0.0001 ^a
	Min-Max	146-956	1-1322	
Hb (g/dl)	Median	10.5	12.2	p<0.0001 ^a
	Min-Max	7.5-12.4	7.9-16.2	
CRP (mg/dl)	Median	99	3.2	p<0.0001 ^a
	Min-Max	4.91-19.25	0-23.3	
Alb<3(g/dl)		10(91%)	39(20.6%)	p<0.0001 ^b
Hypertension		8(72.7%)	101(53.4%)	p=0.3510 ^b
SpO ₂ <90%		4(36.4%)	8(4.2%)	p=0.0020 ^b
Fever ≥ 38.0°C		4(36.4%)	49(25.9%)	p=0.4864 ^b
Insomnia		11(100%)	51(27%)	p<0.0001 ^b
Diarrhea		8(72.7%)	44(23.3%)	p=0.0011 ^b
Constipation		0	16(8.5%)	p=0.6057 ^b

Alb:albumin; CRP:C-reactive protein; Hb: hemoglobin;aMann-Whitney U test, bFisher's exact test

a meta-analysis on the risk factors for postoperative delirium for head and neck surgery with free flap reconstruction, and identified 10 statistically significant risk factors, including old age (>70 years), male sex, duration of surgery, history of hypertension, blood transfusions, tracheotomy, American Society of Anesthesiologists physical status grade of at least III, flap reconstruction, and neck dissection [5,25]. Evaluating dehydration is also important because renal function can be easily lowered and dehydration is difficult to recognize in the elderly [18]. Among the modifiable risk factors, exposure to benzodiazepines appears to be the most strongly associated with delirium [26]. With little evidence to support the efficacy of pharmacotherapy in preventing delirium, a great deal of attention is being paid to non-pharmacological interventions [27-29]. These studies show that multifactorial interventions that address potential modifiable risk factors can reduce the prevalence, incidence, and duration of delirium. Preventive interventions are associated with improved

quality of care for older patients. Notably, at least 30–40% of occurrence is thought to be preventable by multicomponent interventions [30–33].

Preventive measures are very wide, and collaboration among nurses, dentists, and psychiatrists is very important for their success. In our department, a preparatory factor screening sheet for postoperative delirium has been prepared, to be filled prior to hospitalization, with reference to DELirium Team Approach (DELTA) program [33], which was developed with the aim of preventing delirium by providing adequate assessment and care by the team. By performing regular conferences with nurses and psychiatric liaison teams after hospitalization, preventive intervention and enhancement in the early detection of postoperative delirium and its response can be made possible.

Future research should aim to analyze larger samples, and should include the clinical evaluation of the effectiveness of delirium prevention programs.

Conclusion

Postoperative delirium in patients with malignant tumors of the Malignant tumors of the oral and maxillofacial region was clinico-statistically investigated. The incidence of postoperative delirium was 5.5%, and the incidence during head and neck surgery with free flap reconstruction was 16.9%. The risk factors that were significantly different between patients with and without delirium in the statistical analysis were operation time, anesthetic time, blood loss, hypertension, Hb, CRP, Alb, SpO₂, insomnia, and diarrhea. Although it is difficult to accurately predict the development of postoperative delirium, preoperative assessment of risk factors is desirable along with initiation of preventive interventions; postoperatively, it is necessary to early and prompt detection of changes in patient's condition to decrease its severity.

Abbreviations

Alb: albumin; CRP: C-reactive protein; Hb: hemoglobin; TR: tumor resection; ND: neck dissection; R: immediate reconstruction by free flap.

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Conflicts of Interest

The authors have no conflict of interest to declare.

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