A Nationwide Survey of Japanese Palliative Care Physicians' Practice of Corticosteroid Treatment for Dyspnea in Patients With Cancer

To the Editor:

Dyspnea is one of the most common symptoms among patients with advanced cancer.[1] Corticosteroids are recommended for specific conditions such as lymphangitic carcinomatosis, superior vena cava (SVC) syndrome, and airway obstruction,[2,3] and their routine administration is not recommended, except for these indicated conditions, as per clinical guidelines.[2,3] Only few studies have examined the efficacy of corticosteroids for treating dyspnea in patients with cancer,[4,5] and their indications and administration methods have not been standardized despite these being used conventionally. Corticosteroids may also cause serious side effects.[6,7] Therefore, corticosteroid treatment for dyspnea in patients with cancer should be standardized.

As a first step for the standardization of corticosteroids treatment for dyspnea in patients with cancer, we explored current practices of corticosteroid treatment for dyspnea in patients with cancer among Japanese palliative care physicians.

Methods

We conducted a nationwide survey among palliative care physicians in Japan between September and October 2018. We identified 536 certified palliative care physicians from the Japanese Society for Palliative Medicine Web site and divided them into two groups (268 participants each) based on random selection. We administered a questionnaire about dyspnea management of ambulatory patients with cancer to one group and about dyspnea management of patients with cancer at the end-of-life stage to the other. In this letter, we focus on corticosteroid treatment for dyspnea in patients with cancer. Some results of other topics we surveyed have already been published[8] and some are in preparation for publication.

Because a specific questionnaire is currently lacking, we developed an ad hoc questionnaire based on a literature review, discussion among palliative care specialists, and results of pilot testing, including several components of physician-reported practice regarding corticosteroids for dyspnea in adult ambulatory patients with cancer expected to survive for more than several months and with dyspnea of 2–3 on the Modified Medical Research Council scale. The following practices were evaluated:

1) Indications for corticosteroids. Participants chose one from the following options: a) only for specific conditions, such as lymphangitic carcinomatosis, SVC syndrome, and major airway obstruction; b) routinely, regardless of the condition; and c) never.

The following questions were asked about each condition among lymphangitic carcinomatosis, SVC syndrome, and major airway obstruction:

2) Frequency of administering corticosteroids and administration methods (dose increment or decrement regimen). Responses were scored on a five-point Likert scale (1 = rarely and 5 = very frequently).

3) Practice details of corticosteroid administration. Participants chose one from the following options: a) dexamethasone or betamethasone, b) prednisolone, c) methylprednisolone, and d) cortisone. We also inquired about the starting and maintenance doses of corticosteroids primarily selected.

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University), a graphical user interface for R (The R Foundation for Statistical Computing). On the five-point Likert scale, responses of "frequently" and "very frequently" were analyzed with 95% confidence intervals (CIs). We also calculated the mean starting and maintenance corticosteroid doses. This study was approved by the Institutional Review Board of Konan Hospital.

Results

A total of 192 physicians responded to the questionnaire (response rate, 72%).

Indications of Corticosteroids for Dyspnea in Cancer

In total, 188 (98% [95% CI, 95–99]) respondents reported administering corticosteroids for dyspnea. However, their indications were inconsistent. A total of 125 (65% [95% CI, 58–72]) physicians responded that they administered corticosteroids for dyspnea only under specific conditions, whereas 63 (33% [95% CI, 26–40]) responded that they administered corticosteroids routinely for dyspnea.

Practice of Corticosteroids for Dyspnea in Cancer Based on Specific Conditions

Majority of physicians reported administering corticosteroids frequently or very frequently for dyspnea in patients with cancer under specific conditions—166 (87% [95% CI, 81–91]) for lymphangitic carcinomatosis, 150 (78% [95% CI, 72–84]) for SVC syndrome,

and 140 (73% [95% CI, 66−79]) for major airway obstruction.

Regarding the administration method, the proportion of participants who administered dose decrement regimens frequently or very frequently was higher than that of participants who administered dose increment regimens—125 (65% [95% CI, 58−72]) vs. 41 (21% [95% CI, 16−28]) for lymphangitic carcinomatosis, 130 (68% [95% CI, 58−72]) vs. 28 (15% [95% CI, 10−20]) for SVC syndrome, and 121 (63% [95% CI, 56−70]) vs. 29 (15% [95% CI, 10−21]) for major airway obstruction.

Regarding the corticosteroid choice, dexamethasone or betamethasone was reported as the most chosen corticosteroid, administered primarily under the dose decrement and increment regimens—152/162 (94% [95% CI, 89−97]) and 93/96 (97% [95% CI, 91−99]) for pulmonary lymphangitic carcinomatosis, 151/163 (93% [95% CI, 88−96]) and 80/83 (96% [95% CI, 90−99]) for SVC syndrome, and 142/158 (90% [95% CI, 84−94]) and 68/75 (91% [95% CI, 82−96]) for major airway obstruction, respectively.

Regarding responses on the dose decrement regimen, the mean starting and maintenance doses of dexamethasone or betamethasone were 6.5 ± 2.6 mg/day and 2.7 ± 1.3 mg/day for pulmonary lymphangitic carcinomatosis, 7.0 ± 2.7 mg/day and 3.0 ± 1.8 mg/day for SVC syndrome, and 7.5 ± 3.1 mg/day and 3.1 ± 1.6 mg/day for major airway obstruction, respectively. Regarding responses on the dose increment regimen, the mean starting and maintenance doses of dexamethasone or betamethasone were 2.4 ± 1.8 mg/day and 4.2 ± 1.9 mg/day for pulmonary lymphangitic carcinomatosis, 2.3 ± 1.6 mg/day and 5.5 ± 2.0 mg/day for SVC syndrome, and 2.9 ± 2.3 mg/day and 5.0 ± 1.9 mg/day for major airway obstruction, respectively.

Comment

To the best of our knowledge, this is the first nationwide survey among palliative care specialists examining their daily practice of corticosteroid administration for dyspnea in cancer.

The main finding of this survey was that despite the frequent administration of corticosteroids for dyspnea in cancer, their indications and administration methods varied markedly. Particularly, there was variability in whether corticosteroids should be administered only under certain conditions or routinely regardless of the cause. Two-thirds of palliative care specialists reported administering corticosteroids for dyspnea in cancer only under specific conditions, in line with recommendations in guidelines,[3] whereas one-third of them reported administering these routinely. Similarly, in one observational study of patients with cancer receiving specialized palliative care services, corticosteroids were administered for dyspnea in cancer of various etiologies, such as primary or metastatic lung cancer, pleural effusions, lymphangitis carcinomatosis, and respiratory muscle weakness.[9] These results suggest differing opinions among palliative care specialists regarding indications for corticosteroids, although guidelines recommend administering corticosteroids only under certain conditions. Because of the lack of sufficient evidence, indications of corticosteroids for dyspnea in cancer have not yet been established. In future, large prospective studies should be conducted to clarify the efficacy of corticosteroids for dyspnea in cancer of various etiologies.

Regarding the administration method, most participants selected dose decrement regimens in daily practice, wherein they started at 6−8 mg/day of dexamethasone or betamethasone and maintained at 2−3 mg/day. In a feasibility randomized control trial of dexamethasone for dyspnea in cancer, patients received 8 mg dexamethasone twice daily × four days and then 4 mg twice daily × three days,[10] which were higher doses than those in our study. Thus far, no consensus exists on the most effective and safest corticosteroid doses. These findings underline the urgent need for dose identification studies to establish a standardized treatment of corticosteroids for dyspnea in cancer.

Although almost all palliative care physicians administered corticosteroids for dyspnea in patients with cancer, their practices varied markedly, indicating that the best administration method of corticosteroids remains unclear. Future studies to identify indications and ideal doses of corticosteroids are urgently needed to establish treatment standardization for dyspnea in cancer.

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Multicomponent Compression Bandaging for Refractory Bilateral Lower Extremity Edema of Multifactorial Origin in Cancer Patients: A Retrospective Case Series

To the Editor

Edema has numerous causes[1,2] and can negatively affect mobility, comfort, quality of life,[3] and activities of daily living.[4] Treatment for edema generally consists of reversal of underlying disorder, sodium restriction, diuretics, leg elevation, and physical exercise.[1] Diuretics are often erroneously given for all forms of edema, and the long-term use of diuretics may induce chronic edema by disturbing the renin-angiotensin relationship.[5] Diuretics may cause adverse effects (e.g., hypotension or renal insufficiency) without improving edema in certain patients, including those with hypoalbuminemia and/or lymphedema.[4] These challenges highlight the need to use nonpharmacologic approaches when appropriate, rather than resorting to the immediate use of diuretics.[1] In this case series, we report the outcomes of five cancer patients who underwent multicomponent compression bandaging, a standard treatment technique recommended for lymphedema and chronic venous insufficiency, for refractory bilateral lower extremity edema (BLE) of multifactorial origin.

Methods

In this retrospective study, a physiatrist and a physical therapist tracked patients who were referred for lower extremity multicomponent compression bandaging between February 2016 and June 2018. The inclusion criteria for this study were 1) moderate to severe lower extremity edema that was refractory to the usual treatments (i.e., diuretics in combination with physical exercise), 2) referral for multicomponent compression bandaging, and 3) limb circumference measurement availability for at least two days. Of the nine patients who were referred for compression bandaging, we excluded two patients (one with lymphedema and one with chronic venous insufficiency, as noted in clinical notes) because compression bandaging is the standard of care for these conditions.[3,6,7]

J. M. T. and S. N. contributed equally. S. N. is a co-first author.

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