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COMMENTARY

Use of olanzapine for the relief of nausea and vomiting in patients with advanced cancer: a multicenter survey in Japan

Keisuke Kaneishi[1] · Kazunori Nishimura[2] · Norio Sakurai[3] · Kengo Imai[4] · Naoki Matsuo[5] · Naoko Takahashi[6] · Kenichiro Okamoto[7] · Akihiko Suga[8] · Hiromi Sano[9] · Isseki Maeda[10] · Haruhiro Nishina[11] · Takuhiro Yamaguchi[12] · Tatsuya Morita[13] · Satoru Iwase[14]

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Abstract Nausea and vomiting are among the most common and distressing symptoms in patients with advanced cancer. Olanzapine, an antipsychotic agent, is known to have an affinity for multiple neurotransmitter receptors. Previous studies have reported olanzapine to be efficacious in the treatment of nausea and vomiting. Although it has been administered at a number of facilities, its applicability to treat nausea and vomiting in patients with advanced cancer is poorly understood. We investigated the use of olanzapine for nausea and vomiting in patients with advanced cancer at multiple centers. This retrospective study was carried out at seven palliative care units and three facilities with palliative care teams in Japan from 2013 to 2015. The dosage of olanzapine, treatment duration, and duration from initial use until death were collected from the medical records. One hundred and eight patients met our inclusion criteria. The average dose of olanzapine was 3.6 mg (2.5 mg, $n=61$; 5 mg, $n=46$; 10 mg, $n=1$) and average treatment duration was 18.7 days. The average duration from initial use until death was 39.0 days. There were no differences in the duration of administration until death between olanzapine doses (2.5 and 5 mg). Our results suggest that olanzapine have been used in patients with poor prognoses for nausea and vomiting in patients with advanced cancer. Conducting a prospective trial would further yield promising results.

Keywords Olanzapine · Nausea · Vomiting · Cancer · Palliative care

✉ Keisuke Kaneishi
kankannjp@yahoo.co.jp

[1] Department of Palliative Care Unit, JCHO Tokyo Shinjuku Medical Center, 5-1 Tsukudo–cyo, Shinjuku, Tokyo 162-0815, Japan

[2] Department of Palliative Care, Shimada Hospital, Fukuoka, Japan

[3] Department of gastroenterological medicine, Tokyo Rinkai Hospital, Tokyo, Japan

[4] Seirei Hospice, Seirei Mikatahara General Hospital, Hamamatsu, Japan

[5] Hospice, Medical Corporation Junkei-kai Sotoasahikawa Hospital, Akita, Japan

[6] Department of Palliative Care, Japanese Red Cross Medical Center, Tokyo, Japan

[7] Department of Palliative Medicine, Showa University Northern Yokohama Hospital, Yokohama, Japan

[8] Department of Palliative Medicine, Shizuoka Saiseikai General Hospital, Shizuoka, Japan

[9] Department of Palliative Care, Nomura Hospital, Tokyo, Japan

[10] Department of Palliative Medicine, Osaka University Graduate School of Medicine, Osaka, Japan

[11] Department of Surgery and Palliative Care Team, Koto Hospital, Tokyo, Japan

[12] Division of Biostatistics, Tohoku University Graduate School of Medicine, Sendai, Japan

[13] Palliative and Supportive care Division, Seirei Mikatahara Hospital, Hamamatsu, Japan

[14] Department of Palliative Medicine, Institute of Medical Science, The University of Tokyo, Tokyo, Japan

Purpose

Nausea and vomiting are among the most common and distressing symptoms in patients with advanced cancer. These symptoms can easily lead to loss of appetite and depression, which may result in substantial impairment to quality of life. It is important to relieve nausea and vomiting and to assess the causes of these symptoms for appropriate management [1, 2]. However, determining these causes is often complicated, and undergoing an examination is burdensome for patients with advanced cancer.

Olanzapine, an antipsychotic agent, is known to have an affinity for multiple neurotransmitter receptors, including dopaminergic (D1, D2, D3, and D4), serotonergic (5–HT2A, 5–HT2C, 5–HT3, and 5–HT6), muscarinic, histaminergic, and adrenergic (alpha1) receptors [3]. These receptors are present in the chemoreceptor trigger zone as well as the vomiting center, thus, olanzapine has potentially broad antiemetic capabilities [2, 3]. Previous studies have suggested that olanzapine may be efficacious in the treatment of nausea and vomiting related to multiple sources [4–6], especially chemotherapy–related nausea [7], with relatively few adverse effects. In addition, olanzapine is available as an orally disintegrating disk (Zydis®), which can be easily administered, even to patients with nausea and vomiting [3, 6]. For these reasons, olanzapine has been administered at a number of facilities; however, the use of olanzapine for nausea and vomiting in patients with advanced cancer is poorly understood. Each facility administers different doses of olanzapine for nausea and vomiting, and the differences in effectiveness of olanzapine doses are unclear. Thus, we conducted a retrospective study to investigate the use of olanzapine for nausea and vomiting in patients with advanced cancer at multiple centers in Japan.

Methods

This retrospective study was performed at seven palliative care units (Tokyo, Fukuoka, Shizuoka, and Kanagawa) and three facilities with palliative care teams (Tokyo, Shizuoka, and Osaka). We reviewed the medical records of patients admitted from August 2013 to March 2015 by physicians. Patients were included if they had advanced cancer and if they received olanzapine for the relief of nausea and vomiting. Exclusion criterion for this study was the presence of diabetes mellitus (administration contraindication in Japan). A total of 108 patients (61 women and 47 men) met the inclusion criteria. Data for demographic variables, disease sites, maintenance dosage, dosing periods of olanzapine, and duration from initial use until death were collected. The differences between groups were analyzed using the Mann–Whitney *U* test. Results were expressed as the mean ± SD. This study was approved by the Institutional Review Board of each facility.

Results

The average age was 66.5 years (range, 25–95 years). Within the study period, 96 (89 %) patients died, 9 patients (8 %) survived, and 3 patients were classified as status unknown. Primary tumor sites and types included the stomach ($n = 21$); lung ($n = 16$); uterus/ovary ($n = 15$); colon/rectum ($n = 11$); urinary tract/bladder ($n = 8$); pancreas ($n = 6$); liver/bile duct ($n = 7$); breast ($n = 5$); esophagus ($n = 4$); head and neck ($n = 3$); malignant lymphoma, malignant melanoma, renal, and prostate ($n = 2$); and malignant mesothelioma, angiosarcoma, thyroid, nasal sinus, brain, and unknown primary ($n = 1$). The mean dose of olanzapine administered was 3.6 ± 1.4 mg (2.5 mg, $n = 61$; 5 mg, $n = 46$; 10 mg, $n = 1$), and the total average treatment duration was 18.7 ± 19.2 days (median, 13; range, 1–94). The total average duration of first use until death was 39.3 ± 34.3 days ($n = 99$, median; 32, range 2–211). The relationship of olanzapine treatment dosage (2.5 and 5 mg), duration of administration, and duration from initial use until death is presented in Table 1. There were no significant differences in the duration of administration and duration from initial use until death between doses of olanzapine (2.5 and 5 mg).

Discussion and conclusions

This study is, to the best of our knowledge, the first to investigate the use of olanzapine for nausea and vomiting in patients with advanced cancer at multiple facilities. Our findings revealed that on average, patients

Table 1 Relationship of olanzapine treatment dosage (2.5 and 5 mg), duration of administration, and duration until death

	Dose of olanzapine		
	2.5 mg	5 mg	*p*
(Total patients population)			
N (%)	61 (56.5)	46 (42.6)	
Administration (days)	21.2 ± 21.8	15.4 ± 14.9	0.15
(Patients who died)			
N (%)	54 (54.5)	44 (44.4)	
Administration (days)	20.5 ± 20.7	15.5 ± 15.1	0.09
Period until death (days)	36.6 ± 24.9	35.5 ± 36.3	0.34

who received olanzapine for nausea and vomiting were in severe physical conditions with poor prognosis. The average duration from initial use until death was almost 1 month. This suggests that olanzapine could be also useful for patients with limited prognosis. Regardless of the severity of condition or prognosis, olanzapine could be used for an average of 2 weeks in patients with advanced cancer. Oral administration of medication is cumbersome for most patients with advanced cancer. Therefore, olanzapine (Zydis®) may be more easily administered and useful for the relief of nausea and vomiting. Moreover, it could be used for relatively long treatment duration in patients with advanced cancer who are in a severe condition. In 99 % of patients, the dose of administered olanzapine was either 2.5 or 5 mg. There was no difference in the duration of administration or duration from initial use until death by olanzapine dose. This suggests that the difference in olanzapine dosage (2.5 or 5 mg) did not make a major impact on the condition and prognosis in patients with advanced cancer.

Our study had certain limitations, including the inherent limitations of a retrospective study. It did not directly indicate the dose-dependent efficacy and safety of olanzapine, and the sample size might not have been large enough to draw valid conclusion.

We realize that our results are tentative; nonetheless, we believe that this data from over 100 patients who received olanzapine for nausea and vomiting at seven palliative care units and three facilities with palliative care teams may be useful in clinical settings. Our results identified how olanzapine was administered for nausea and vomiting in patients with advanced cancer in multiple centers. Further prospective trials are required.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no competing interests.

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