Original Article

Predictors of Responses to Corticosteroids for Cancer-Related Fatigue in Advanced Cancer Patients: A Multicenter, Prospective, Observational Study

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Abstract

Context. Although corticosteroids are widely used to relieve cancer-related fatigue (CRF), information regarding the factors predicting responses to corticosteroids remains limited.

Objectives. The aim of this study was to identify potential factors predicting responses to corticosteroids for CRF in advanced cancer patients.

Methods. Inclusion criteria for this multicenter, prospective, observational study were patients who had metastatic or locally advanced cancer and had a fatigue intensity score of 4 or more on a 0−10 Numerical Rating Scale (NRS). Univariate and multivariate analyses were conducted to identify the factors predicting two-point reduction or more in NRS on day 3.

Results. Among 179 patients who received corticosteroids, 86 (48%; 95% CI 41%−56%) had a response with two-point reduction or more. Factors that significantly predicted responses were performance status score of 3 or more, Palliative Performance Scale score more than 40, absence of ascites, absence of drowsiness, absence of depression, serum albumin level greater than 3 mg/dL, serum sodium level greater than 135 mEq/L, and baseline NRS score greater than 5. A multivariate analysis showed that the independent factors predicting responses were baseline NRS score greater than 5 (odds ratio [OR] 6.6, 95% CI 2.8−15.4), Palliative Performance Scale score more than 40 (OR 4.4, 95% CI 2.1−9.3), absence of drowsiness (OR 3.4, 95% CI 1.7−6.9), absence of ascites (OR 2.3, 95% CI 1.1−4.7), and absence of pleural effusion (OR 2.2, 95% CI 1.0−5.0).

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Conclusion. Treatment responses to corticosteroids for CRF may be predicted by baseline symptom intensity, performance status, drowsiness, and severity of fluid retention symptoms. Larger prospective studies are needed to confirm these results. J Pain Symptom Manage 2016;52:64−72.

Key Words
Fatigue, corticosteroids, predictors, cancer, palliative care

Introduction

Cancer-related fatigue (CRF) is the most frequently exhibited symptom by patients with advanced cancer. Moderate-to-severe fatigue was previously estimated to be present in more than 70% of patients in the last month of life, with its intensity increasing closer to death.[1]

Corticosteroids have commonly been used for symptom relief in the treatment of advanced cancer patients based largely on clinical experience,[2−5] rather than on established evidence from well-designed trials. Two randomized controlled trials recently confirmed the short-term treatment efficacy of corticosteroids in improving CRF in a palliative care setting.[6,7] A randomized, placebo-controlled trial revealed that the oral administration of dexamethasone at a dose of 4 mg twice per day improved the intensity of CRF.[6] The participants in this study were ambulatory patients with a relatively good condition in outpatient clinics for palliative care, pain management, and oncology treatment. This type of patient selection in a randomized control trial[6] may have caused a limitation for the applicability of the findings to terminally ill cancer patients, particularly those with a poorer general condition (e.g., hemoglobin < 9g/dL and life expectancy less than four weeks) who are likely to be excluded from randomized trials. Clarifying clinical effects in real-world nonselected patients and identifying the predictors of responses to corticosteroid therapy would be of great value for clinicians in day-to-day practice to provide information for clinical decisions when using corticosteroids.[8,9] However, to the best of our knowledge, the potential predictors of responses to corticosteroids for CRF have not yet been systemically explored. To date, a few large surveys have been conducted in which palliative care specialists reported that presence of fever, digestive cancer, and lung cancer were identified as the predictive factors of efficacy.[10]

The primary aim of the present study was to identify the potential predictors of responses to corticosteroids for CRF in nonselective terminally ill cancer patients receiving specialized palliative care services. We also explored the clinical effects of a corticosteroid treatment in this population.

Methods

This was a multicenter cohort study involving advanced cancer patients in Japan. All consecutive patients who received newly initiated corticosteroids for CRF were enrolled and monitored. The treating palliative care specialists in each institution decided the starting corticosteroid therapy on the basis of their clinical judgment. This study was conducted in accordance with the ethical standards of the Declaration of Helsinki and the ethical guidelines for epidemiologic research of the Ministry of Health, Labor, and Welfare in Japan and was approved by the local institutional review boards of all participating institutions.

Subjects

Study subjects were advanced cancer patients receiving specialized palliative care services at 22 sites in Japan. Patients were enrolled consecutively from August 2012 to November 2014.

Patients were eligible if they were 20 years or older, had a histologically, cytologically, or clinically confirmed malignancy, had metastatic or locally advanced cancer, were receiving specialized palliative care services (i.e., admitted to inpatient palliative care units or referred to a palliative care consultation team), had a fatigue intensity score of 4 or more on a 0−10 Numerical Rating Scale (NRS) (worst during the last 24 hours, 0 = no fatigue to 10 = worst possible fatigue), and initially receiving corticosteroid therapy for fatigue. We chose a cutoff point of four as an inclusion criterion based on a previous study in which this cutoff point was suggested to indicate moderate fatigue.[11] Patients were excluded if they were unable to report NRS because of delirium, dementia, or organic brain disorders, had contraindications to corticosteroids, or had already received corticosteroids for any reasons.

Study Design and Procedure

In this multicenter, prospective, observational study, measurement variables were recorded at two time points as a part of routine practice: baseline (day 1) and in the evening on day 3 after the administration of corticosteroids. If patients were unable to answer NRS on day 3, the reason was recorded: progression