The use of a responder analysis to identify differences in patient outcomes following a self-care intervention to improve cancer pain management

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Abstract

Previously, we demonstrated, in a randomized clinical trial, the effectiveness of a psychoeducational intervention to decrease pain intensity scores and increase patients' knowledge of cancer pain management with a sample of oncology patients with pain from bone metastasis. In the present study, we evaluated for changes in mood states (measured using the Profile of Mood States), quality of life (QOL; measured using the Medical Outcomes Study Short Form-36 (SF-36)), and pain's level of interference with function (measured using the Brief Pain Inventory (BPI)) from baseline to the end of the intervention first between the intervention and the standard care groups and then within the intervention group based on the patients' level of response to the intervention (i.e., patients were classified as non-responders, partial responders, or responders). No differences were found in any of these outcome measures between patients in the standard care and intervention groups. However, when patients in the intervention group were categorized using a responder analysis approach, significant differences in the various outcome measures were found among the three respondent groups. Differences in the physical and mental component summary scores on the SF-36 and the interference items on the BPI, among the three respondent groups, were not only statistically significant but also clinically significant. The use of responder analysis in analgesic trials may help to identify unique subgroups of patients and lead to the development of more effective psychoeducational interventions.
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1. Introduction

Numerous studies have documented the undertreatment of cancer pain and its negative consequences on patient's mood, functional status, and quality of life (QOL; (Cleeland et al., 1994; Glover et al., 1995; Burrows et al., 1998; Cleeland, 1998)). However, the number of randomized clinical trials (RCTs) that have tested the effectiveness of patient interventions to improve cancer pain management is extremely limited (for reviews see Allard et al., 2001; Miaskowski, 2003; Miaskowski, 2004) given the fact that 50% of oncology outpatients and 80–90% of patients in the terminal stages of cancer experience moderate to severe pain (Miaskowski et al., 2005).

In 2004, we published the results of a RCT that demonstrated the effectiveness of a psychoeducational

intervention called the PRO-SELF[©] Pain Control Program compared with standard care to decrease pain intensity scores and improve analgesic prescriptions in oncology outpatients with pain from bone metastasis (Schumacher et al., 2002b; West et al., 2003; Kim et al., 2004; Miaskowski et al., 2004). To date, this is the only intervention study that has resulted in both statistically and clinically significant reductions in pain intensity scores, statistically significant improvements in the number of appropriate analgesic prescriptions (i.e., more prescriptions of around-the-clock with as needed opioids), and statistically significant increases in patients' knowledge regarding pain management.

Recent work under the auspices of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) identified important core outcomes for studies of chronic pain (Turk et al., 2003; Turk and Dworkin, 2004). In addition to pain intensity scores, measures of pain's level of interference with function, mood, and QOL should be included in an evaluation of the effectiveness of an intervention for chronic pain. In the above mentioned RCT of a cancer pain management intervention (Miaskowski et al., 2004), these additional outcomes were evaluated at the beginning and at the end of the 6-week intervention. Initial comparisons of changes in mood states, QOL, and pain's level of interference with function between the standard care and the intervention groups failed to demonstrate significant treatment effects.

However, in a recent paper, Dionne and colleagues (Dionne et al., 2005) suggested that the use of "responder approaches in analgesic studies" might offer another valid, reliable, and clinically meaningful way to analyze data from RCTs. These approaches may address important differences at the level of the individual than are traditionally described using summaries of group means and standard deviations. Therefore, the purposes of this study, in a sample of oncology outpatients with pain from bone metastasis who received the psychoeducational intervention, were: to evaluate for changes in mood states, QOL, and pain's level of interference with function from baseline to the end of the intervention based on the patient's response to the intervention (i.e., patients were classified as non-responders, partial responders, or responders). Data on changes in these outcome measures, between the standard care and intervention groups, are presented for comparative purposes.

2. Methods

2.1. Sample and settings

Two hundred and twelve oncology outpatients, who were experiencing pain from bone metastasis, were recruited from seven outpatient settings in Northern California (i.e., a university-based cancer center, two community-based oncology practices, one health maintenance organization, one outpatient radiation therapy center, one veteran's affairs facility, one military hospital). The participants were adult oncology outpatients (>18 years old) who were able to read, write, and understand English. All participants had a Karnofsky Performance Status (KPS) score of ≥50; an average pain intensity score of ≥2.5; and radiographic evidence of bone metastasis. The study was approved by the Human Subjects Committee at the University of California, San Francisco, and at each of the study sites. All of the patients and family caregivers signed a written informed consent.

2.2. Intervention

Specific details of the study procedures are described elsewhere (Schumacher et al., 2002a; West et al., 2003; Miaskowski et al., 2004). In brief, patients were approached in the outpatient setting by a recruitment nurse who explained the study and obtained written informed consent. Patients were stratified by site and on the basis of whether they participated by themselves or with a family caregiver. Both patients and clinicians at the study sites were blinded to the patient's group assignment. Patients were randomly assigned to either the PRO-SELF[©] or the standard care group. At the time of enrollment, patients completed a demographic questionnaire, the KPS score (Karnofsky, 1977), and for one week before the first study visit, patients rated their level of pain intensity on a daily basis.

Patients in the standard care group received the patient version of the Cancer Pain Guideline published by the Agency for Health Care Policy and Research (AHCPR) (Jacox et al., 1994) and were seen by a research nurse in their homes at weeks 1, 3, and 6. Telephone interviews were conducted at weeks 2, 4, and 5. The focus of the visits and phone calls was on monitoring the patients' level of adherence with completing the Pain Management Diary.

Patients in the PRO-SELF[©] group received the psychoeducational intervention by a different group of specially trained oncology nurses. At week 1, the PRO-SELF[©] nurse conducted the academic detailing session with the patient and the family caregiver (Avorn and Soumerai, 1983; Soumerai and Avorn, 1990). This academic detailing session was tailored to meet the individual learning needs of the patient and family caregiver based on their responses to a knowledge and attitude survey about cancer pain management (Ferrell et al., 1993). The nurse identified the specific areas of knowledge deficit and focused the education in these areas. In addition, patients were given written instructions regarding pain and side effect management; were taught how to use a weekly pillbox; and were taught how to use a script to assist them in communicating with their physician or nurse about unrelieved pain and the need for a change in their analgesic prescription (West et al., 2003).

During weeks 2, 4, and 5, the PRO-SELF[©] nurse contacted patients in the intervention group by phone and reviewed their pain intensity scores and medication intake. The educational content of the PRO-SELF[©] Program was reinforced and patients were coached about how to modify their pain management plan or how to contact their physicians or nurses to improve pain outcomes. Most of the coaching took place during the phone calls and follow-up visits. The PRO-SELF[©]