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A history of aggression is a risk factor for postoperative confusion in elderly male drinkers

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Abstract
Purpose. We investigated the relationship between preoperative psychological state and postoperative confusion in elderly drinkers.
Methods. We studied 81 male patients, ranging in age from 65 to 80 years, who were scheduled to undergo total hip arthroplasty and total knee arthroplasty. The patients were divided into two groups; non-drinkers and patients who drank 25 g or more of alcohol daily. All patients were given a neuropsychological screening evaluation, including a Mini-Mental State test, the Japanese version of the State-Trait Anxiety Inventory (STAI), a depression scale test, and evaluation of a history of aggression and postoperative confusion.
Results. Postoperative confusion during the first 72 h after the end of the operation occurred in 7 of the 50 non-drinkers (14%) and in 11 of the 31 drinkers (35%) ($P = 0.01$). There were no significant differences in STAI (state anxiety and trait anxiety), Mini-Mental State, and depression scale scores between the non-drinkers and drinkers, or between patients with and without postoperative confusion. All 8 patients who had a history of aggression developed postoperative confusion. There was no significant difference in the incidence of postoperative confusion between drinkers who did not have a history of aggression and non-drinkers.
Conclusion. A history of aggression in elderly male drinkers is associated with postoperative confusion.

Key words Alcohol · Postoperative confusion · Aggression · Cognitive function · Depression · Anxiety

Introduction

Postoperative confusion is common in elderly surgical patients and may be associated with increased morbidity, length of hospital stay, and patient care costs [1]. Alcohol drinking is a risk factor for postoperative confusion [2]. Reduced central cholinergic, serotonergic, and gamma-aminobutyric acid (GABA) activity have been reported in alcohol drinkers [3]. Alterations in the cholinergic, serotonergic, and GABA systems may result in postoperative confusion in elderly patients [4]. In addition, alteration of the hypothalamic-pituitary-adrenal (HPA) axis has been reported in chronic alcohol drinkers [5]. Functional impairment in the HPA axis causes delirium in elderly patients [6]. We demonstrated that an increase in postoperative interleukin-6 and cortisol in elderly patients was associated with the development of postoperative confusion [7]. In addition, we previously reported that patients with alcohol problems who developed postoperative confusion had an increased cortisol response to surgery [8]. Thus, it appears that elderly drinkers are at risk for developing postoperative confusion.

Alcohol drinking is associated with a high rate of psychiatric symptoms. Alcohol drinkers often exhibit impairments in cognitive function [3]. Elderly patients with cognitive impairment are more vulnerable to postoperative confusion [1]. Approximately 50% of alcoholics have episodes of depression [9]. Alcohol drinking is capable of causing depressive symptoms both on drinking and on withdrawal of alcohol [9]. The depression is reported to be a risk factor for postoperative confusion in elderly patients [10]. Increased rates of anxiety disorders in alcohol drinkers are also reported [11]. Anxiety symptoms resembling generalized anxiety disorder and phobic problems are common during intoxication and alcohol withdrawal [12]. Preoperative anxiety is also associated with postoperative confusion [13]. Aggression, for the purposes of this study, was defined as a personality change caused by alcohol drinking. Aggressive behavior is reported to be associated with disturbance in the HPA axis, although the relationship between a history of aggression and postoperative confusion in alcohol drinkers is not clear. To our knowledge, there have been no reports about the relationship

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between postoperative confusion and the preoperative psychiatric state in elderly drinkers. In this study, we investigated the relationship between postoperative confusion and a preoperative cognitive, depressive, anxiety state, and a history of aggression in elderly drinkers.

Patients and methods

The study was approved by the medical ethics committee of our institution. Informed consent was obtained from all patients. We studied 81 male patients, ranging in age from 65 to 80 years. The patients were interviewed preoperatively regarding daily alcohol consumption, the duration of regular drinking, daily drinking, and depression. Families were questioned about a past history of alcohol-related aggression. Alcohol-related aggression was measured using the Buss-Perry Aggression Questionnaire [14]. The patients were then divided into two groups according to their actual consumption: group A, moderate and heavy drinkers ($n = 31$), who had consumed 25 g or more of alcohol a day for several years, and who drank more than three drinks per week; and group B ($n = 50$) non-alcohol drinkers [15]. All patients in the study underwent elective total hip arthroplasty (THA) and total knee arthroplasty (TKA) at Hakodate Watanabe Hospital and Hirosaki National Hospital. Patients with a history of liver cirrhosis, mild or severe cerebrovascular or cardiovascular disease or dementia, or the use of psychoactive medication or anticholinergic drugs were excluded.

Anesthesia was induced with $1.5\,mg \cdot kg^{-1}$ of intravenous propofol and $2\,\mu g \cdot kg^{-1}$ fentanyl, and was maintained with an infusion of propofol at the rate of $5–6\,mg \cdot kg^{-1} \cdot h^{-1}$ until skin closure; $4\,\mu g \cdot kg^{-1}$ fentanyl was given for all patients until skin incision, followed by further increases according to responses to vital signs such as systolic blood pressure and heart rate, which were controlled to within 20% of preoperative values. Acetated Ringer's solution was infused at a rate of $5–6\,ml \cdot kg^{-1} \cdot h^{-1}$ to all patients. No patients received packed red blood cell transfusions. Postoperatively, all patients were treated with a nonsteroidal analgesic (diclofenac sodium 50-mg suppository) every 8 h for incisional pain. If they complained of pain, they were treated with pentazocine. Nasal oxygen ($6\,l \cdot min^{-1}$) was administeted for 24 h after the end of the anesthesia. The patients were monitored with a pulse oximeter. If, on the first postoperative day, any patients demonstrated an arterial oxygen saturation (Sp_{O_2}) value of less than 95%, these patients were excluded from this study.

Postoperative confusion was assessed using a confusion assessment method (CAM) [16]. The assessment has four key features: (1) acute change in mental status with a fluctuating course, (2) inattention, (3) disorganized thinking, and (4) an altered level of consciousness. A diagnosis of confusion requires the presence of both of the first two features. The patients were examined at least once daily with CAM diagnostic criteria for confusion until the seventh day after the operation; assessment of confusion was performed whenever a patient was found have changed mentally by the nursing staff. The nurses were not aware of the purpose of the study. Confused patients were treated with 5 mg haloperidol. Pain scores were evaluated by nurses every 24 h after that time. Pain was estimated using a 100-mm visual analogue scale (VAS; 0 mm representing no pain and 100 mm representing the worst imaginable pain). The pain score was not evaluated if confusion occurred; the pain score in confused patients was evaluated 5 h after haloperidol treatment.

Psychometric testing was performed in the afternoon prior to surgery. The Japanese version of the State-Trait Anxiety Inventory (STAI) was used to assess the anxiety state of the patients [17]. State anxiety (transient anxiety that varies according to the situation) and trait anxiety (stable personality disposition reflecting general level of fearfulness) were evaluated. A score for state anxiety of more than 42 and a score for trait anxiety of more than 44 are indicative of an anxious state. Cognitive function was assessed by using the Mini-Mental State (MMS) test [18]. The MMS examination is a general cognitive screening test that investigates orientation to time and place, calculation ability, level of attention, short-term recall language ability, and the ability to copy a geometric design. The maximal score is 30 points and a score of less than 23 is indicative of cognitive impairment. Depression was assessed according to the depression scale of Koenig et al. [19], in which the maximal score is 11 points and a score of 4 or more is indicative of clinical depression.

Data values were expressed as means ± SD. Comparisons between groups in regard to VAS pain score, mean duration of anesthesia and surgery, and mean volume of blood loss were analyzed by one-way analysis of variance (ANOVA). Comparisons of STAI, MMS, and depression scale values before and after the operation and between groups were analyzed by ANOVA followed by Dunnett's test. The incidence of acute confusion was analyzed by χ^2 testing. P values of less than 0.05 were considered significant.

Results

Patients in group A had been in the habit of drinking 39.4 ± 18.2 g alcohol per day (range, 25.2–56.0 g per day). Liver abnormalities were mild in group A: SGOT, $47.0 \pm 23.5\,IU \cdot l^{-1}$; SGPT, $62.6 \pm 21.6\,IU \cdot l^{-1}$; and γ-

Table 1. Profile of patients, and clinical data during anesthesia in this study

	Group A	Group B
Number of patients	31	50
Age (years)	72.1 ± 4.4	71.9 ± 3.8
Daily alcohol consumption (g)	39.4 ± 18.2*	0
Weight (kg)	55.8 ± 10.6	55.8 ± 9.5
Number of smokers	13	8
Duration of surgery (min)	125.3 ± 35.3	113.2 ± 24.4
Duration of anesthesia (min)	189.4 ± 40.1	176.1 ± 27.5
Blood loss (g)	167.5 ± 57.4	148.8 ± 51.1
Fentanyl consumption (μg)	248.0 ± 31.7	229.1 ± 34.4
Pentazocine consumption (mg)	10.5 ± 15.2	8.9 ± 10.8
VAS pain score POD 1	32.6 ± 12.1	29.4 ± 11.0
VAS pain score POD 2	20.3 ± 10.8	17.9 ± 6.8
VAS pain score POD 3	11.9 ± 5.5	13.7 ± 8.3

* $P < 0.05$, between groups A and B
Data values are expressed as means ± SD

glutamyltransferase, 77.8 ± 46.1 IU·l^{-1} and were normal in group B: SGOT, 16.7 ± 6.1 IU·l^{-1}; SGPT, 19.9 ± 5.6 IU·l^{-1}, and γ-glutamyltransferase, 30.4 ± 14.9 IU·l^{-1}. There were no significant differences in age, mean duration of anesthesia, or surgery, or mean volume of blood loss between groups A and B (Table 1). There were no hemodynamic differences, in systolic and diastolic blood pressure or in heart rate, between groups A and B. Total fentanyl consumption was 248.0 ± 31.7 μg for group A, and 229.1 ± 34.4 μg for group B, with no significant difference between groups A and B. There were no clinically significant differences in postoperative pain scores between groups A and B for 3 days after the operation (Table 1).

Postoperative confusion during the first 72 h after the end of the operation occurred in 11 of the 31 patients (35%) in group A and in 7 of the 50 patients (14%) in group B. The incidence of postoperative confusion was significantly ($P = 0.01$) higher in group A than in group B (crude odds ratio, 3.3; adjusted odds ratio, 3.1). The peak incidence of postoperative confusion was on the day after the operation in both groups A and B. In group A, the daily alcohol consumption (49.2 ± 10.6 g) of patients with postoperative confusion was significantly higher than that (34.1 ± 8.3 g) of the patients without postoperative confusion. All 8 patients who had a history of aggression developed postoperative confusion. The incidence of postoperative confusion in patients who did not have a history of aggression in group A was 13%, which was not significantly different from that in group B. In both groups A and B, we found no significant differences in age between patients with and without postoperative confusion. There was no significant relationship between postoperative pain scores and confusion in either group A and or group B.

STAI (state anxiety and trait anxiety) scores were 41.0 ± 7.8 and 34.6 ± 8.1 in group A and 38.6 ± 9.6 and 33.5 ± 7.3 in group B, and there were no significant differences between groups A and B (Table 2). We compared STAI scores in patients with and without postoperative confusion. However, there was no significant difference in STAI scores between patients with and without postoperative confusion, in either group A and or group B.

Table 2. Scores for State-Trait Anxiety Inventory (STAI), depression score, and Mini-Mental State (MMS) examination in Groups A and B

	Group A	Group B
STAI		
State anxiety	41.0 ± 7.8	38.6 ± 9.6
Trait anxiety	34.6 ± 8.1	33.5 ± 7.3
Depression scores	3.2 ± 1.8	2.8 ± 1.8
MMS	25.7 ± 2.1	26.2 ± 2.1

Data values are expressed as means ± SD

Depression scores were 3.2 ± 1.8 in group A and 2.8 ± 1.8 in group B, and there was no significant difference between groups A and B. Depression scores in patients with and without postoperative confusion were 4.1 ± 1.9 and 2.7 ± 1.9 ($P = 0.053$) in group A and 3.4 ± 1.6 and 2.7 ± 2.0 ($P = 0.22$) in group B (Table 3). We found that, in group A, depression scores correlated ($r = 0.47$; $P = 0.006$) with the daily alcohol consumption, with a regression line of $y = 0.05x + 1.16$ (Fig. 1). In this study, six heavy drinkers, who drank more than 60 g of alcohol daily, were all depressed, and five of them developed postoperative confusion.

The MMS score was 25.7 ± 2.1 in group A and 26.2 ± 2.1 in group B and there was no significant difference in scores between the non-drinkers and drinkers. The MMS scores in patients with and without postoperative confusion were 26.1 ± 1.8 and 25.5 ± 2.4 in group A and 26.3 ± 2.4 and 26.2 ± 1.7 in group B; there was no

Table 3. Daily alcohol consumption, State-Trait Anxiety Inventory (STAI), depression score, and Mini-Mental State (MMS) examination in patients with and without postoperative confusion

	Group A		Group B	
	Confusion (+) (n = 11)	Confusion (−) (n = 20)	Confusion (+) (n = 7)	Confusion (−) (n = 43)
Daily alcohol consumption (g)	49.2 ± 10.6*	34.1 ± 8.3	0	0
STAI				
State anxiety	42.7 ± 9.0	39.9 ± 8.2	41.1 ± 11.4	38.2 ± 8.6
Trait anxiety	35.5 ± 9.4	34.1 ± 7.6	35.9 ± 13.7	33.1 ± 9.0
Depression scores	4.1 ± 1.9	2.7 ± 1.9	3.4 ± 1.6	2.7 ± 2.0
MMS	26.1 ± 1.8	25.5 ± 2.4	26.3 ± 2.4	26.2 ± 1.7
VAS pain score POD 1	34.0 ± 13.7	31.6 ± 8.6	30.2 ± 13.4	29.3 ± 8.4
VAS pain score POD 2	23.7 ± 9.4	17.8 ± 6.0	17.5 ± 9.2	18.0 ± 5.5
VAS pain score POD 3	12.6 ± 6.3	11.4 ± 4.1	12.7 ± 8.8	13.8 ± 7.1

* $P < 0.05$ vs patients without postoperative confusion
Data values are expressed as means ± SD

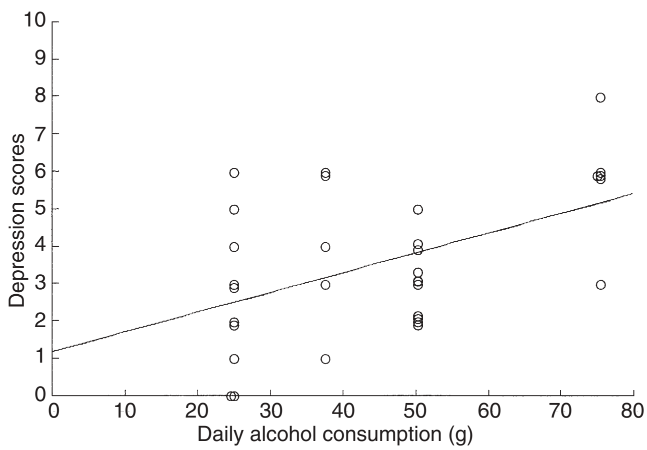

Fig. 1. Relationship between depression scores and daily alcohol consumption. In group A, depression scores were correlated with daily alcohol consumption, with a regression line of y = 0.05 x + 1.16

significant difference in MMS scores between patients with and without postoperative confusion in either group A or group B (Table 3).

Discussion

The present study showed that the incidence of postoperative confusion in elderly male drinkers was significantly higher than that in non-drinkers, and the daily alcohol consumption of confused elderly male drinkers was significantly higher than that of elderly male drinkers without confusion. Thus, alcohol drinking in elderly men is a risk factor for postoperative confusion. This study demonstrated that all the patients who had a history of aggression developed postoperative confusion. In addition, there was no significant difference in the incidence of postoperative confusion between drinkers who did not have a history of aggression and non-drinkers. Thus, a history of aggression in elderly male drinkers appears to be an important factor in the development of postoperative confusion. Alcohol-related aggression is a personality change caused by alcohol drinking [20]. A large percentage of patients with alcohol abuse have problems in the control of aggression [20]. Aggressive behavior is reported to be correlated with heavy alcohol use [20]. In this study, the alcohol consumption per day was significantly higher in patients who developed postoperative confusion than that in patients who did not develop postoperative confusion. Thus, it seems that alcohol drinking induces aggressive behavior by affecting the central nervous system. Patients with a history of aggression have disturbances in the HPA axis [20]. The disturbances in the HPA axis appear to contribute to a low threshold for postoperative confusion, because the occurrence of confusion is associated with increased postoperative plasma cortisol concentrations [7,21]. In addition, the alcohol-induced increases in aggression can be potentiated by benzodiazepine agonists and prevented by their antagonists [22]. GABA also appears to have an important role in the neurochemical control of aggressive behavior.

Depression is a risk factor for postoperative confusion [10]. A high prevalence of depression is found in chronic alcohol drinkers [9]. Approximately 50% of chronic alcohol drinkers are reported to meet the criteria for major depression or bipolar affective disorder [9]. In this study, we could find no significant difference in depression scores between drinkers and non-drinkers, and we found no relationship between depression and postoperative confusion in the elderly male drinkers. However, we found a relationship between a depressive state and daily alcohol consumption. It is possible that depressive symptoms in elderly drinkers may contribute to heavy drinking. In this study, six heavy drinkers were all depressed, but the number of heavy drinkers was small. We found no differences in cognitive function or preoperative anxiety between our elderly male patients with and without postoperative confusion. Cognitive impairment in chronic alcohol drinkers was shown to be related to heavy alcohol consumption [3]. Light-to-moderate alcohol consumption is associated with a reduced risk of dementia [22]. Fifty to sixty-seven percent of chronic alcohol drinkers had high scores on anxiety measures [12]. Moreover, patients, preoperatively, feel anxiety about an operation. However, we found that postoperative confusion in elderly male drinkers was not associated with their preoperative anxiety.

In this study, no patients demonstrated an Sp_{O_2} value of less than 95% during or after surgery. We found no significant differences in age or pain scores between patients with and without postoperative confusion. Thus, the postoperative confusion was mainly associated with alcohol drinking. As alcohol consumption is underestimated in self-reports, one might expect that some patients reporting as light drinkers, might, in fact, belong to the heavy drinking group. However, the present study showed a significant difference in the incidence of postoperative confusion between non-drinkers and drinkers. Thus, a problem in self-reporting seemed unlikely.

The MMS is a widely used instrument for assessing cognitive function. The sensitivity and specificity were reported to be 80% and 98% [24]. As the MMS provides a global measure of cognitive function, our data may not have indicated the impairment of a specific cognitive function. In addition, the MMS is affected by intelligence and social class [24]. However, as the MMS requires little time to complete, it appears to be a useful screening test to evaluate cognitive function in the elderly, in a study such as ours. Anxiety is difficult to measure accurately, as it is an emotion. The incidence of preoperative anxiety varies from 10% to 80%, depending mainly on the method of assessment. The STAI used to assess the anxiety in this study is the most commonly used instrument, and has been shown to demonstrate a heightened level of preoperative anxiety [25]. The STAI questionnaire is a global test and measures trait and state of anxiety. In this study, depression was assessed using the brief depression scale of Koenig et al. [19], because the questionnaire is simple and easy to answer for elderly patients. Its sensitivity and specificity were reported to be 83% and 77% [19], and this brief depression scale is a sensitive and reliable method for the assessment of depression.

In conclusion, in elderly male drinkers with a history of aggression, this history was associated with postoperative confusion.

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