

Comorbid depression and anxiety symptoms in chronic pain patients and their impact on health-related quality of life

Comorbidade de sintomas ansiosos e depressivos em pacientes com dor crônica e o impacto sobre a qualidade de vida

Martha M. C. Castro¹, Lucas C. Quarantini², Carla Daltro³, Milke Pires-Caldas⁴, Karestan C. Koenen⁵, Durval Campos Kraychete⁶, Irismar R. de Oliveira⁷

¹ Professora da Escola Bahiana de Medicina e Saúde Pública e da Universidade Federal da Bahia (UFBA).

² Médico da Unidade de Psiquiatria, Hospital Universitário Professor Edgard Santos, UFBA.

³ Professora do Departamento de Medicina Interna da Escola Bahiana de Medicina e Saúde Pública (EBMSP).

⁴ Psicóloga da Unidade de Psiquiatria, Hospital Universitário Professor Edgard Santos, UFBA.

⁵ Professora do Departamento de Saúde, Sociedade e Desenvolvimento Humano, Escola de Saúde Pública de Harvard, Boston, Ma, EUA.

⁶ Coordenador do Ambulatório de Dor da UFBA.

⁷ Professor titular do Departamento de Neurociências e Saúde Mental, UFBA.

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Abstract

Background: Pain is an unpleasant sensory and emotional experience. Both chronic pain and depression result in substantial disability reduced HRQoL and increased health care costs and utilization. **Objectives:** To evaluate the strength of the association between depressive and anxiety symptoms and chronic pain, and to investigate the impact of these symptoms on health-related quality of life (HRQoL) in chronic pain individuals. **Methods:** Pain was assessed by means of a Visual Analogue Scale (VAS). Depressive and anxiety symptoms were assessed by the Hospital Anxiety and Depression (HAD) scale. Quality of life was assessed by means of the SF-36. **Results:** Four hundred patients were studied, mean age 45.6 ± 11.4 years and 82.8% female gender. According to HAD, 70% had anxiety and 60% depression symptoms. SF-36 showed mean scores $\leq 50\%$ for all the domains. Patients with severe pain/extreme (70.4%) had a higher frequency of anxiety than those with pain selvagem/moderada (59,5%). This was a statistically significant ($p = 0.027$). However, the frequency of depression did not reach statistical significance when both groups were compared $p = 0.109$. **Discussion:** Depressive/anxiety symptoms and pain together have worse clinical outcomes than each condition alone.

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Keywords: Chronic pain, depression, anxiety, health-related quality of life.

Resumo

Contexto: Dor é uma experiência emocional e sensorial desagradável. Tanto a dor crônica como a depressão reduzem de forma significativa a qualidade de vida, além de aumentar muito os custos dos cuidados com a saúde. **Objetivos:** Analisar a associação entre sintomas depressivos e de ansiedade em relação à dor crônica e investigar o impacto desses sintomas na saúde e na qualidade de vida em indivíduos com dor crônica. **Métodos:** A dor foi avaliada por meio de uma Escala Analógica Visual (VAS). Os sintomas depressivos e a ansiedade foram avaliados pela Escala Hospitalar de Ansiedade e Depressão (HAD). A qualidade de vida foi avaliada por meio do SF-36. **Resultados:** Quatrocentos pacientes foram estudados, com idade média de $45,6 \pm 11,4$ anos e 82,8% são do sexo feminino. De acordo com a HAD, 70% tinham ansiedade e 60%, os sintomas de depressão. A SF-36 apresentou escores $\leq 50\%$ para todos os domínios. Os pacientes com dor intensa/extrema apresentaram maior frequência (70,4%) de ansiedade do que aqueles com dor selvagem/moderada (59,5%). Essa foi uma associação estatisticamente significante ($p = 0,027$). No entanto, a frequência de depressão não atingiu significância estatística quando ambos os grupos foram comparados ($p = 0,109$). **Conclusão:** Os sintomas depressivos/ansiedade e dor, em conjunto, apresentaram piores desfechos clínicos de cada estado sozinho. É necessária mais investigação para determinar se o tratamento da dor ajuda os sintomas dos pacientes depressivos e se o alívio dos sintomas depressivos melhora a dor e sua morbidade.

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Palavras-chave: Dor crônica, depressão, ansiedade, qualidade de vida.

Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage¹ and is the most common presenting somatic symptom in medical outpatients². Chronic pain plays a significant role in incapacitation, making it impossible for individuals to perform physical activities³. In addition, this condition is usually comorbid with psychiatric disorders, especially major depression^{4,5}. Both conditions are often inadequately treated and result in substantial disability, reduced health-related quality of life (HRQoL) and increased health care costs and utilization^{6,7}.

Previous studies of the relationship between chronic pain and psychiatric disorders have been largely conducted in Western Europe

and North America. Given the suggestion that the association between somatic symptoms, including pain conditions, and psychiatric illness may be influenced by cultural factors⁸ however the generalizability of these findings to non-Western populations is an important question⁹. Recently, a worldwide study examining a population-based sample from 18 developed and developing countries, has carefully examined the relationship between chronic pain and mental disorders^{9,10}. Unfortunately, Brazil was not included in this important study. Thus, many questions related to clinical characteristics and the burden of psychiatric comorbidity in chronic pain individuals still remain in this country. The strength of the relationship between chronic pain and major depression is unclear^{11,12} especially with regard to HRQoL and depressive/anxiety symptoms.

The aim of this study was to evaluate the strength of the association between depressive/anxiety symptoms and chronic pain and investigate the impact of depressive/anxiety symptoms in chronic pain individuals on HRQoL. We hypothesized that depressive/anxiety patients with chronic pain would report a significantly lower quality of life as compared with individuals with chronic pain who do not have depression/anxiety symptoms.

Methods

From February 2003 and November 2006, 400 consecutive adults seeking treatment at the Pain Clinic at the University Hospital Federal University of Bahia, Brazil, were included in the study. The following variables were evaluated: age, sex, marital status, education level, religion, current occupation, the duration, frequency and intensity of pain, medical diagnosis of the pain, and time and response to treatment. Age was divided into two groups according to median in order to investigate the influence of age in the quality of life.

The intensity of the pain was measured using a Visual Analogue Scale (VAS) in which the intensity of pain was classified as 0 to 10, as follows: 0-1 = no pain; 2-3 = mild pain; 4-5 = moderate pain; 6-7 = intense pain and 8-10 = extreme pain¹³.

Depressive and anxiety symptoms were assessed by Hospital Anxiety and Depression (HAD, Brazilian version) scale^{14,15}. HAD scale is questionnaire with the dimensions anxiety and depression containing 14 items, 7 referring to anxiety and 7 to depression, with a cut-off point of 8 for anxiety and 9 for depression. All items refer exclusively to the emotional state and do not reflect somatic symptoms.

Health-related quality of life was assessed by applying the Medical Outcome Study Short-Form 36 Health Survey (SF-36) translated and validated into Portuguese. This is a generic instrument composed of 36 items that evaluate the following domains: physical functioning (the ability to take care of oneself and to perform routine daily activities); role limitations due to physical health (the impact of physical health in performing activities); bodily pain (level of pain experienced while performing routine daily activities); general health perceptions (how the individual perceives his/her health); vitality (energy and fatigue); social functioning (impact of physical conditions on his/her social life); role limitations due to emotional problems (the extent to which emotional problems interfere in routine daily activities); and mental health (effect of mood on his/her life). To analyze the eight domains of the scale, a score ranging from 0 (most affected) to 100 (not affected) is used¹⁶.

All patients gave their signed, informed consent prior to admission to the study. The study was approved by the local Institutional Review Board.

Statistical analysis

The program Statistical Package for the Social Sciences (SPSS) was used to construct the database and perform the statistical calculations.

The continuous variables were presented as means \pm standard deviations (SD) and the categorical as proportions (relative frequency).

Student's t-test or Mann-Whitney was used to compare the variables between the two groups and qui-square test was used to compare proportions. Significance was established at $P < 0.05$.

Results

Four hundred patients were enrolled in this study, 331 of whom were female (82.8%) and 69 (17.2%) male. The mean age of the patients was 45.6 ± 11.4 years. Most patients were married or had stable partners, considered themselves Catholics and had completed high school. Only 32.3% of patients in this study were employed during the period evaluated (Table 1).

Table 1. Características gerais de 400 pacientes atendidos na Clínica de Dor do Hospital Universitário entre 2003 e 2006

Variable	Results
	Mean \pm SD
Age (years)	45.6 \pm 11.4
	N (%)
Gender	
Female	331 (82.8%)
Male	69 (17.2%)
Marital status	
Single	128 (32.1%)
Married	195 (48.5%)
Separated/divorced	50 (12.6%)
Widowed	27 (6.8%)
Education	
Illiterate	17 (4.3%)
Primary school	71 (18.1%)
Elementary school	90 (22.3%)
High school	190 (47.3%)
University	32 (8.0%)
Religion	
No religion	27 (6.8%)
Catholic	221 (55.1%)
Protestant/Evangelical	107 (26.8%)
Spiritualist	36 (9.0%)
Others	9.0 (2.3%)
Current occupation	
Unemployed/no occupation	57.0 (14.3%)
Retired	60.0 (15.0%)
On sick leave	154.0 (38.4%)
Employed	129.0 (32.3%)

With respect to the classification of pain, 70.8% of patients reported pain that varied in magnitude, but occurred on a daily basis; 32.0% rated their pain as severe and 48.5% had been undergoing treatment in this center for more than three months the 38% moderate relief of pain.

When the results of the HAD scale for assessing anxiety and depression were analyzed, it was found that 21% did not have symptoms of anxiety or depression, while 7% were found to be only depressed and 18% were only anxious. On the other hand 54.0% showed scores higher than established norms for both anxiety and depression. Evaluation of the SF-36 showed that the mean scores of patients in this study were 50% or less for all the domains of the scale (Table 2).

Table 2. Results of the SF-36 scale of the patients

SF-36 scale domains	Mean \pm SD
Physical functioning	36.2 \pm 22.6
Role limitations due to physical health	17.8 \pm 27.9
Bodily pain	31.8 \pm 17.4
General health perceptions	44.4 \pm 21.8
Vitality	41.3 \pm 22.6
Social functioning	49.5 \pm 27.9
Role limitations due to emotional problems	30.0 \pm 36.6
Mental health	48.7 \pm 23.2

During analysis, age was dichotomized according to the median into < 45 years of age ($n = 185$) and ≥ 45 years of age ($n = 215$). No statistically significant differences were found between these two age groups with respect to the scores of any of the domains of the SF-36. Likewise, when a univariate analysis of these domains was carried out with respect to gender and marital status, no statistically significant differences were found between the two groups.

To compare the domains of the SF-36 scale, we constructed a table that shows the first quartile (25%), the second quartile or median (50%) and third quartile (75%) (Table 3).

When the results of the SF-36 QOL scale were compared according to HAD scores, it was observed that patients without anxiety and depression showed a greater quality of life when compared with those with anxiety and/or depression and this difference was statistically significant (Table 4).

Table 3. Domains of the SF-36 scale and anxiety and depression symptoms according to intensity of pain

Variables	Pain intensity		P
	Mild and moderate 148 (37.9%)	Intense and extreme 243 (62.1%)	
Symptoms of anxiety	88 (59.5%)	171 (70.4%)	0.027
Symptoms of depression	65 (43.9%)	127 (52.3%)	0.109
SF-36 domains			
Physical functioning	40.4 ± 23.6	32.8 ± 20.7	0.003
Role limitations due to physical health	22.7 ± 32.0	15.0 ± 24.8	0.027
Bodily pain	37.2 ± 17.5	28.0 ± 15.7	< 0.001
General health perceptions	50.8 ± 20.8	39.7 ± 21.0	< 0.001
Vitality	45.8 ± 22.1	38.0 ± 22.6	< 0.001
Social functioning	55.3 ± 28.4	46.0 ± 27.1	0.001
Role limitations due to emotional problems	34.1 ± 38.4	27.1 ± 34.7	0.097
Mental health	54.6 ± 23.5	45.1 ± 22.2	< 0.001

Table 4. Domains of the SF-36 scale according to anxiety and depression symptoms

Domínios da SF-36	Without anxiety and depression n = 119	Anxiety and depression symptoms n = 176	P
Physical functioning	44.3 ± 24.8	29.6 ± 18.3	p < 0.001
Limitations due to physical health	25.4 ± 33.9	12.7 ± 23.5	p = 0.001
Bodily pain	36.7 ± 17.0	26.8 ± 16.1	p < 0.001
General health perceptions	55.7 ± 21.9	36.6 ± 18.7	p < 0.001
Vitality	54.8 ± 20.9	30.2 ± 19.7	p < 0.001
Social functioning	64.2 ± 28.9	36.6 ± 22.5	p < 0.001
Limitations due to emotional problems	45.7 ± 40.6	13.8 ± 25.7	p < 0.001
Mental health	65.7 ± 20.8	34.6 ± 17.4	p < 0.001

Discussion

Our study had two aims: 1) examining the prevalence and strength of association between depressive/anxiety symptoms and chronic pain, and 2) describing the clinical burden of comorbid depressive/anxiety and chronic pain. Related to aim 1, we found evidence of a high prevalence of depression/anxiety. Related to aim 2, evidence shows that the clinical burden associated with depression and anxiety and chronic pain is significantly greater than for those with chronic pain alone. Specifically, respondents with depression and anxiety had significantly poorer HRQoL than the other group without those symptoms.

The prevalence of depressive symptoms in our sample was significantly higher and similar to what was found in other clinical samples that ranged from 30% to 60%¹⁷. The same comparison had occurred with anxiety symptoms. Those data confirm previous observations in which depressive and anxiety symptoms frequently coexist in patients with chronic pain¹⁸⁻¹⁹. This study also revealed that pain was more likely to be disabling when depressive/anxiety symptoms were present. Among those reporting comorbid chronic pain with

depression and anxiety, they had more severe scores in all items in the SF-36 QOL, particularly those related to physical and emotional limitations. These findings on HRQoL are consistent with those of others who have reported significant decrements in quality of life associated with depressive disorders²⁰. Depression and depressive symptoms has been associated with an impressively large number of poor pain outcomes and worse prognosis; patients with pain and comorbid depression experienced more intense pain, longer duration of pain, more amplification of pain symptoms and more pain complaints²¹. In addition, functional limitations (activity restrictions) and resulting disability, such as days in bed while ill and hospitalizations, increased in patients with pain and depression. Similarly, depression and pain produced additive impairments in social functioning, higher unemployment^{22,23} rate and diminished patient satisfaction.

The linkage between chronic pain and its affective components (i.e., depression and anxiety) has been known from the time of the ancient Greeks²⁴. Psychological mechanisms have been suggested to explore the relationship among these clinical conditions. Studies showed that fear of exacerbating pain by movement and catastrophizing pain predict more severe pain and disability in patients with chronic low back pain. Thus, catastrophizing may mediate the relationship among all three conditions and lead to increasing physical and mental symptoms. As a result, a persons' perception of pain may be amplified in the context of depression and anxiety^{25,26}.

On the one hand, biologic explanations emphasize the common neurobiology and neuroanatomical mechanisms of these conditions. The development of pain, depression, and anxiety share the participation of neurotransmitters' such as serotonin, norepinephrine, gamma-amino-butyric-acid, glutamate, adenosine, cannabinoids, and many other neuropeptides. Functional magnetic resonance imaging (MRI) studies of subjects with chronic pain and depression (or anxiety) have shown common areas of brain activation²⁷. Additional mechanisms that may at least in part elucidate the link between pain, depression, and anxiety is related to the activation of the sympathetic nervous system, involvement of the hypothalamic-pituitary-axis, and downregulation of benzodiazepine receptors in the frontal cortex²⁸.

There are several limitations to be considered in interpreting these findings. First, the cross-sectional design excludes the opportunity to examine chronological relationships between depression, anxiety and pain. Second, the study was conducted in a teaching hospital, where, is supposed, more severe cases are treated; therefore results may not be generalizable for other care settings. Third, we exclusively used self-report measures as opposed to interview-administered assessment and the results were compared with other studies what evaluated major depression. Finally, because chronic pain patients frequently report alterations in concentration, energy, and sleep, questions have been raised related to the probability of false-positives when assessing the prevalence of major depression within this population²⁹.

Conclusion

The combination of depression, anxiety and pain is associated with worse clinical outcomes than each condition alone. More research is needed to determine if treatment of pain helps the patients' depressive symptoms and, in the same way, whether relief of depressive symptoms improves pain and its related morbidity. These questions open an avenue for future investigations related to the role of psychotherapy approach of chronic pain patients and combined pharmacological approaches.

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