Quality of sleep assessment in patients with cancer pain

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Abstract

Introduction: Cancer is ranked as the third cause of death in Mexico. Cancer patients have pain and disturbances in sleep quality. **Purpose:** To evaluate sleep's quality in patients with cancer pain. **Materials and methods:** The study compared two groups. Group A, cancer pain patients ($n = 30$), and Group B, healthy subjects (control group) ($n = 30$). Demographics, sleep quality (using the Pittsburgh Sleep Quality Index, PSQI), somnolence (Epworth Questionnaire), pain intensity (using the visual analogue scale [VAS] and verbal rating scale [VRS]), depression and anxiety (using the Beck questionnaires) were considered as variables. **Results:** Pain cancer patients reported mean pain intensity (VAS) of 4 ± 1 . Patients with advanced cancer reported higher pain intensity. In Group A the PSQI reported a score of 10 ± 5 , in Group B the PSQI had a score of 6 ± 3 ($p = 0.002$). Somnolence reported significant differences ($p = 0.01$). **Conclusions:** Our results suggest a relationship between sleep disorders, cancer pain and cancer stage.

Key words: Sleep. Pain. Cancer. Pittsburgh. Epworth.

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Introduction

Cancer has been considered to constitute a global public health problem¹. In 2002, the World Health Organization reported that 24.6 million people suffered from it². In our country, malignant tumors were estimated to constitute the third cause of national mortality in 2005³.

Pain in cancer patients occurs in 80 to 90% of cases and is of multifactorial origin^{4,5}. The causality of this symptom has been associated with the malignant disease, antineoplastic therapy and concomitant conditions⁵. Pain in these patients has been documented to be associated with tumor disease in 92.5% of cases, to have an average severity of 3.6 to 4.3 on the visual analogue scale (VAS), to have exacerbations with a severity of 6.6 to 7.7 on VAS, to have an average duration of 5.9 months, to be of the breakthrough type in 64.4% of cases and to occur in more than one site in 24.8% of cases⁶.

In addition to the above, cancer patients have been documented to have a great diversity of associated symptoms⁵, including sleep disorders. These disturbances are estimated to occur in 29 to 95% of cases. The frequency of sleep disturbances in these patients depends on the type, stage and treatment of the neoplasm⁷.

In this sense, various sleep disorders have been identified in the patient with cancer pain, with the following standing out: difficulty in falling asleep and in the ability to stay asleep, early awakening, increase in the number of waking hours, poor sleep efficiency, and an increase in daytime sleepiness^{8,9}. Thus, these patients have been documented to have poor sleep quality^{10,11} and that this series of disturbances affect their living conditions.

On the other hand, feelings of hopelessness, opioid pharmacotherapy and interference of pain with mood have been observed to be factors that can influence on the quality of sleep¹². Therefore, it is of vital importance to document the quality of sleep in patients with cancer, in order to improve their living conditions and provide them with a comprehensive therapeutic approach in an optimal and rational way. Based on this series of considerations, the purpose of this work is to assess the quality of sleep in patients with pain of oncological origin.

Materials and Method

Selection of study patients

Following the Mexican regulations for health research and the ethical parameters for research in human

subjects¹³⁻¹⁵, and once the approval of the protocol by the Ethics and Research Committee of the institution was obtained, a comparative, cross-sectional cohort study was conducted in patients who attended a pain clinic.

In agreement with the central limit theorem, two groups were compared: group A, formed by cancer patients with cancer pain ($n = 30$), and group B, formed by healthy individuals ($n = 30$). To be included, the subjects had to be: a) older than 18 years, b) free of psychiatric disorders, c) willing to participate in the study, d) able to answer or complete the assessment instruments, and e) experiencing pain of oncological origin (Fig. 1).

Patients with: a) pain localized in the facial region, b) pain caused by autoimmune diseases, c) fibromyalgia, d) phantom limb sensation and/or pain, and/or e) migraine-type headache were excluded from the study. Those with incomplete evaluation instruments were censored.

Characteristics of the evaluation instrument

The evaluation instrument used in this study was applied to both groups on a single occasion by direct interview, and contained the following elements:

- Demographic variables. Information on study subjects' gender, age, marital status and level of education was collected.
- Karnofsky performance status (KPS). This scale rates the functional abilities of cancer patients in an ascending order with multiples of 10. The zero score corresponds to physical death, while a score of 100 corresponds to normal functioning with no evidence of disease^{16,17}.
- Characteristics of the neoplasm. The type (solid tumors and hematopoietic tumors), stage (I to IV) and treatment (chemotherapy and radiotherapy) of the oncological disease were documented.
- Pain assessment scales. In accordance with the practice parameters for the treatment of cancer pain¹⁸, the following scales were used to assess the severity of pain: the 100-mm visual analogue scale (VAS; 0 mm corresponds to absence of pain and 100 mm to the worst possible pain) and the four-point Verbal Rating Scale (VRS) (no pain, mild pain, moderate pain and severe pain).
- Pittsburgh Sleep Quality Index (PSQI). The Colombian version of this instrument was used^{19,20}. The PSQI evaluates seven areas or fields associated with sleep, each one of these fields is scored from 1 to 7 (C1-C7) and

Figure 1. Study subjects selection flowchart. Two groups were formed: a control group (n = 30) and one group of subjects with cancer pain (n = 30).

assess: subjective quality of sleep (C1), sleep latency (C2), sleep duration (C3), usual sleep efficiency (C4), sleep disorders (C5), use of sleeping medications (C6) and daytime dysfunction (C7). Each component is given a value of 0 to 3 points; the sum of these values corresponds to the overall PSQI rating. A score higher than 5 points is indicative of poor sleep quality.

- Epworth Daytime Sleepiness Scale. This instrument evaluates overall daytime sleepiness present in patients; it consists of 8 items, which are rated on a 0-3 scale (0, no sleepiness; 1, mild; 2, moderate; and 3, severe sleepiness). The sum of these items provides an overall rating, which, from 0 to 6 points corresponds to sufficient sleep, from 7 to 8 points corresponds to average population somnolence score, and 9 or more points corresponds to daytime sleepiness that requires medical attention²¹.
- Psycho-affective state. This assessment took into consideration the Mexican validations of Beck's inventories for depression²² and anxiety²³. Beck's depression inventory (BDI) is used to measure the severity of depression symptoms, while the anxiety inventory (BAI) measures the severity of anxiety

symptoms. Both instruments have 21 items and, depending on the score obtained, these symptoms are classified as minimal, mild, moderate or severe.

Statistical analysis

Central tendency and dispersion measures of the study variables were identified. The results obtained for both groups were compared. Parametric variables were applied Student's t-test and regression analysis; non-parametric variables were applied the chi-square test and ANOVA. P-values ≤ 0.05 were considered significant. For statistical analysis, a software compatible with the Windows™ platform was used (SPSS v.11®; SPSS, Inc.; Chicago, Ill, USA).

Results

General demographic variables

The demographic results of both groups are represented in table 1 and figure 2; no statistically significant differences were identified between groups. A higher

Table 1. Study subjects demographic variables (n = 60)

Variable	Group A (n = 30)		Group B (n = 30)		p-value*	
	n	%	n	%		
Women	18	60	20	66	0.42	
	Mean $\pm$ SD		Mean $\pm$ SD		Mean difference	p-value†
Age (years)	58 $\pm$ 13.3		57 $\pm$ 13.7		0.96	0.65
Level of education (in years)	10 $\pm$ 4.9		9 $\pm$ 4.9		1.2	0.35

Group A is comprised of individuals with cancer pain; group B is comprised of healthy subjects (control group).

p*, P-value obtained with the Chi-square test (Pearson).

p†, P-value obtained with paired Student's t-test.

SD: standard deviation; n: number of subjects.

Figure 2. Marital status in both groups is shown (n = 30 + 30 = 60). Group A (subjects with cancer pain) and group B (control). No statistically significant differences are identified.

proportion of women was found in both groups. Average age, in both groups, was within the sixth decade of life. Similarly, average level of education in both groups was 9 to 10 years of education.

Characteristics of pain in cancer patients

In this group of patients, we identified that: 77% had a solid tumor and 23% had a hematopoietic tumor; 10% had neoplasms at stage I, 17% at stage II, 40% at stage III and 33% at stage IV; 20% were on treatment with chemotherapy, 16.7% with radiotherapy, 3.3% received both

modalities and 66.7% none of them; and KPS showed an average of 80 (standard deviation [SD]: 13) (Table 2).

Regarding the characteristics of pain, somatic pain was observed in 40% of patients, visceral in 50% and neuropathic in 10%. In addition, average pain severity on VAS was identified to be 4 (SD: 1). On VRS, 3.3% did not show pain, 43.3% showed mild pain, 50% moderate and 3.3% severe pain (Table 3). In patients with solid tumors, pain severity on VAS was on average 4.09 (SD: 1.2), and in those who had hematopoietic tumors, 4.29 (SD: 1.9); no statistically significant differences were identified between both types of neoplasm.

Table 2. Neoplasm type and stage (Group A, n = 30)

		Type of neoplasm					
		Solid		Hematopoietic		Accumulated values	
		n	%	n	%	Total	% of total
Stage of the neoplasm	I	2	9	1	14	3	10
	II	3	13	2	29	5	17
	III	11	48	1	14	12	40
	IV	7	30	3	43	10	33
	Total	23	77	7	23	30	100

The table corresponds to Group A. Number (n) and proportion (%) of tumor stages by type of neoplasm.

Table 3. Pain severity (VAS and VRS) with regard to the type of pain (Group A, n = 30)

	Pain Severity										
	VAS			VRS							
				No pain		Mild pain		Moderate pain		Severe pain	
Type of pain	Mean		SD	N	%	N	%	N	%	N	%
Somatic	4	±	2	0	-	3	10	8	27	1	3
Visceral	4	±	1	1	3	8	27	6	20	0	-
Neuropathic	4	±	1	0	-	2	7	1	3	0	-
Mixed	0		-	0	-	0	-	0	-	0	-

The table corresponds to Group A subjects.

N: number of subjects; SD: standard deviation; VAS: visual analogue scale; VRS: verbal rating scale.

On the other hand, patients with stage I tumors had an average severity of 4 (SD: 0), those with stage II disease showed an average severity of 3.4 (SD: 1.5), those with stage disease III had an average severity of 4.1 (SD: 1.5), and subjects with stage IV tumors had an average severity of 4.5 (DS: 1.6). No significant differences were observed regarding the stage of the neoplasm and the severity of pain evaluated by VAS. As regards the VRS, there was only one patient (stage III) who reported absence of pain, 13 cases were identified with mild pain (1 stage I, 2 stage II, 6 stage III and 4 stage IV), 15 cases were documented with moderate pain (2 stage I, 3 stage II, 5 stage III and 5 stage IV), and there was one case with severe pain (stage IV). No significant differences were observed with regard to the neoplasm stage and the severity of pain on the VRS scale.

VAS-measured pain severity showed an average of 4.6 (SD: 2.3) in patients who received chemotherapy, 3.5 (DS: 0.5) in those who received radiotherapy,

3 (DS: 0.5) in those who received both treatments and 4.1 (DS: 1.3) in those who were not treated. No significant differences were observed regarding pain severity (VAS) and the antineoplastic approach (chemotherapy and radiotherapy) (Table 4). As for pain severity according to VAS and KPS, we identified that the lower the KPS score, the higher the pain severity (linear R: 0.5; $p = 0.002$) (Fig. 3).

Characteristics of sleep quality in cancer patients

Among the patients with cancer pain: a) the PSQI score was on average 9.8 (SD: 4.6), b) there were statistically significant differences between “good” and “poor sleepers” ($p = 0.007$), and c) daytime sleepiness had a score of 4.3 (DS: 3.0). As pain severity according to VAS increased, the PSQI score (linear R: 0.51; $p = 0.004$) and the score obtained in the Epworth scale

Figure 3. The figure correlates visual analogue scale (VAS)-measured severity of pain with the with the Karnofsky performance status (KPS) scale. A positive correlation between both variables can be identified: the higher the severity of pain, the lower the Karnofsky score (linear R: 0.5; $p = 0.002$).

(linear R: 0.4; $p = 0.025$) were observed to increase (Fig. 4). Furthermore, as the KPS score decreased, the PSQI score was identified to increase (linear R: 0.67; $p = 0.000$) (Fig. 5).

Similarly, in patients with hematopoietic tumors, a higher PSQI score was observed (mean: 13 ± 5.4) than in patients with solid tumors (mean: 8.8 ± 4), with these differences being significant ($p = 0.03$). The PSQI classification into “good” and “poor sleepers” showed no differences regarding the type of neoplasm. The score obtained with stage IV disease showed differences in comparison with the scores observed with stage II and III disease (IV vs. II, $p = 0.02$; IV vs. III, $p = 0.005$); these differences were not observed with regard to the classification of this instrument. In comparison with cancer patients who did not receive chemotherapy or radiotherapy, patients who underwent these treatments showed no statistically significant differences with regard to the scores obtained on PSQI and Epworth.

Comparative analysis between cancer patients and control subjects

Among the patients with pain, PSQI average score was 9.8 (SD: 4.6), while in control patients it was 6.3 (DS: 2.9);

Table 4. Pain severity with regard to neoplasm characteristics

	VAS	
	Mean	SD
Type of neoplasm		
Solid	4	1
Hematopoietic	4	2
Stage of the neoplasm		
I	4	0
II	3	2
III	4	1
IV	5	2
Chemotherapy		
Yes	4	2
No	4	1
Radiotherapy		
Yes	4	1
No	4	2

Group A data are shown.

SD: standard deviation; VAS: visual analogue scale.

these differences were statistically significant ($p = 0.001$) (Table 5). By means of the PSQI classification, statistically significant differences were observed between “good” and

Figure 4. The figure shows pain severity assessed with the visual analogue scale (VAS) and its correspondence with Pittsburgh sleep quality index or Epworth somnolence scale. The scores obtained on both PSQI (linear R: 0.51; $p = 0.004$) and Epworth scale (linear R: 0.4; $p = 0.025$) were observed to significantly increase as pain severity according to VAS increased.

Figure 5. The figure shows the scores obtained on the Karnofsky performance status (KPS) scale and on Pittsburgh sleep quality index (PSQI). The score obtained on PSQI (linear R: 0.67; $p = 0.000$) was observed to increase as the KPS score decreased.

“poor sleepers” among the patients with pain ($p = 0.007$); this difference was not observed in the control subjects. Between both groups (A vs. B), “good sleepers” showed

no significant differences; conversely, “poor sleepers” did show statistically significant differences (group A: 27 cases vs. group B: 21 cases; $p = 0.001$) (Fig. 6).

Table 5. Quality of sleep assessment and daytime somnolence.

	Group A (n = 30)	Group B (n = 30)	Mean difference (A-B)	p-value*
	Mean $\pm$ SD	Mean $\pm$ SD		
PSQI	10 $\pm$ 5	6 $\pm$ 3	3.4	0.002
Epworth	4 $\pm$ 3	3 $\pm$ 2	1.7	0.011

Group A is comprised of individuals with oncological-origin pain; group B is comprised of healthy subjects (control group).

p*, P-value obtained with a paired Student's t-test.

PSQI: Pittsburgh sleep quality index; SD: standard deviation.

Figure 6. Pittsburgh sleep quality index (PSQI) overall score is presented with categorization in two groups (“good sleepers” vs. “poor sleepers”), with cutoff point at a 5-point overall score. The results of both groups (group A [subjects with cancer pain], n = 30, and group B [control], n = 30) are compared. A higher number of “poor sleepers” are observed to belong to the group of subjects with cancer pain, with the difference being statistically significant (p = 0.001).

Among cancer patients, daytime sleepiness had a score of 4.3 (SD: 3.0), whereas in the control subjects it was 2.6 (SD: 1.9); this difference was statistically significant (p = 0.012). Similarly, a higher PSQI score was identified to correspond to a higher Epworth score (linear R: 0.6; p = 0.000).

Regarding the psycho-affective state, average BAI score obtained by patients with cancer was identified to be 6.4 (SD: 6.2), while in the control subjects it was 1.1 (SD: 1.7), with the difference being statistically significant (p = 0.000). In addition, a higher BAI score was identified to correspond to a higher PSQI score (linear R: 0.72; p = 0.000). As for the depression scale, cancer patients were observed to have an average score of 7.33 (SD: 8.0), whereas in the control subjects it was 0.6 (SD: 1.0), with the difference being statistically significant (p = 0.000). Similarly, a higher BDI score was

found to correspond to a higher PSQI score (linear R: 0.65; p = 0.000).

Discussion

In our country, malignant tumors were estimated to constitute the third cause of national mortality in 2005³. Pain in these patients occurs in 80 to 90% of cases and is multifactorial in origin^{4,5}. In addition, the frequency of sleep disturbances occurs in 29 to 95% of cases and depends on the type, stage and treatment of the neoplasm⁷. These patients have been documented to have poor sleep quality^{10,11}, and this series of disturbances affects their living conditions.

In this report, the number of PSQI-defined “poor sleepers” was observed to be significantly higher in patients with pain of oncological origin. In this sense,

Gooneratne et al. (2007) reported that, in comparison with healthy subjects, 56% of patients with cancer pain were considered “poor sleepers”. Moreover, said study specifies that the onset of sleep disturbances observed in cancer patients was associated with the neoplasm diagnosis²⁴.

The increase in pain severity according to VAS has been documented to favor poor sleep quality²⁵. Mystakidou, et al. (2007) have documented that, in the cancer patient, the severity of pain according to VAS is associated with sleep quality, quality of life and pain perception¹⁰. Coincidentally, in this study we observed that a higher severity of pain significantly increases the PSQI score.

In addition to the above, this study identified that a higher overall PSQI score or more severe pain are associated with more sleepiness on the Epworth scale. In this sense, Sela et al. (2005) have reported that fatigue is associated with difficulty falling asleep and waking up earlier⁸. This association has been described by other investigators²⁶.

In this report, the PSQI classification of subjects into “good” and “poor sleepers” was observed not to show differences with regard to the type of neoplasm. In this sense, the existing literature appears not to have documented the effect of the type of neoplasm on sleep quality. However, KPS has been reported to be associated with poor quality of sleep.²⁶ This statement is consistent with the findings identified in this study.

Davidson et al. (2002) compared the presence of sleep disturbances in patients treated with chemotherapy, radiotherapy or surgery in comparison with cancer patients without treatment; in this study, no significant differences were reported between both groups²⁷. Accordingly, in this report we observed that, in comparison with cancer patients who did not receive chemotherapy or radiotherapy, patients with these treatments showed no statistically significant differences with regard to the PSQI and Epworth-obtained scores.

A high correlation has been documented between the presence of anxiety and difficulty falling asleep⁸. Similarly, hopelessness and analgesia are factors that have been associated with poor sleep quality in patients with cancer at advanced stages¹⁰. In this sense, depression and anxiety indices were observed to be associated with poor sleep quality in the present work. These findings are consistent with those previously reported by other authors.^{8,10,26,28} This phenomenon is of special relevance, since depression, hopelessness, the use of sleeping pills and a poor quality of sleep

have a high correlation with the “wish to die” in cancer patients²⁸.

Sleep disorders have been identified to have an impact on pain severity, on the psycho-affective state and on the quality of life of patients^{8,10,26}. In addition to the above, various works suggest that sleep and pain severity have a reciprocal association; thus, the decrease in pain severity improves the quality of sleep and vice versa^{29,30}. For this reason, identification of sleep disorders in patients with cancer pain can be an element that improves the living conditions of these patients. Furthermore, the assessment of the interaction of these physiological variables (sleep and pain) will possibly guide us to the obtainment of new strategies in the treatment of pain and sleep disorders.

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