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Assessment of the neuropathic component in a chronic low back pain syndrome

Ispitivanje neuropatske komponente bola kod hroničnog lumbalnog bolnog sindroma

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Abstract

Background/Aim. Chronic low back pain syndrome (CLBPS) is the most common cause of functional disability and loss of working ability in developed countries. Some research shows that neuropathic pain (NP) is present in almost 50% of patients with CLPBS. The aim of this study was to determine the characteristics of NP and its impact on quality of life (QoL) in patients with CLBPS. **Methods.** Patients were tested using three questionnaires for NP: Pain Detect Questionnaire, Leeds Assessment of Neuropathic Symptoms and Signs, and *Douleur Neuropathique 4 questions*. Thirty-two patients diagnosed with NP based on current clinical criteria and with positive results for NP on all three NP questionnaires formed an experimental group. A control group consisted of 32 patients with CLBPS who did not fulfill clinical criteria for NP and were negative for NP on all three questionnaires. Hamilton depression and anxiety rating scales (Ham-D and Ham-A, respectively) and Short Form (SF)-36 questionnaire were also applied. **Results.** According to magnetic resonance imaging (MRI), disc herniation was typically detected in the experimental group, while degenerative changes were commonly found in the control group. Patients from the experimental group had significantly greater intensity of pain, pain radiation in the legs, and the pain was usually presented as episodes of sudden attacks with mild pain between them. The most distinctive features of NP were allodynia, electric shock sensation, and hypoesthesia to prick. Patients from the experimental group also had significantly higher depression and anxiety scores, as well as worse QoL compared to the control group, especially in mental domains. Predictors of worse QoL in the patients with CLBPS were a higher level of anxiety and depression. **Conclusion.** The presence of allodynia, electric shock-like sensations, and hypoesthesia to prick in patients with CLBPS suggest NP. CLBPS patients with NP had worse scores in mental domains of QoL compared to CLPBS patients without NP.

Key words:
anxiety; back pain; depression; neuralgia; quality of life.

Apstrakt

Uvod/Cilj. Hronični lumbalni bolni sindrom (HLBS) je najčešći uzrok funkcionalne onesposobljenosti i gubitka radne sposobnosti u razvijenim zemljama. Neka istraživanja pokazuju da je neuropatski bol (NB) prisutan u gotovo 50% bolesnika sa HLBS. Cilj rada bilo je određivanje karakteristika NB i njegovog uticaja na kvalitet života (KŽ) kod bolesnika sa HLBS. **Metode.** Bolesnici sa HLBS bili su testirani pomoću tri upitnika za procenu NB (*Pain Detect Questionnaire*, *Leeds Assessment of Neuropathic Symptoms and Signs* i *Douleur Neuropathique 4 questions*). Trideset dva bolesnika koja su imala kliničku dijagnozu NB prema važećim kriterijuma i koji su imali pozitivne rezultate na sva tri upitnika za procenu NB svrstani su u eksperimentalna grupu, a 32 bolesnika sa HLBS koji nisu ispunili kliničke kriterijume za NP i bili negativni i prema kliničkim kriterijumima i prema korišćenim upitnicima činili su kontrolnu grupu. Takođe, u ispitivanju su korišćene Hamiltonove skale za procenu depresije i anksioznosti (Ham-D i Ham-A), kao i *Short Form* (SF)-36 upitnik za procenu KŽ. **Rezultati.** Prema rezultatima magnetne rezonance, diskus hernija je bila češće prisutna kod bolesnika u eksperimentalnoj grupi, dok su u kontrolnoj grupi najčešće zabeležene degenerativne promene. Bolesnici iz eksperimentalne grupe su imali znatno veći intenzitet bola, bol sa propagacijom u nogama, koji se obično javljao u obliku epizoda iznenadnih jakih

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napada sa blagim bolom između epizoda. Najspecifičnije karakteristike NB bile su alodinija, senzacija nalik električnom udaru i hipestezije pri bockanju. Ovi bolesnici su imali znatno veće skorove depresije i anksioznosti, kao i lošiji KŽ u odnosu na bolesnike iz kontrolne grupe. Prediktori lošijeg KŽ kod bolesnika sa HLBS su bili veći stepen anksioznosti i depresije. **Zaključak**. Prisustvo alodinije, osećaja strujnih udara i hipestezija na bockanje ukazuju na HLBS. Bolesnici sa HLBS i NB imaju lošiji KŽ u odnosu na bolesnike sa HLBS bez NB.

Ključne reči:
anksioznost; leđa, bol; depresija; neuralgija; kvalitet života.

Introduction

Chronic low back pain syndrome (CLBPS) is defined as a presence of pain lasting for at least 12 weeks and is located in the back area between the lower edge of the ribs and gluteal region, with or without radiation to the legs [1]. The prevalence of CLBPS is 4–10%, and it has been increasing over the years [2]. CLBPS typically leads to a significant reduction of a patient's quality of life (QoL). It is the most common cause of functional disability and loss of working ability in developed countries. Increasing treatment costs, loss of productivity, and decrease in working days are associated with CLBPS [3].

Baron et al. [4] reported in their review that neuropathic pain (NP) was present in 16–55% of patients with CLBPS. NP in CLBPS commonly occurs because of the damage of the nerve fibers due to degenerative changes of the intervertebral disc (local NP), the release of local inflammatory mediators in the area of the degenerated disc (inflammatory, root NP), and, finally, because of the mechanical root compression (root NP) [5]. Compared to nociceptive pain, NP seems to be associated with higher pain intensity, larger number of comorbidities, more severe comorbidities, reduced QoL, and higher treatment costs [4]. One recent study noted that the treatment costs for patients who have the neuropathic component of pain in the lower part of the back were 67% higher than for those who had only nociceptive pain [6].

The aim of this study was to determine the frequency, characteristics, and impact of NP on QoL in patients with CLBPS.

Methods

This study was approved by the Ethics Committee of the University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina. Prior to research, informed consent was obtained from all patients. At the Neurology Clinic in Banja Luka, 168 patients with CLBPS were examined from January 2015 until December 2015. Nine patients were excluded because of the presence of another disorder that could significantly affect their QoL and the results of this research. Thus, 159 patients were included in the further examination. Among them, a definite clinical diagnosis of NP according to the NP criteria proposed by Haanpää et al. [7] was made in 59 patients. We tested all 59 patients with three questionnaires for NP diagnosis: Pain Detect Questionnaire (PD-Q), Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), and *Douleur Neuropathique 4 questions* (DN4). The questionnaires were filled in by all patients in the presence of a neurologist, who was available for them in case of difficulties in understanding certain questions. Score ≥19 on the PD-Q, score ≥12 on the LANSS, as well as score ≥ 4 on the DN4, indicated the presence of NP [8–10]. Finally, for further analysis, we selected 32 patients who had a diagnosis of NP based on criteria by Haanpää et al. [7] and had positive results for NP on all three NP questionnaires (experimental group). The control group consisted of 32 patients with CLBPS who did not fulfill clinical criteria for NP diagnosis given by Haanpää et al. [7] and were negative for NP on all three questionnaires.

We examined sociodemographic characteristics of our patients including gender, current age, education, occupation, marital and employment status. Following features of the CLBPS were also examined: age at onset of the disease, disease duration, degree of disability, presence of comorbid disorders, and current therapy.

Identification of the affected nerve root and the severity of the nerve injury were established by electromyography (EMG) [11]. All examinations were performed by the same examiner (ZV) on the Oxford Synergy equipment. The temperature of the tested limb was above 31ºC. Nerve conduction study (NCS) was performed using surface stimulation and registration electrodes. The following parameters were assessed: motor conduction velocity (MCV), the amplitude of the compound muscle action potentials (CMAP) and minimal F wave latency of motor nerves (peroneal and tibial nerves), sensory conduction velocity (SCV), and amplitude of sensory nerve action potentials (SNAP) of sensory nerves (sural nerve). Using the needle electrode, *extensor digitorum brevis*, *flexor hallucis brevis*, *tibialis anterior*, *gastrocnemius* and *vastus medialis* muscles were examined on both sides. We also performed magnetic resonance imaging (MRI) in all CLBPS patients.

Hamilton depression rating scale (Ham-D) was used to assess symptoms of depressiveness, where a score > 8 indicated the presence of depression [12]. Hamilton anxiety rating scale (Ham-A) was used to estimate anxiety, where a score > 18 indicated the presence of anxiety [13].

As a measure of health-related QoL, each patient filled in the Serbian version of the Short Form (SF)-36 questionnaire [14], which is a generic measure that combines eight general health domains: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). Besides the total SF-36 score, physical composite score (PCS) and mental composite score (MCS) are two main scores to summarize these eight domains. All scores are interpreted with a 0-100 scale, where higher numbers represent better QoL.

All examined variables were analyzed using the Kolmogorov-Smirnov test in order to determine whether they were distributed normally. For the comparison of nominal and ordinal variables, the χ^2 test or Fisher test was used. The difference between two continuous nonparametric variables was investigated using the Mann-Whitney *U*-test, while the Student's *t*-test was used for continuous parametric variables. All parameters that differed between patients with and without NP were included in the multiple linear regression analysis (stepwise method) as independent variables, while the SF-36 score was considered a dependent variable. The level of statistical significance was 0.05 for a statistically significant difference and 0.01 for a highly statistically significant difference.

Results

Sociodemographic and clinical characteristics of patients included in the study are given in Table 1. According to magnetic resonance imaging (MRI), disc herniation was typically detected in the experimental group, while degenerative changes were commonly found in the control group.

Patients from the experimental group had significantly greater intensity of pain, pain radiation in the legs, and the pain was usually presented as episodes of sudden attacks with mild pain between them (Table 2). The most distinctive features of NP were allodynia, electric shock sensation, and hypoesthesia to prick. Patients from the experimental group also had significantly higher depression and anxiety scores

Table 1

Sociodemographic and clinical characteristics of patients with chronic low back pain (CLBP) syndrome with (experimental group) and without (control group) neuropathic pain

Characteristic	Experimental group (n = 32)	Control group (n = 32)
Gender (% of males)	53.1	56.2
Age (years), mean ± SD	46.6 ± 8.5	47.2 ± 9.5
Education (% of patients)		
lower	18.8	18.8
middle	56.2	59.4
higher	25.0	21.9
Employment (% of patients)		
physical work	50.0	59.4
intelectual work	50.0	40.6
Employment status (% of patients)		
employed	75.0	81.2
unemployed	25.0	18.8
Marital status (% of patients)		
lives with a partner	81.2	81.2
lives alone	18.8	18.8
Age at CLBPS onset (years), mean ± SD	42.2 ± 8.2	43.0 ± 8.6
Disease duration (years), mean ± SD	4.4 ± 1.4	4.2 ± 2.0
CLBP (% of patients)		
unilateral	78.1	78.1
bilateral	21.9	21.9
Root involve according to EMG (% of patients)*		
none	0.0	21.9
L4	21.9	9.4
L5	34.4	31.2
S1	43.8	37.5
Severity of radiculopathy according to EMG (% of patients)**		
absent	0.0	21.9
mild	9.4	62.5
moderate	56.2	15.6
severe	34.4	0.0
Root involvement according to MRI (% of patients)		
L3	21.9	12.5
L4	34.4	34.4
L5	43.8	53.1
Type of the lesion according to MRI (% of patients)*		
disc herniation	100.0	0.0
degenerative changes	0.0	100.0

SD – standard deviation; EMG – electromyography; MRI – magnetic resonance imaging. * $p < 0.05$; ** $p < 0.01$.

(Table 3), as well as worse QoL compared to the control group, especially in mental domains (Table 4). Predictors of worse QoL in the patients with CLBPS were a higher level of anxiety and depression (Table 5).

Table 2

Main characteristics of pain in patients with chronic low back pain (CLBP) syndrome with (experimental group) and without (control group) neuropathic pain

PDQ questionnaire	Experimental group (n = 32)	Control group (n = 32)
Actual pain (mean ± SD) **	4.5 ± 0.8	3.5 ± 1.0
Strongest pain (mean ± SD) **	7.2 ± 1.0	5.9 ± 1.2
Average pain (mean ± SD) **	4.8 ± 0.7	3.9 ± 1.0
Course of pain (% of patients) **		
persistent pain with slight fluctuations	21.9	62.5
persistent pain with pain attacks	15.6	31.2
pain attacks with pain between them	62.5	6.2
Pain radiation (% of patients) **	100.0	46.9
Pain localization (% of patients) **		
leg only	71.8	6.2
leg and the lower back	28.1	93.8

PDQ – Pain Detect Questionnaire; SD – standard deviation.
**** $p < 0.01$.**

Table 3

The presence of anxiety and depression in patients with chronic low back pain (CLBP) syndrome with (experimental group) and without (control group) neuropathic pain

Scale	Experimental group (n = 32)	Control group (n = 32)
Ham-D score (mean ± SD)*	7.9 ± 5.2	5.6 ± 3.4
Depressive patients (% of patients)	34.4	21.9
Ham-A score (mean ± SD)*	11.5 ± 8.3	7.7 ± 6.4
Patients with anxiety (% of patients)	31.2	18.8

Ham-D – Hamilton depression rating scale; Ham-A – Hamilton anxiety rating scale; SD – standard deviation.
**** $p < 0.05$.**

Table 4

Quality of life measured by Short Form (SF)-36 questionnaire in patients with chronic low back pain (CLBP) syndrome with (experimental group) and without (control group) neuropathic pain

Domain of the SF-36 scale	Experimental group (n = 32)	Control group (n = 32)
Physical functioning (PF) score (mean ± SD)	72.7 ± 9.8	73.1 ± 8.2
Role physical (RP) score (mean ± SD)	12.5 ± 19.1	13.3 ± 19.0
Bodily pain (BP) score (mean ± SD)**	41.7 ± 8.0	48.3 ± 6.9
General health (GH) score (mean ± SD)	32.7 ± 7.7	34.0 ± 10.0
Vitality (VT) score (mean ± SD)**	50.2 ± 15.4	62.7 ± 18.0
Social functioning (SF) score (mean ± SD)**	50.6 ± 15.4	62.3 ± 11.6
Role emotional (RE) score (mean ± SD)	51.0 ± 50.1	66.6 ± 44.8
Mental health (MH) score (mean ± SD)*	57.1 ± 22.5	69.5 ± 19.9
Physical composite score (PCS) (mean ± SD)*	41.8 ± 8.7	46.1 ± 7.6
Mental composite score (MCS) (mean ± SD)**	48.3 ± 20.1	59.1 ± 19.0
Total SF-36 score (mean ± SD)*	46.1 ± 14.8	53.8 ± 13.3

SD – standard deviation.
**** $p < 0.05$; ** $p < 0.01$.**

Table 5

Predictors of the total Short Form (SF)-36 score in patients with chronic low back pain (CLBP) syndrome – multiple regression analysis (stepwise method)

Varables included	Beta	*p*
Ham-D **	-0.81	< 0.01
Ham-A **	-0.39	< 0.01
R^2 adjusted	0.75	

***Note*: Excluded variables were: the presence of neuropathic pain, nerve root involvement according to electromyography (EMG), severity of nerve root injury according to EMG and magnetic resonance maging (MRI).**
Ham-D – Hamilton depression rating scale; Ham-A – Hamilton anxiety rating scale.
**** $p < 0.01$.**

Discussion

The prevalence of NP in patients with CLBPS in our study was 35%, which is in accordance with the results of most previous studies [4]. All of our patients had a definite clinical diagnosis of NP according to the criteria of Haanpää et al. [7], which included the patient's history, neurological examination, EMG testing, and MRI of the lumbosacral spine. The wide range of NP prevalence in patients with CLBPS in the literature (16–55%) could be the result of methodological differences between studies (especially in the definition of NP, pain assessment tools, and examined body parts) [4]. One previous study underlined that the prevalence of NP in CLBPS was even 90% [15].

Significant differences in sociodemographic characteristics of patients with CLBPS and NP vs. CLBPS without NP were not noted. These results are very similar to the findings of other studies [16]. NP may appear in patients with CLBPS independently of gender and age. According to our EMG results, patients with NP usually had at least one affected nerve root and more severe nerve root injuries. All patients with NP had a disc herniation in contrast to the control group, where degenerative spine changes predominated. Accordingly, pain radiation and the presence of pain in one or both legs were significantly more frequent in patients with NP. These findings are in accordance with the research conducted by Attal et al. [17]. It was suggested that the percentage of patients with NP increased with the degree of distal pain radiation. Around 8% of patients with localized back pain, 15% of patients with pain limited above knees, 39% of patients with the presence of pain under the knees, and 80% of patients with pain radiation to the foot/feet had NP [17].

Patients with NP had significantly more severe pain intensity compared to the control group, which corresponds to the results of previous publications [18, 19]. Except for the mentioned difference in pain intensity, significant differences were also noted in the course of the disease, pain radiation, and localization. Patients with NP were most likely to have pain in the form of severe pain attacks with mild pain between them, while patients without NP more often had persistent pain with slight fluctuations. Using three questionnaires for NP diagnosing, we observed that the most significant features of NP were allodynia, electric shock-like sensations, and hypoesthesia to prick. To date, only a few studies have been published in which two or more questionnaires were applied at the same time and on the same group of patients, but even in these papers, patients with different etiology of peripheral NP have been included in the trials [20–22]. It seems that standardized questionnaires for NP seem to be insufficiently sensitive and specific for detecting NP in patients with CLBPS. These results imply the need for further development of the specific NP questionnaire for CLBPS.

The worst QoL score in both groups of patients was RP, which is in accordance with some previous studies [23–26]. These studies also reported slightly lower scores for physical domains in contrast to mental ones, which is in line with our results. According to the SF-36 questionnaire, patients with CLBPS and NP had worse QoL compared to the patients without NP [18, 27, 28]. Lower scores on mental domains in patients with NP and the fact that patients with NP had significantly higher rates of depression and anxiety than the control group underline the significance of the bidirectional relationship between NP and anxiety/depression. The presence of depression and anxiety was reported to be in a positive correlation with the presence of pain and functional disability and a negative correlation with patients' QoL [27, 29–31]. Multiple linear regression analysis showed that the presence of depression and anxiety was a predictor of worse QoL in our patients with CLBPS and that these two variables could explain as much as 75% of the total SF-36 score variability. Several studies indicated that QoL in patients with CLBPS is more impaired due to psychosocial factors than due to pain intensity and functional disability [28, 32]. All these results support the biopsychosocial model of the development of CLBPS, where the psychosocial factors tend to be more important than the initial injury of anatomical structures [28]. Depression and anxiety should be an important treatment "target" in CLBPS patients in order to significantly improve their QoL. Although depression and anxiety are the main psychosocial factors that play an important role in the occurrence and maintenance of CLBPS, social factors like those related to the work environment (demanding work conditions, job dissatisfaction) should not be underestimated. However, the association between NP and type of patients' work was not found in our cohort.

The main limitation of our study could be a relatively small sample size. However, this study is well defined and represents the first study where frequency and characteristics of NP in CLBPS were examined by three questionnaires, as well as its influence on QoL. Furthermore, the control group was included (patients with CLBPS without NP). Another advantage is the fact that patients who had comorbid disorders, which could affect their QoL, were excluded from the study.

Conclusion

The presence of allodynia, electric shock-like sensations, and hypoesthesia to prick in patients with CLBPS suggest NP. CLBPS patients with NP had worse scores in mental domains of QoL compared to patients without NP.

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