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Relationship Between Age and Frequency of Side Effects Associated with Postoperative Analgesia

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Summary : Study Objective: Although patient-controlled analgesia (PCA) is a valid analgesic method, it is necessary to pay attention to associated side effects, especially in elderly patients. It is unclear whether the incidence of side effects increases with age. In this study, we examined the incidence of side effects by age to confirm whether the frequency of side effects varies depending on age group.

Patients: Patients who underwent gastroenterological surgery at Hiroshima University Hospital between 2009 and 2013 and received postoperative analgesia using PCA [either epidural PCA (PCEA) or intravenous PCA (IVPCA) were included].

Measurements: The degree of pain using the visual analog scale, number of PCA requests, and frequency of side effects, including nausea, vomiting, pruritus, urinary disturbance, drowsiness, low blood pressure, delirium, and respiratory depression, was determined from PCA records.

Main Results: A total of 2,881 patients were enrolled and categorized into PCEA (n = 1,965) or IVPCA (n = 916) group based on postoperative analgesia. The incidence of delirium significantly increased with age in both groups (P < 0.001). In the PCEA group, the incidence of nausea, vomiting, and itching decreased, whereas that of hypotension significantly increased with age. Visual analog scale scores both at rest and during activity on postoperative day 2 were not correlated with age in either group. There was a significant negative correlation with age in both groups for the number of PCA requests on postoperative day 2.

Conclusions: The incidence of postoperative delirium increases with age regardless of pain relief method. Side effects related to postoperative analgesia are not necessarily more likely to occur with age.

Key words : patient-controlled analgesia, side effects, age, opioid, epidural, postoperative analgesia

Introduction

From the viewpoint of recovery after surgery, it is important to take strong measures for pain relief in the acute postoperative period. An essential tool for postoperative pain relief is patient-controlled analgesia (PCA). Intravenous PCA (IVPCA) that involves intravenous administration of opioids such as morphine and fentanyl and epidural PCA (PCEA) are effective analgesic methods. On the other hand, opioids and epidural blocks have various side effects, and when using PCA, which allocates the administration of analgesics to the patients, it is necessary to pay close attention to the occurrence of side effects; thus, monitoring is essential. We have been managing acute postoperative pain with PCA for many years. We encountered difficulties in monitoring side effects due to PCA because of time and manpower constraints. Therefore, we created an acute pain service

team in 2009, which included nurses, pharmacists, clinical engineering technicians, and anesthesiologists, to manage acute postoperative pain.¹⁾ In particular, we closely monitored side effects by collaborating with nurses. By obtaining information on the effects and side effects of PCA from patients twice a day, it was possible to detect and manage side effects promptly.

Adverse reactions in elderly patients tend to occur due to decrease in physical reserve. However, it is unknown whether the incidence of side effects due to PCA is related to age. It is also unclear whether differences in side effects that are likely to occur depend on age. Therefore, in this study, we examined the relationship between age group and the distribution of side effects to confirm whether the frequency of side effects differs with age.

Patients and Methods

After obtaining the permission of the ethical committee of Hiroshima University Hospital, patients who underwent abdominal surgery at Hiroshima University Hospital between 2009 and 2013 and who received postoperative

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analgesia using PCA were included in this study. We retrospectively assessed the following items from PCA records: pain intensity using the visual analog scale (VAS), number of PCA requests, and side effects including delirium, nausea and vomiting, low blood pressure, urinary disturbance, drowsiness, respiratory depression, and pruritus.

Patients were given intravenous anesthetics (remifentanyl and propofol) or an inhalational anesthetic (sevoflurane or desflurane) in combination with epidural anesthesia. PCEA was used for postoperative analgesia. Patients for whom epidural anesthesia was contraindicated received general anesthesia, and postoperative pain was relieved with IVPCA. Our PCA chemical solutions and pump settings are as follows: PCEA: 0.15% ropivacaine with 2 µg/mL fentanyl (for patients <80 years old) or 1 µg/mL (for patients >80 years old), background infusion rate 3 mL/h, demand dose 2 mL, and lockout interval 15 min; IVPCA: morphine (1 mg/mL), no background infusion, demand dose 1 mg, and lockout interval 5 min.

We analyzed data by categorizing patients into PCEA or IVPCA group based on postoperative analgesia. We compared the investigation items in patients divided by age (10-year intervals from the 20s to the 90s). Pearson’s correlation analysis was used to determine the relationship between the number of PCA requests or VAS score and age. The Cochran–Armitage test was used to determine the relationship between the recorded side effects and age.

Results

A total of 2,882 patients were enrolled and categorized into PCEA (n = 1,965) or IVPCA (n = 916) group based on postoperative analgesia received by them. Patient demographic data are shown in the Table. Age was significantly lower and the proportion of females higher in

the PCEA group. The distribution of each side effect against each age group in both PCEA and IVPCA groups is shown in Fig. 1. Among the side effects noted, the incidence of delirium significantly increased with age in both groups (P < 0.001). The incidence of nausea and vomiting and pruritus significantly decreased with age in the PCEA group (P < 0.001 and P = 0.008, respectively). The incidence of low blood pressure significantly increased with age in the PCEA group (P = 0.009), whereas it was significantly higher in young patients in the IVPCA group (P = 0.03). No significant changes were observed with age for urinary disturbance or drowsiness. Furthermore, VAS scores both at rest and during activity on postoperative day (POD) 2 were not correlated with age in either group (PCEA: at rest, P = 0.80; during activity, P = 0.16; IVPCA: at rest, P = 0.601; during activity, P = 0.442) (Fig. 2). There was a significant negative correlation with age in both groups for the number of PCA requests on POD 2 (PCEA, P < 0.001; IVPCA, P = 0.004) (Fig. 3).

Discussion

Among the side effects studied, delirium showed an increasing trend with age. Although pain and pain management strategies are considered important factors related to the development of postoperative delirium in elderly patients,^{2,3} VAS score was not correlated with age, and the number of requests for PCA was fewer in the elderly. These results suggested that the higher incidence of delirium in elderly patients was not associated with postoperative pain or analgesia. Advanced age has generally been indicated as a risk factor for delirium,^{4,5} and thus, aging itself may be related to this finding. Although IVPCA is related to a slightly higher incidence of delirium, the difference is clinically negligible. Therefore, epidural analgesia is not necessarily required

Age group	n		Delirium		Nausea and vomiting		Low blood pressure		Urinary disturbance		Drowsiness		Respiratory depression		Pruritus	
	PCEA	IVPCA	PCEA	IVPCA	PCEA	IVPCA	PCEA	IVPCA	PCEA	IVPCA	PCEA	IVPCA	PCEA	IVPCA	PCEA	IVPCA
20	38	21	2.6%	0.0%	63.0%	45.5%	0.0%	0.0%	13.6%	0.0%	9.1%	33.3%	0.0%	0.0%	54.5%	83.3%
30	83	71	0.0%	0.0%	38.3%	50.0%	0.0%	4.5%	6.1%	18.2%	3.0%	9.1%	0.0%	9.1%	66.7%	59.1%
40	165	104	0.0%	1.0%	43.0%	40.7%	3.0%	5.1%	11.9%	17.9%	0.0%	15.4%	0.0%	0.0%	80.6%	51.3%
50	310	123	1.3%	2.4%	39.5%	37.9%	3.3%	2.8%	15.8%	16.7%	4.2%	25.0%	0.0%	0.0%	77.5%	63.9%
60	659	241	2.0%	4.6%	29.0%	45.7%	7.6%	1.3%	20.1%	15.2%	0.7%	25.3%	0.0%	0.0%	65.8%	60.8%
70	519	255	6.2%	7.8%	35.5%	41.1%	7.5%	0.0%	18.7%	23.1%	3.7%	23.1%	0.0%	1.1%	63.6%	57.1%
80	184	95	13.6%	14.7%	25.9%	29.1%	5.9%	0.0%	16.2%	20.0%	1.5%	16.7%	0.0%	6.7%	51.5%	60.0%
90	7	6	42.9%	50.0%	0.0%	0.0%	50.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	50.0%	100.0%
p value			<0.001	<0.001	<0.001	0.15	0.009	0.03	0.11	0.31	0.49	0.54			0.008	0.91

Figure 1. Distribution of the incidence of each side effect

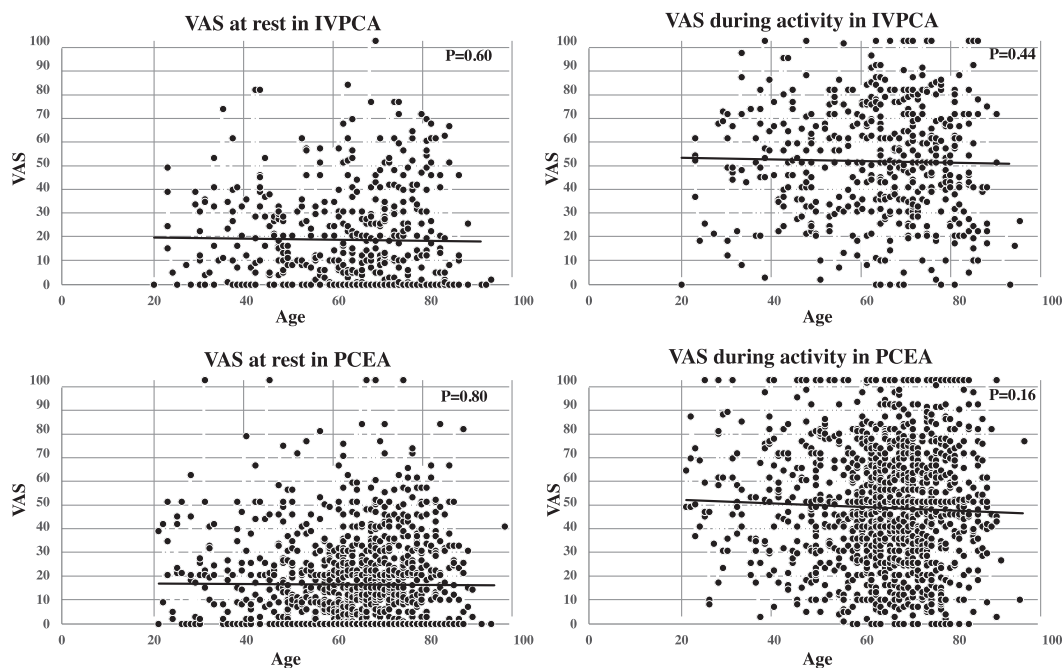


Figure 2. Relationship between Age and VAS

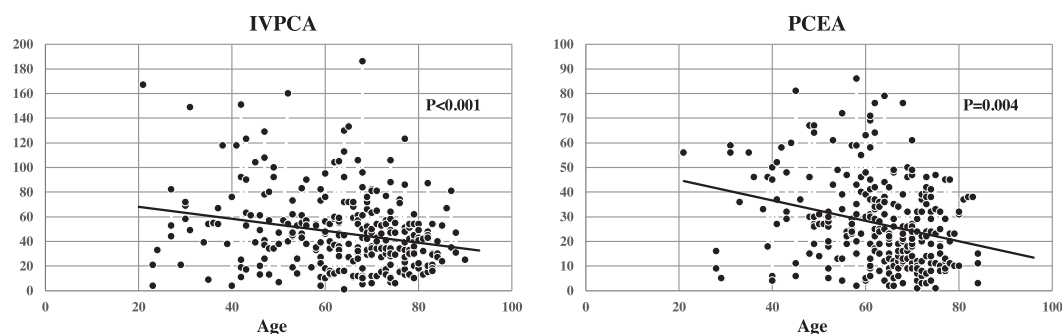


Figure 3. Relationship between Age and PCA dose request

for elderly patients just because the risk for delirium is lower. Rather, epidural analgesia can cause catheter problems when delirium occurs.

The incidence of postoperative nausea and vomiting (PONV) was significantly higher in young patients in the PCEA group. Because no significant trend was observed in the IVPCA group, this result may be related to epidural analgesia. Although local anesthetic-based epidural analgesia after gastrointestinal surgery did not affect the incidence of PONV,⁶⁾ it is possible that fentanyl is associated with the development of PONV because the drug solution we use in PCEA contains fentanyl. The reason the frequency of PONV negatively correlated with age is not clear. Moslemi et al.⁷⁾ reported no difference in the frequency of PONV in PCEA with fentanyl added to the local anesthetic and IVPCA with fentanyl for postoperative analgesia after gynecological surgery. On the other hand, Hayek et al.⁸⁾ investigated the effects of age and sex on intrathecal opioid requirements in patients

with chronic noncancer-related pain. They showed that pain and opioid requirements are significantly less in elderly patients. In our study, the overall frequency of PONV not divided by age group was almost the same in both groups, and the frequency of PONV was the same regardless of age in the IVPCA group. These results suggest that regarding the mechanism of PONV as a side effect of opioids, there may be age-dependent changes in the action of opioids at the spinal cord level. In terms of PONV, PCEA may be more efficacious in elderly patients.

Although pruritus was negatively correlated with age in the PCEA group, both groups showed high frequency of pruritus in all age groups, indicating that pruritus occurs at a considerably high rate as an adverse effect of opioids regardless of age. The incidence of opioid-induced pruritus has been reported as 10%–50% when administered intravenously compared with 30%–100% after spinal or epidural administration.⁹⁾ Regarding the incidence of pruritus, there seems to be no major difference between

either analgesic method in elderly patients.

In the PCEA group, elderly patients developed significantly more hypotension. Because both PCA setting and concentration of local anesthetic are the same in all age groups, it is conceivable that in elderly patients, blood pressure reduction due to epidural block is likely to occur due to a decrease in circulating reserve capacity. Therefore, blood pressure should be more closely monitored when using PCEA in elderly patients.

A limitation of this study is that as a retrospective study, some data in the PCA records we used may have been incomplete or unavailable. However, because of the large number of patients, we believe the results of this study have clinical significance. To the best of our knowledge, there are no studies showing the age-dependent frequency of side effects associated with IVPCA or PCEA.

In conclusion, the incidence of PONV and pruritus decreased with age, whereas that of hypotension and delirium increased with age in the PCEA group. On the other hand, the incidence of only delirium increased with age in the IVPCA group. Side effects related to postoperative analgesia are not necessarily more likely to occur in elderly patients.

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