INFLUENCE OF DEPRESSION AND ANXIETY ON PAIN INTENSITY IN PATIENTS WITH CHRONIC PAIN AND DEPRESSION

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ABSTRACT:
Depression in chronic pain often manifests with symptoms of anxiety.

Purpose: The aim of the study is to investigate the influence of depression, state and trait anxiety on pain intensity in patients with chronic pain and depression.

Materials and Methods: Sixty-one patients with chronic pain and depression were studied. The study was phased. The second stage was carried out three months after the first. All participants received antidepressant treatment. The severity of depression was assessed with HAMD-17, the level of state and trait anxiety – with Spielberger’s STAI and pain intensity – with VAS. The trait anxiety was studied during the first stage. Regression analysis was used to perform the purpose of the study.

Results: The mean age of the sample was 55.6066±10.90608. Women comprised 91.8% of the sample, and men – 8.2%. A reduction in the mean values of the indicators in the second stage was reported. A regression analysis during the first stage showed that 60% of the variations in pain intensity were explained by the influence of the three variables (R=,616; R²=,379). Depression had the greatest impact and degree of influence on pain (t=3,372; p=.001), compared to state anxiety (t=,513; p=.015). The influence of trait anxiety was negligible (t=.484; p=.630). The results of the analysis of the second stage were similar (R=.644, R²=.415). The influence of depression was significant (p=.011; t=2,626), compared to that of state anxiety (t=2,012; p=.049).

Conclusions: Depression is the main variable influencing pain intensity. The search for symptoms of depression and their treatment is crucial for the management of chronic pain.

Keywords: chronic pain, depression, state anxiety, trait anxiety, pain intensity, regression analysis.

INTRODUCTION:
The phenomena of pain and depression have common neurobiological and psychological bases [1], explaining the widespread combination between chronic pain and depression as comorbidity [2]. Depression in chronic pain negatively affects the overall functioning of patients and predicts their future disability [3].

The biopsychosocial model defines chronic pain as a product of the complex interaction of heterogeneous groups of factors: biological, psychological and socio-demographic. Psychosocial factors play a leading role in the development of acute pain into chronic[4]. Depressive symptoms manifested in an episode are among the main psychological factors involved in the maintenance and persistence of chronic pain. Depression is associated with decreased pain tolerance and increased pain intensity [5].

Anxiety symptoms often accompany depression in chronic pain [6]. The manifestation of symptoms of anxiety predetermines not only the persistence of pain during its acute and subacute period but also the manifestation of depression during its chronic period. Anxiety symptoms are more common in patients with chronic pain and depression than without depression [7]. Even mild symptoms of anxiety affect the course of a depressive episode and make treatment of pain more challenging [8]. The combination of symptoms of anxiety, depression and pain in chronic pain patients worsens the clinical outcomes than each condition manifested alone [9]. This determines the need for a comprehensive assessment of the condition of patients with chronic pain. In addition to the physical characteristics of pain, psychological factors such as depression and anxiety need to be assessed in order to be effectively managed.

The aim of our study was to investigate the influence of depression, state and trait anxiety on pain intensity in comorbid patients with chronic pain and depression.

MATERIALS AND METHODS:
A randomized study of 61 patients with chronic non-malignant pain of different origins and depression hospitalized at the “St. Marina” University Hospital – Varna was carried out over a period of one year (from August 2019 to July 2020). The design of the study has been approved by
the Ethics of Scientific Research Committee at Medical University “Prof. dr. Paraskev Stoyanov” – Varna. The study was phased in two stages. The second stage was carried out three months after the first.

The assessment of the mental state of the patients studied was made according to the criteria for a depressive episode of the international classification of diseases tenth revision (ICD – 10). Between the two stages of the study, all patients conducted antidepressant treatment. Using quantitative methods, the severity of depression, the degree of state and trait anxiety and the intensity of pain were assessed. All indicators, with the exception of trait anxiety, were assessed during both stages of the study. The latter was only investigated during the first stage of the study as it was considered a constant characteristic. The following scales were selected for the purpose of the study: 1) Hamilton Depression Rating Scale (HAM-D-17) for assessment of the severity of depression; 2) Spielberger’s State and Trait Anxiety Inventory (STAI) – scale (S) for state anxiety degree (STAI – form Y1) and scale (O) for trait anxiety degree (STAI – form Y2); and 3) Visual Analog Scale (VAS) for assessment of the intensity of pain.

The regression analysis was performed in order to find causal relationships between the studied indicators: severity of depression, state anxiety, trait anxiety and pain intensity in the studied group of patients with chronic pain and depression.

RESULTS:
Sixty-one subjects with chronic pain and depression were studied. Participants’ age ranged from 24 to 76 years. The mean age of the studied sample and its standard deviation were respectively 55.6066 and 10.90608 (M=55.6066, SD=10.90608). The sex distribution in the study group was uneven. The share of the surveyed women was predominant – 91.8% (n = 56), compared to that of men – 8.2% (n=5). (fig. 1.)

Fig. 1. Sex distribution of the sample with chronic pain and depression.

The results of the sample distribution according to the antidepressant treatment in the first stage of the study showed that 73.78% (n=45) of the patients were on maintenance treatment, 18.03% (n=11) of them had discontinued their treatment for some reason, and the rest 8.19% (n=5) had never taken antidepressants (fig. 3.). All patients received regular maintenance treatment with antidepressants between the two stages of the study.

Fig. 3. Distribution of the sample according to the antidepressant treatment – first stage.

The distribution of the sample according to the regular medical treatment of pain showed that 63.93% of the patients took medication only during pain, and 36.07% were on maintenance treatment. (fig. 2.)

Fig. 2. Distribution of the sample according to the regularity of the drug treatment of pain.

The dynamics in the mean values of the indicators in the two stages of the study are shown in table 2. A decrease in the mean values of the indicators (severity of depression, degree of state anxiety and pain intensity) in the second stage of the study was reported. Trait anxiety was assessed only during the first stage. The reduction in the mean value of the severity of depression was the most pronounced one as a result of antidepressant treatment between the two stages of the study. (table 1)
The distributions by frequency by the scales used are close to normal.

The assessment of the severity of depression using the HAM-D-17 scale showed that in the first stage of the study, 54.2% of patients had mild depression, 37.8% of patients had moderate depression and 8% – had severe depression. In the second stage of the study, a decrease in the severity of depression was reported: 62.4% were with mild depression, 31.1% were with moderate depression, and 6.5% were with severe depression. (fig. 4.)

Fig. 4. Distribution of the sample according to the severity of depression.

The studied sample was comprised mostly of patients with high trait anxiety. Their share was 80.33%, and the remaining 19.67% had moderate anxiety. (fig. 5.)

Fig. 5. Distribution of the sample according to the trait anxiety degree.

The distribution of the sample according to state anxiety showed that in the first stage of the study, 64% of patients had a high degree of state anxiety, 27.8% of patients had a moderate degree of state anxiety, and 8.2% had a mild degree of state anxiety. In the second stage, a decrease in the share of patients with a high and mild degree of state anxiety was reported, respectively 62.5% and 6.4%. Thus, dynamics of the results was on account of the increased share of patients with a moderate degree of state anxiety – 31.1%. (fig. 6.)

Fig. 6. Distribution of the sample according to the state anxiety degree.
One dependent and three independent variables are involved in the regression analysis. A dependent variable was the intensity of pain. The independent variables were: trait anxiety (TA), state anxiety (SA) and severity of depression (D). The influence of independent variables on the dependent variable for the first stage was studied. The model and the results of the analysis are presented in Table 2.

**Table 2.** Regression analysis: model for the first stage of the study.

| Model | R     | R²    | Corrected R² | Standard Error |
|-------|-------|-------|--------------|----------------|
| 1     | .616  | .379  | .347         | 2.21073        |

a. Independent variables: TA, SA, D.

b. Dependent variable: Intensity of pain.

The results showed:
- The multiple correlation coefficient between independent variables and dependent was R = 616, i.e. nearly 60% of variations in pain intensity in the first stage of the study could be explained by the influence of these three variables: trait anxiety, state anxiety and severity of depression.
- The proportion of variation in the dependent variable as a result of the influence of the independent variables was R²=.379. (table 2)

The results revealing the force of action (severity and degree of influence) of the independent variables on the dependent one are represented in Table 3.

**Table 3.** Force of action of the independent variables on the dependent variable during the first stage of the study.

| R²=.379 | β/standardized beta/ | t    | p   |
|---------|---------------------|------|-----|
| TA      | 0                   | -0.484 | 0.63 |
| SA      | 0.316               | 2.513 | 0.015 |
| D       | 0.399               | 3.372 | 0.001 |

a. Independent variables: TA, SA, D.
b. Dependent variable: intensity of pain.

The results related to the severity of influence (t) of the independent variables on the dependent showed:
- Depression had the greatest impact on pain (t = 3,372)
- State anxiety was next in the severity of pain (t = 2,513)
- Trait anxiety had an insignificant severity of pain influence (t = -.484). (table 3)

The results for the degree of significance (p) of the independent variables on the dependent were similar:
- Depression had the greatest degree of significance (p = 001)
- State anxiety was the next variable in degree of importance (p = .015)
- Trait anxiety had a negligible degree of significance (p=.630). (table3)

One dependent and two independent variables were included in the regression analysis for the second stage of...
The study group was dominated by patients with moderate and high state anxiety. The same trend was reported during the second stage of the study. Therefore, symptoms of anxiety accompany the depressive episode in the studied sample with chronic pain and depression (fig. 6.). Tension, anxiety, and bad premonitions of impending events were the more frequent the more intense the pain [15].

The results showed:
- Depression was the main variable affecting the variations of pain intensity. The influence of depression on pain intensity was $t=2.626$, and the degree of significance was low ($p=0.011$).
- The influence of state anxiety on variations of pain intensity was weaker ($t=2.012$), and the degree of significance was low ($p=0.049$). (table 5)

**DISCUSSION:**

The age distribution in the study group with chronic pain and depression was uneven. Most of the patients were between the ages of 45 and 66. The results were similar to the data of a study revealing a high prevalence of chronic pain among adults after the age of 40 [13]. Other research shows that with the increase in age, the prevalence of pain symptoms increases, and with increasing age by one year, the risk of pain manifestation in patients with depression increases by 2% [10]. Therefore, age is a risk factor not only for the manifestation of chronic pain but also for its combination with depression.

The share of women (91.8%) predominated over the share of men (8.2%) (fig. 1.). Given that depressive disorder and chronic pain, isolated from each other, are more common among women, it could be assumed that women are the more vulnerable sex to their manifestation as comorbidity [11]. Women report higher rates of chronic pain conditions and depression and higher pain severity than men [13].

More than half of the studied patients (73.78%) received maintenance treatment with antidepressants. The share of the patients who were on treatment with antidepressants in the past due to symptoms of depression was 18.03%. Patients with a new-found depressive episode were registered. The share of those patients who have never consulted a psychiatrist and have never received antidepressant treatment in the past was 8.19% (fig. 3.). A study found that 35% of the surveyed patients with chronic pain had clinically manifested and unrecognized symptoms of depression [14]. These data reveal the need for systematic monitoring of the patients’ mental state in order to actively look for symptoms of depression and reassess antidepressant therapy.

All study participants were evaluated for clinically significant symptoms of depression according to the criteria for a depressive episode of ICD – 10. The severity of depression, assessed with the HAM-D-17 scale, decreased significantly in the second stage from 16.1475 to 13.3607 (table 1). Therefore, an improvement in the severity of depression has been reported as a result of regular maintenance antidepressant treatment for a period of three months. This dynamics of the results in the studied group with depression was also demonstrated in the distribution of patients according to the severity of depression. The second stage of the study marked an improvement in the severity of depression. The share of patients with mild depression increased (62.4%), compared to a decrease in the shares of patients with moderate (31.1%) and severe depression (6.5%) (fig. 4.). Study proves correlations between severity of depression and degree of pain intensity, i.e. the more severe the depression, the more intense the pain [15].

The study group was dominated by patients with moderate and high state anxiety. The same trend was reported during the second stage of the study. Therefore, symptoms of anxiety accompany the depressive episode in the studied sample with chronic pain and depression (fig. 6.). Tension, anxiety, and bad premonitions of imminent events were the more frequent the more intense the pain [15].

The proportion of variation in the dependent variable for the second stage of the study was $R = 0.644$ and, compared to the one calculated for the first stage ($R = 0.616$), was a better result. (table 2, table 4)

The results of the analysis of the force of action of independent variables on the dependent variable for the second stage of the study are represented in table 5.

**Table 4. Regression analysis: model for the second stage of the study.**

| Model | $R$ | $R^2$ | Corrected $R^2$ | Standard Error |
|-------|-----|-------|-----------------|---------------|
| 1     | 0.644 | 0.415 | 0.395 | 2.00834 |

a. Independent variables: SA, D.
b. Dependent variable: intensity of pain.

The results showed:
- The multiple correlation coefficient between the independent variables and the dependent variable for the second stage of the study was $R = 0.644$ and, compared to the one calculated for the first stage ($R = 0.616$), was a better result. (table 2, table 4)
- The proportion of variation in the dependent variable as a result of the influence of the independent variables was $R^2 = 0.415$ – also a good result. (table 4)

The results of the analysis of the force of action of independent variables on the independent variable for the second stage of the study are presented in table 5.

**Table 5. Force of action of the independent variables on the dependent variable during the second stage of the study.**

| $R^2 = 0.379$ | $\beta$/standardized beta | $t$ | $p$ |
|---------------|---------------------------|-----|-----|
| SA            | 0.299                     | 2.012 | 0.049 |
| D             | 0.391                     | 2.626 | 0.011 |

a. Independent variables: SA, D.
b. Dependent variable: intensity of pain.

The results showed:
- The influence of depression on variations of pain intensity was $t=2.012$, and the degree of significance was weak ($p=0.049$). (table 5)
pending danger are more common in patients with chronic pain and depression than without depression [7]. Some authors suggest state anxiety to be a predictive factor for chronic pain and pain related disability [16].

The studied sample with chronic pain and depression was characterized by a high mean value of trait anxiety (M=49.2295). The predominant part of it (80.33%) had a high degree of trait anxiety (fig. 5.). It is proposed that "the STAI-T be considered a non-specific measure of negative affectivity rather than trait anxiety per se" [17]. Other researchers have associated high trait anxiety with more symptoms of anxiety and more intense pain. They prove an additive rather than synergistic effect between state-trait anxiety and subjective pain intensity [18]. These findings reveal the need for more evidence in support of the prognostic role of high trait anxiety in the manifestation of depression in patients with chronic pain.

The regression analysis was performed in order to find causal relationships between the studied parameters in the group with chronic pain and depression. In the first stage of the study, the influence of three independent variables (trait anxiety, state anxiety and severity of depression) was assessed on the dependent variable (pain intensity). The results showed that nearly 60% of the variations in pain intensity could be explained by the combined effect of the three variables: trait anxiety, state anxiety and severity of depression (table 2.). The greatest influence on the pain intensity had the severity of depression, followed by the state anxiety. Trait anxiety had an insignificantly influence (table 3). This trend was maintained for the second stage of the study. The trait anxiety was not included in the analysis. The multiple correlation coefficient between the independent variables and the dependent one for the second stage of the study had a better result than that for the first stage (table 4). Therefore, the combined effect of the severity of depression and state anxiety largely explains the variations in pain intensity. The severity of depression was the main variable influencing the variations in pain intensity. The influence of state anxiety on the variations in pain intensity was insignificant (table 5).

Other evidence for the influence of depression on pain intensity has been found in the literature. Depression in chronic pain is associated with greater pain intensity. In a study of a sample of patients with burning mouth syndrome, researchers found that the intensity of pain was mainly influenced by depression. They also proved that the levels of anxiety (state and trait) influence the severity of depression[19]. Another study of patients with rheumatoid arthritis examined the influence of psychosocial factors (severity of depression, state and trait anxiety, and social support) on pain intensity. The results showed that psychosocial factors explained 18.9% of the variations in pain intensity assessed with VAS [20]. The effect of the severity of depression on pain intensity was also studied by other scientists. They defined the severity of depression as a strong predictor of the severity of pain and proved the reciprocal relationship between pain and depression [21].

CONCLUSION:
Depression is the main variable influencing pain intensity. The combined effect of depression and anxiety has a significant impact on the intensity of pain in comorbid patients with chronic pain and depression. Symptoms of depression and anxiety in patients with chronic pain should not be considered separately, as they are part of a general condition that influences the pain intensity. Therefore, the search for symptoms of depression and their treatment is crucial to the management of chronic pain.

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