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Evaluation of the quality of care of elderly patients with chronic and breakthrough pain treated with opioids: SAND study

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Transparency statement

Declaration of funding

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Declaration of financial/other interests

AJJ and AS-Y belong to the Medical Department of Kyowa Kirin Farmacéutica, S.L.U. BS was hired by the Andalusian Foundation for the Treatment of Pain, to conduct the design, monitoring, statistical analysis, and management of the publications of the study. Remaining authors have no relationships to be declared. CMRO peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Author contributions

MJR and LMT participated in the design, inclusion of patients and drafting of the paper. RdIT, JO, JMT, DB, AJJ and AS-Y critically revised the paper for intellectual content. BS designed the study, completed the quality control and the statistical analysis of the study and drafted the paper. All authors approved the version to be published and agree to be accountable for all aspects of the work.

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OBJECTIVE:
The objective of this study was to evaluate the quality of care of elderly patients with treatment for chronic pain (CP) and breakthrough pain (BTP).

METHODS:
A cross-sectional observational study was conducted in 20 pain units, selecting patients aged 70 years or older with baseline controlled CP in treatment with opioids and a diagnosis of BTP. Patients were classified as first episode of BTP or patient in follow-up. The patients completed the SF-12 quality of life questionnaire, Brief Pain Inventory, Lattinen Index, and Edmonton Symptoms Assessment Scale. The patient’s satisfaction with the treatment was evaluated through a visual analogue scale (VAS).

RESULTS:
A total of 199 patients were included with 67.7% women (132). Attending the first visit for BTP were 28.5% (55) and 71.5% (138) were on follow-up visits. Below the mean score for the Spanish general population on the physical component of the SF-12 was 95% and 44% below the mean score on the mental component. Worse scores were observed for women in the bodily pain dimension (p=0.032) and in the overall physical component (p=0.045). Patients satisfied with the treatment for BTP were 62.9% (112). In the multivariate analysis, SF-12 physical component scores (p=0.017) and patient’s satisfaction with BTP treatment was better in follow-up visits (p=0.031).

CONCLUSIONS:
All clinical parameters compared between first visit for the treatment of BTP and follow-up visits have been improved, so the quality of care was considered also improved. Elderly women and non-oncologic patients were observed as the population with worse symptom control.

Keywords: Quality of life; Elderly; Breakthrough pain; Satisfaction.
INTRODUCTION

The International Association for the Study of Pain defines chronic pain as "pain that persists beyond the normal healing time of tissues, which is supposed to be three months".1-3 Because of the differences observed in pain characteristics and responses to treatment, two groups of patients with chronic pain can be defined: oncological and non-oncological.

Pain is one of the most common symptoms in cancer patients, and its prevalence varies depending on the stage of the disease.4 Chronic non-oncological pain presents mainly in patients with degenerative joint pathologies and neuropathic syndromes. Its prevalence in the general population varies between 1 and 12%, mostly in middle-aged patients, with no differences between genders or races. The pathologies that produce more disability or dysfunction are lumbago and cephalalgia. The economic consequences of chronic pain are significant, being one of the main causes of disability.5-7

The most affected by chronic pain are the elderly, due to the higher prevalence of chronic, degenerative, and oncological diseases in this age group. Consequently, due to the aging of the population, it is expected that the prevalence of chronic pain will also increase in the coming years.

In patients with chronic pain, a type of pain known as breakthrough pain (BTP) is frequently observed. BTP is defined as a "transitory exacerbation of pain that appears spontaneously or related to a particular trigger, predictable or unpredictable, despite the existence of a stable and adequately controlled baseline pain".8 BTP is a clinical entity with a relatively recent definition (1990), whose recognition has permitted to improve diagnostic and therapeutic approaches.

In cancer patients, BTP prevalence increases as the disease progresses, worse the functional status and if osseous and plexus structures are affected because of tumor expansion, reaching figures of up to 66%. The appearance of BTP as been recognized as an indicator of poor prognosis.9-11

BTP has a very significant repercussion on the quality of life of patients and is also associated with a higher usage of health care resources consumption.12-14

Due to the extensive etiological diversity of BTP, its treatment should need a multiple approach. Opioids have been described as the main pain-crisis-relief factor in 44.61% of patients, 26-44% finds relief through avoidance of the event that causes the pain, but 12-20% do not seem to find adequate relief with pharmacologic or non-pharmacological treatments.14

Despite the numerous therapeutic options for the treatment of BTP, it is common that up to 77% of patients are undiagnosed or are not adequately treated.15

There is little information available about the long-term use of opioids for BTP due to the limited temporal design in clinical trials.16 Data regarding the current management of BTP in oncological and non-oncological patients are also limited. Consequently, it is necessary to obtain more information from real-life clinical practice, with respect to the management of patients with BTP and its results in terms of quality of life.

Due to the aging of the population and the increase in life expectancy, the prevalence of symptoms associated with cancer and chronic and degenerative diseases, such as chronic pain, will rise in the next decade. It is important that with this increase in life expectancy, the
preservation of the quality of life of patients and greater satisfaction with the treatment received should become in priorities for their daily management. These aspects can be considered indicators of the quality of medical care, as a direct consequence of proper control of patient’s symptoms. However, these parameters are not usually taken into account by health professionals. Therefore, the objective of this study was to assess the quality of care of elderly patients with chronic pain and associated BTP, determined by assessing their quality of life and their satisfaction with the treatment they received at the time of the visit, and compare the results between those attending for the first time for BTP control and those being on follow-up of the treatment, so we can verify if the quality of care has globally been improved.

MATERIALS AND METHODS

Study design and ethical standards

A cross-sectional observational study was designed. Patients were included between May 2015 and March 2016. The Coordinating Committee on Ethics in Biomedical Research of Andalusia approved the project. All patients received information about the study and agreed to participate by signing the consent form. The basic ethical principles contained in the latest version of the Declaration of Helsinki were followed.

Specialists belonging to 20 pain units in Spain participated in the study. The researchers completed in the case report form the information of the study, preserving the anonymity of the patients only identified by an order-of-inclusion number.

Selection criteria

The patients were included consecutively by selecting at least the first 10 cases attending the center and who met the selection criteria. The source of the data was the clinical history of the patient and the data collected at the selection visit. No complementary tests were requested for the study. Patients had to be ambulatory, of any race and gender, older than 70 years, with chronic baseline pain history for more than six months, and on treatment with opioids. The baseline pain had to be adequately controlled at the time of selection, with a score less than or equal to 4 on the visual analogue scale (VAS), graded from 0 (no pain) to 10 (maximum pain). Patients must have been diagnosed of BTP following the definition of Portenoy and the Association of Palliative Medicine, being the first diagnosis of BTP in the visit of the study otherwise the patient was on follow-up. Patients with cognitive impairment severely affected by their underlying disease, not collaborating, or unable to complete the necessary data for the study by themselves or with help were excluded.

Sociodemographic and clinical variables

The patient’s date of birth, gender, and socioeconomic level (low, middle, or high) was recorded. The weight and height of the patient was determined at the time of the visit.

Information about the clinical history of the patient and the currently administered treatments were collected. From this information, the patient was classified as oncological or non-oncological, based on whether there was a history of cancer. The type of chronic pain (somatic, visceral, neuropathic, mixed, or unknown) and the main cause of the chronic pain (tumor, spinal problems, trauma, complex regional pain syndrome, arthrosis, peripheral neuropathy, or other) were recorded. Information about 10 main characteristics of BTP was
collected, as described in Table 2, plus the average number of episodes and their duration.

**Assessment of the study objectives**

Patients were classified into two groups as if they attend the center for the first BTP diagnosis of it was a follow-up visit for BTP control.

The SF-12v2 questionnaire was used to assess the quality of life. This is a short version of the SF-36 Health Questionnaire with 12 questions. The score-specific program of the authors of the questionnaire was used for the analysis, (QualityMetric Health Outcomes™ Scoring Software 4.5), obtaining the scores of the eight dimensions and the two summary scores of the physical and mental components. The population normal values used for the comparisons were those of the United States of America (USA) as has been published that no significant differences in the normal values exists among both countries. A patient was considered to be at risk of depression when the mental component score (MCS) of the SF-12v2 was less than or equal to 42 points. This cut-off was the result of the comparison of the MCS scores with a short form of CESD (Center of Epidemiologic Studies Depression scale) and the NIMH (National Institute of Mental Health) Diagnostic Interview Schedule (DIS) criteria for clinical depression. Using the receiver operating curve analysis, the sensitivity and specificity across the full range of MCS scores were evaluated and were found the best all-around cut-off for the MCS at scores of 42 or below.

The patient’s satisfaction with the treatment received for chronic pain and BTP at the time of the visit was evaluated using a VAS, graded from 0 to 10 points, where the value 0 represented the expression “Not satisfied” and the value 10, “Very satisfied”. The patient was asked about his/her satisfaction with the treatment of chronic pain and BTP. If the VAS score was less than 5, the patient was asked to indicate the main cause of his/her dissatisfaction (the pain does not relief, I have difficulty with the dosage, the treatment produces adverse effects or other causes).

Patients completed the Brief Pain Inventory (BPI) to assess pain intensity and the impact on patient functionality. Two dimensions were assessed in the BPI: 1) **pain intensity**, evaluating the maximum and minimum pain, the average pain, and the current pain, on a scale of 0 to 10, where the value 0 represented no pain and the value 10 the maximum pain; and 2) **the impact on activities of daily living**, that measured how seven daily activities were affected, including general activity, mood, walking ability, normal work, relations with other persons, sleep, and enjoyment of life. This dimension was scored as the mean score of the seven questions.

The Lattinen Index (LI) is a recently validated, widely used tool for the evaluation of pain in the Spanish-speaking world, consisting of five Likert subscales graded from 0 to 4, that scored pain intensity, pain frequency, consumption of analgesics, degree of disability, and hours of sleep. The score for each dimension and the total score—the sum of the scores for each of the dimensions—were obtained. The minimum score could be 0, with a maximum of 20 points; the higher the score was the worse the state of the patient.

The Edmonton Symptoms Assessment Scale (ESAS) was used to evaluate the control of symptoms associated, including pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, dyspnea, and insomnia. The evaluation was referred to the last 24 hours. Symptom control was considered adequate when the symptom score was less than or equal to 4 points on a 10-point scale, where a value of 10 represented the highest intensity of the symptom. A patient was considered to be adequately controlled when the score was less than
or equal to 4 points in all 10 symptoms.\textsuperscript{24-25}

\textbf{Treatment}

This was a non-interventional study; therefore, the selected patients received treatment and/or medical care for their clinical condition according to the clinical criterion of the specialist. Information was collected on current treatments for chronic pain and BTP, as well as regarding any medications the patient was receiving at the time of the visit.

\textbf{Sample size calculation}

The population normal value of the physical component of the SF-12 questionnaire for subjects between 65 and 75 years old was estimated to be 45.05 points for Spanish population, with a standard deviation (SD) of 10.17.\textsuperscript{26} Considering the null hypothesis that there were no differences in the scores of the physical component of the SF-12 questionnaire between the subjects included in the study and the population norm for subjects of the same age, with a two-tailed alpha significance level of 0.05, a sample of 199 patients had 88.8\% power to detect significant differences in the mean score. The calculation was performed considering a difference of 4.6 points as being significant.

\textbf{Statistical analysis}

A descriptive analysis of the variables included in the study was completed with a frequency and percentage distribution for the qualitative variables, and calculation of mean, standard deviation, minimum, and maximum for the quantitative variables. The comparisons between qualitative variables were performed using Fisher’s exact test or Chi-square test. Student’s t-test was applied for the comparisons of independent groups in the quantitative variables. When the differences in the quality of life or the satisfaction of the patient as a function of different characteristics were evaluated, the factorial analysis of variance model was applied, implementing Bonferroni or Games-Howell correction, depending on the homogeneity of the variances, for the control of the error from multiple comparisons. For the analysis of the SF-12 questionnaire, the analysis-specific program of the owners of the questionnaire was applied.\textsuperscript{19}

An exploratory multivariate linear regression analysis was performed in which the variables gender, socioeconomic level, oncological or non-oncological patient, intensity of BTP, and type of visit (first visit or follow-up) were included to assess their relationship with the VAS scores of the patient’s satisfaction with the treatment for chronic pain and BTP, and the physical and mental components of the SF-12v2, which were considered in each three equation as dependent variables.

The significance level was set at 0.05. The statistical software SPSS 14.0 was used for the analysis.
RESULTS

Two hundred one patients were included in the study, with 199 patients being valid for the analysis. Each center included an average of 11 patients (95% CI 7–15), with a median of 10 patients.

Demographic data and medical history

Relating the sex, 32.3% were men (63) and 67.7% women (132), with a mean age of 77 years (95% CI 76.6–78.1) without differences between genders. For 62% (119), the socioeconomic level was middle, followed by low for 25.5% (49) and high for 12.5% (24).

The body mass index (BMI) was higher in women (p = 0.002), with a mean difference of 2.08 kg/m$^2$ (95% CI 0.78–3.39), being 27.3 kg/m$^2$ in men (95% CI 26.4–28.3) and 29.4 kg/m$^2$ in women (95% CI 28.5–30.3). The BMI could not be determined in nine patients (4.5%). Overweight was observed in 40.5% (77) were overweight, with a BMI greater than 25 and less than or equal to 30 kg/m$^2$, and 36.3% (69) were obese, with a BMI greater than 30 kg/m$^2$. No differences were observed between men and women in the proportion of patients within overweight and obese categories.

Table 1 summarizes the proportion of patients with history of disease according to gender. Significant differences were observed in the proportion of genitourinary (p < 0.0001) and oncological (p < 0.001) history, with a higher proportion in men. A greater proportion of women had allergic history (p = 0.025).

In total, 85.4% (170) of the patients were non-oncological, and the remaining 14.6% (29) oncological. In these patients, the time since tumor diagnosis was 4.4 years (95% CI 2.2–6.6), with a median of 2.6 years and a range of 0.08 to 18.6 years.

Among the patients included in the study, 28.5% (55) consulted as a first episode of BTP, and 71.5% (138) were on a follow-up visit for BTP control. In six patients, these data were not recorded (3%). No differences were observed in neither demographic nor clinical history between first episode of BTP visits or patients in follow-up.

Characteristics of chronic pain

The most common cause of chronic pain was spinal problems in 41.2% (73 cases), followed by osteoarthritis in 34.5% (61 patients), tumor in 10.2% (18 cases), peripheral neuropathy in 5.6% (10 cases), complex regional pain syndrome in 1.1% (two patients), trauma in 0.6% (one patient), and other causes in 6.8% (12 patients).

The most common type of chronic pain was mixed in 53.3% of the cases (104), followed by somatic pain in 31.8% (62 cases), neuropathic pain in 10.8% (21 cases), and visceral pain in 4.1% (8 cases). Somatic pain occurred more often in non-oncological patients, 34.7%, versus 10.3% in oncological patients (p < 0.05). No significant differences were observed among the remaining types of pain between oncological and non-oncological patients. No differences were observed between first episode of BTP visits or patients in follow-up.

Characteristics of BTP

Table 2 summarizes the characteristics of BTP in non-oncological and oncological patients. The
mean number of episodes of BTP per day was 3.2 (SD 2) in the total group of patients, with a
mean duration of 31.7 minutes (SD 34.3).

Significant differences were observed in the location of BTP (p < 0.0001), with the
head/face/mouth and abdomen the most common locations in the oncological patients.

The intensity of BTP was severe in 66.9% of non-oncological patients, whereas in oncological
patients was 44.8% (p < 0.05). BTP appeared more frequently during the daytime in non-
oncological patients compared with oncological patients (64.9% versus 44.8%, respectively, p <
0.05). The somatic type of BTP was more frequent in non-oncological patients, and the mixed
type was more frequent in oncological patients (p = 0.005).
No differences were found between patients in the first visit for BTP or in follow-up visits for
BTP.

**Treatments for chronic pain and BTP**

In 170 patients (85.4%), a single active ingredient was administered to treat chronic pain. In 27
patients (13.6%), two active ingredients were administered, and in six patients (3%), three
active ingredients were administered.

Treatments administered in monotherapy for chronic pain were: oxicodone 31.2%
(53), fentanyl 25.3% (43), tapentadol 23.5% (40), tramadol 8.8% (15), buprenorphine 6.5% (11),
oxicodone/naloxone 2.9% (5), morphine 1.2% (2) and hidromorphone 0.6% (1). Other
associated medications administered for chronic pain were: celecoxib (1), clonazepan (1),
etoricoxib (2), ibuprofen (1), metamizol (2), paracetamol (5), pregabaline (3).

For the treatment of BTP, 170 patients (85.4%) received only one active ingredient. In 15
patients (7.5%), two active ingredients were administered, and in two patients (1%), three
active ingredients were administered.

The most frequently administered drug for BTP, and in monotherapy was fentanyl in 79.4%
(135 patients), with sublingual being the most common route of administration (89.6%); followed by tramadol in 9.4% (16 patients); oxycodone in 3.5% (six patients); metamizol in
2.9% (five patients); dexketoprofen and morphine in 1.2% each (two patients); and diclofenac,
naproxen, and acetaminophen in one patient each.

**Evaluation of quality of life**

Table 3 shows the scores obtained in the SF-12v2 questionnaire by gender in the physical and
mental component, and each dimension. Significant differences were observed between men
and women in the scores of the bodily pain dimension (p = 0.032), 2.9 points lower in women
(95% CI 0.3-5.5), and the overall score of the physical component (p = 0.045, with differences
of 2.5 points (95% CI 0.06-5). Figures 1 and 2 show the scores of the physical and mental
components observed in the study, compared with the normal population score (2009,
Normative values USA) 15 per age group (Figure 1) and per gender (Figure 2). Below the normal
population values in the physical component of the SF-12v2 were 95% of the patients, 4%,
within the normal range, and 1% above the normal range. In the mental component, 44% were
below the population values, 26% within the normal range, and 30% above the normal range.

Forty percent of the patients were at risk for depression, compared with 20% in the healthy
population16. This proportion was 31% for men and 43% for women of the study, compared
with 16% and 22%, respectively, in the normal population.
An exploratory multivariate linear regression analysis was performed in which the variables gender, socioeconomic level, oncological or non-oncological patient, intensity of BTP, and type of visit (first visit or follow-up) were included (Table 4). The physical and mental components scores of the SF-12v2 questionnaire were analyzed in two equations as a function of these parameters. Patients who attended a follow-up visit had an improved physical component score in the SF-12 v2 (p = 0.017), improving their satisfaction by 3.2 points on average (95% CI 0.6-5.8). Higher intensity of BTP was related to a worse physical component score (p = 0.01). No significant differences were observed in the mental component of the SF-12v2.

**Evaluation of the patient’s satisfaction with treatment**

32.7% (64) were not satisfied with the treatment for chronic pain, 37.1% (66 patients) were not satisfied with the treatment for BTP. VAS mean score for satisfaction with CP treatment was 6.1 (IC95% 5.8-6.4), and 5.8 (IC95% 5.4-6.1) for the VAS of satisfaction with the treatment for BTP. No differences between genders or the oncological or non-oncological groups were observed. The main cause of dissatisfaction with the treatment of chronic pain was the lack of efficacy in 81.8% (36 patients), difficulties with the dosage or the appearance of adverse effects, both reasons in 9.1% (four patients). The main cause of dissatisfaction with the treatment for BTP was also the lack of efficacy in 82.2% (37 patients), other causes in 11.1% (five patients), and the occurrence of adverse effects in 6.7% (three patients).

Patients were grouped according to the treatment received for chronic pain or for BTP in patients treated in monotherapy with fentanyl or with other drugs. The degree of satisfaction of patients treated with fentanyl for BTP was significantly better (p <0.0001), with a difference of 2 points on the VAS (95% CI 1.2-2.8).

An exploratory multivariate linear regression analysis was performed, in which the variables gender, socioeconomic level, oncological or non-oncological patient, intensity of BTP, and type of visit were included (Table 4). The degree of satisfaction with the treatment for BTP was analyzed as a function of these parameters. Patients in follow-up visit were more satisfied with the treatment for BTP (p = 0.031), improving their satisfaction by 1 point on average (95% CI 0.1-1.9). Oncological patients were also more satisfied with the treatment received for BTP (p = 0.004), with a difference of 1.6 points (95% CI 0.5-2.6) compared with non-oncological patients.

**Evaluation of patient’s functionality – BPI and LI**

No significant differences were observed in the mean scores of the two dimensions of BPI between genders or between oncological and non-oncological patients, or for the patients in first visit for BTP or in follow-up visits. The intensity of pain dimension had a score of 5.17 points (95% CI 4.93-5.4) in the total group of patients. The mean score of the BPI dimension impact on activities of daily living was 5.75 points (95% CI 5.45–6.04).

The LI was 8 points (95% CI 7.6-8.3), with a median of 8 points, a minimum of 2 points, and a maximum of 14 points. Scores were not collected from four patients (2%). Significant differences between men and women were observed, with scores 1.3 points (95% CI 0.6-2) higher in women than in men (p < 0.0001). There were no differences in the scores between oncological and non-oncological patients, nor between first visits for BTP or follow-up visits.
Evaluation of symptoms control – ESAS

Figure 3 shows the proportion of patients in whom each symptom evaluated on the ESAS was considered controlled per gender if the patient was oncological or non-oncological. Control of all symptoms was achieved in 8.6% of the patients (17 patients). No significant differences were observed between men and women or between oncological and non oncological patients or for the patients in first BTP visit or in follow-up visits.

The mean score of the VAS scale for pain in the last 24 hours in ESAS scale resulted lower for the patients in follow-up compared with patients in first visit (mean difference 0.9, 95%CI 0.1-1.6).

DISCUSSION

The study was conducted with the objective of evaluating the quality of care of our patients with BTP, using indirect and complex measures such as the assessment of quality of life and satisfaction with the treatment. Quality of life questionnaires are multidimensional, evaluating the physical and mental component of the quality of life of each individual patient. The evaluation of the patient’s satisfaction with treatment integrates the patient’s assessment of efficacy, safety, ease of use, and other difficult-to-quantify aspects.

The results of the SAND study present a scenario of an elderly patient who comes to the pain unit for the control of BTP: most such patients are women, of middle socioeconomic level, non-oncological, with chronic pain. The study also provides information about the return of patients to our clinic, where 71.5% were patients in follow-up visits for BTP control and 28.5% were new cases of BTP. Mixed pain was the most prevalent type of pain (53.3%), followed by the somatic type (31.8%), the latter being more frequent in non-oncological patients. Chronic pain in the spine or arthrosis constituted 75.7% of the consultations for pain.

The characteristics of BTP are comparable to those published in the scientific literature.10,14 We observed no major differences in the characteristics of oncological BTP compared with non-oncological patients. BTP in non-oncological patients appeared more frequently during the daytime and this could have great impact on the quality of life, particularly on their functionality.

85.4% of the patients received monotherapy treatment for BTP. This finding allowed us to select patients treated with monotherapy and to analyze the patients’ satisfaction in relation to a particular treatment. Patients who received treatment with fentanyl for BTP were more satisfied with the treatment. Only 37.1% were not satisfied with the treatment for BTP. The main cause of dissatisfaction was the lack of efficacy, followed by the appearance of adverse effects.

This study enabled us to identify the group of patients who require greater attention in our clinics, through the results of the quality of life evaluation. Women obtained worse scores in the bodily pain dimension and in the overall score of the physical component; both are aspects that can be improved with further intensification in the treatment of the pain. This greater deterioration was also observed through the LI. Among the patients in the SAND study, 95% were found to be below the SF-12v2 quality of life scores in the physical component and 44%, in the mental component. The proportion was higher in women in both dimensions (98% vs. 92% and 47% vs. 38%). Based on the results of this evaluation, we consider that the patient with chronic pain and BTP experiences a great deterioration in his/her quality of life that resulted worse than healthy subjects of the same age group (Figures 1, 2). There is a direct relationship between the deterioration of the quality of life and consumption of economic...
resources for patient management, and therefore, the economic repercussions of caring for these patients are higher.

It is important to emphasize that 40% of the patients in the SAND study were at risk for depression, compared with 20% of the population of the same age. This result reflects that it is important to recognize the depression in the patients and attend to this need with multidisciplinary treatment, as well as to control all their symptoms associated with pain as these symptoms may have a major impact on the quality of life of the patients. As it was observed, the control of all symptoms was achieved in only 8.6% of the patients, as shown in Figure 3, and the proportion of each symptom controlled in the patients was mostly lower in women. Although these data are not statistically significant when evaluated individually, as a whole, this factor can negatively influence the multidimensional assessment of the quality of life and the patient’s satisfaction with the treatment received.

The cross-sectional design of the study limits the comparison of the quality of life and satisfaction within the patients, as we are comparing different patients in the first visit for the treatment of BTP with other patients in follow-up, as aggregate data. The approach was only exploratory to get quick information to verify if the population of BTP patients improved in these parameters when were treated in our clinics. No information about the time of evolution of BTP in patients in follow-up visits was collected, so the analysis did not control this factor. The design also helped to identify the patient who needs more attention that resulted in elderly women and non-oncological patients. It is needed prospectively designed studies for the verification of the improvement of the patients and their quality of care for each particular case.

In conclusion, we observed that in the follow-up visits the SF-12 physical component and the satisfaction with the treatment of pain improved; however, more attention is required to improve the mental component and risk of depression, especially in the women who come to our clinics. The control of the symptoms associated with chronic pain need to be improved. Future studies are necessary to prospectively assess whether therapeutic protocols improve pain control and overall satisfaction in our patients.
References:


Table 1. History of disease by patient’s gender.

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</tr>
<tr>
<td>Hematologic</td>
<td>4</td>
<td>6.3</td>
<td>10</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>3</td>
<td>4.8</td>
<td>8</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>7</td>
<td>11.1</td>
<td>26</td>
</tr>
<tr>
<td>Surgery</td>
<td>28</td>
<td>44.4</td>
<td>55</td>
</tr>
<tr>
<td>Allergy**</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Oncologic*</td>
<td>18</td>
<td>28.6</td>
<td>11</td>
</tr>
</tbody>
</table>

N: Number of patients; * Statistically significant difference p<0.0001; **Statistically significant difference p=0.025.
Table 2. Breakthrough Pain characteristics in oncologic and non-oncologic patients.

<table>
<thead>
<tr>
<th></th>
<th>No-onologic</th>
<th>Oncologic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>BTP status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First episode</td>
<td>50</td>
<td>32.1</td>
<td>8</td>
</tr>
<tr>
<td>Follow up</td>
<td>106</td>
<td>67.9</td>
<td>20</td>
</tr>
<tr>
<td>BTP location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td>1</td>
<td>0.6</td>
<td>2</td>
</tr>
<tr>
<td>Cervical</td>
<td>8</td>
<td>5.1</td>
<td>0</td>
</tr>
<tr>
<td>Shoulder</td>
<td>3</td>
<td>1.9</td>
<td>0</td>
</tr>
<tr>
<td>Upper limb</td>
<td>1</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>Thorax</td>
<td>14</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal*</td>
<td>5</td>
<td>3.2</td>
<td>7</td>
</tr>
<tr>
<td>Lumbar</td>
<td>98</td>
<td>62.8</td>
<td>13</td>
</tr>
<tr>
<td>Lower limb</td>
<td>26</td>
<td>16.7</td>
<td>3</td>
</tr>
<tr>
<td>BTP onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gradual</td>
<td>66</td>
<td>39.1</td>
<td>11</td>
</tr>
<tr>
<td>Abrupt</td>
<td>103</td>
<td>60.9</td>
<td>18</td>
</tr>
<tr>
<td>Intensity of pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Moderate</td>
<td>14</td>
<td>8.3</td>
<td>5</td>
</tr>
<tr>
<td>Intense*</td>
<td>113</td>
<td>66.9</td>
<td>13</td>
</tr>
<tr>
<td>Excruciating</td>
<td>42</td>
<td>24.9</td>
<td>11</td>
</tr>
<tr>
<td>Relation of pain with</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>34</td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>Yes is incident</td>
<td>128</td>
<td>79</td>
<td>17</td>
</tr>
<tr>
<td>When appears the pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Night-time</td>
<td>7</td>
<td>4.2</td>
<td>2</td>
</tr>
<tr>
<td>Daytime*</td>
<td>109</td>
<td>64.9</td>
<td>13</td>
</tr>
<tr>
<td>Not related</td>
<td>52</td>
<td>31</td>
<td>14</td>
</tr>
<tr>
<td>How appears the pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unpredictable</td>
<td>60</td>
<td>36.8</td>
<td>16</td>
</tr>
<tr>
<td>Predictable</td>
<td>103</td>
<td>63.2</td>
<td>13</td>
</tr>
<tr>
<td>Type of BTP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatic*</td>
<td>67</td>
<td>40.4</td>
<td>2</td>
</tr>
<tr>
<td>Visceral</td>
<td>4</td>
<td>2.4</td>
<td>2</td>
</tr>
<tr>
<td>Neuropathic</td>
<td>22</td>
<td>13.3</td>
<td>5</td>
</tr>
<tr>
<td>Mixed*</td>
<td>73</td>
<td>44</td>
<td>20</td>
</tr>
</tbody>
</table>

N: Number of patients. * Statistically significant difference p<0.05.
Table 3. Scores of the SF-12 v2 Quality of Life Questionnaire components and their dimensions by gender.

<table>
<thead>
<tr>
<th></th>
<th>Gender</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Physical Functioning</td>
<td></td>
<td>33.32</td>
<td>9.14</td>
<td>30.93</td>
<td>7.64</td>
</tr>
<tr>
<td>Role Physical</td>
<td></td>
<td>28.05</td>
<td>10.2</td>
<td>25.82</td>
<td>7.68</td>
</tr>
<tr>
<td>Bodily Pain*</td>
<td></td>
<td>34.31</td>
<td>9.86</td>
<td>31.43</td>
<td>7.99</td>
</tr>
<tr>
<td>General Health</td>
<td></td>
<td>37.62</td>
<td>10.2</td>
<td>34.74</td>
<td>8.93</td>
</tr>
<tr>
<td>Physical Component*</td>
<td></td>
<td>30.23</td>
<td>9.45</td>
<td>27.72</td>
<td>7.24</td>
</tr>
<tr>
<td>Vitality</td>
<td></td>
<td>44.54</td>
<td>9.65</td>
<td>43.16</td>
<td>9.05</td>
</tr>
<tr>
<td>Social Functioning</td>
<td></td>
<td>39.69</td>
<td>8.35</td>
<td>37.53</td>
<td>7.07</td>
</tr>
<tr>
<td>Role Emotional</td>
<td></td>
<td>41.61</td>
<td>19.23</td>
<td>38.39</td>
<td>19.58</td>
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<tr>
<td>Mental Health</td>
<td></td>
<td>42.96</td>
<td>8.55</td>
<td>41.06</td>
<td>8.7</td>
</tr>
<tr>
<td>Mental Component</td>
<td></td>
<td>47.52</td>
<td>11.78</td>
<td>45.05</td>
<td>12.45</td>
</tr>
</tbody>
</table>

N: Number of patients; M: Mean; SD: Standard Deviation. * Statistically significant differences p<0.05.
Table 4. Three exploratory multivariate linear regression analysis of variables related to Scores of the SF-12 v2 Quality of Life Questionnaire Physical and Mental components and the VAS satisfaction of the patient with the treatment of BTP.

<table>
<thead>
<tr>
<th>Exploratory variables</th>
<th>SF-12 Physical Component</th>
<th>SF-12 Mental Component</th>
<th>VAS Patient’s satisfaction with treatment for BTP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95%CI)</td>
<td>p</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>Sex (Male vs Female)</td>
<td>-2.5 (-5.2 to 0.1)</td>
<td>0.06</td>
<td>-2.1 (-6.3 to 2.1)</td>
</tr>
<tr>
<td>Socioeconomic level</td>
<td>-1.1 (-3 to 0.9)</td>
<td>0.287</td>
<td>0.9 (-2.3 to 4.1)</td>
</tr>
<tr>
<td>Non-oncologic vs oncologic</td>
<td>-0.1 (-3.5 to 3.2)</td>
<td>0.939</td>
<td>-0.3 (-5.6 to 5)</td>
</tr>
<tr>
<td>Pain intensity (VAS)</td>
<td>-2.7 (-4.8 to -0.7)</td>
<td>0.01</td>
<td>-1.5 (-4.8 to 1.8)</td>
</tr>
<tr>
<td>First BTP visit vs Follow-up visit</td>
<td>3.2 (0.6 to 5.8)</td>
<td>0.017</td>
<td>-3.2 (-7.4 to 0.9)</td>
</tr>
</tbody>
</table>

OR: Odds ratio; 95%CI: 95% Confidence Interval. VAS visual Analogic Scale of 0 to 10 cm.
Scores

<table>
<thead>
<tr>
<th></th>
<th>Physical Health</th>
<th>Mental Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-74</td>
<td>32</td>
<td>63</td>
</tr>
<tr>
<td>75+</td>
<td>17</td>
<td>62</td>
</tr>
</tbody>
</table>

**SAND study**

**Population Norm**

**SF-12 PHYSICAL COMPONENT**

**MALE**

- % Above Normal Range: 92
- % At Normal Range: 5
- % Below Normal Range: 3

**FEMALE**

- % Above Normal Range: 98
- % At Normal Range: 2
- % Below Normal Range: 0

**SF-12 MENTAL COMPONENT**

**MALE**

- % Above Normal Range: 73
- % At Normal Range: 33
- % Below Normal Range: 29

**FEMALE**

- % Above Normal Range: 47
- % At Normal Range: 22
- % Below Normal Range: 51

Legend:
- Green: % Above Normal Range
- Yellow: % At Normal Range
- Red: % Below Normal Range