Painful physical symptoms in hospitalized patients with acute depressive episode: results from a naturalistic study

Telesni bolečinski simptomi pri hospitaliziranih bolnikih z akutno epizodo depresije: rezultati naturalistične raziskave

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Abstract

Background: Depressive symptoms in patients with chronic pain (organic or functional) are well recognized. However, studies on pain were mostly conducted in non-psychiatric settings, and there is a paucity of data on painful physical symptoms (PPS) in patients with depression, especially in acute depressive episode (ADE). The aim of the study was to find out the prevalence of PPS in patients with ADE and to compare socio-demographic and clinical variables in patients with and without PPS.

Methods: 150 somatically healthy patients, hospitalized due to ADE were screened for PPS. Data on PPS location and severity, basic socio-demographic characteristics, illness severity, therapy, suicidality, and comorbid alcohol abuse were collected.

Results: 71 % of patients with ADE reported at least one painful physical symptom. Headache was the most common complaint. Patients with PPS had more severe depressive symptoms, lower level of functioning, and were prescribed more analgesics. However, no differences in socio-demographic characteristics, antidepressant therapy, suicidality or alcohol dependence were found.

Conclusions: The results show high prevalence of PPS in somatically healthy hospitalized patients with ADE and partly concur with results from similar studies. The high use of analgesics in patients with depression and painful physical symptoms opens the issue of rational pharmacotherapy.

Izvleček

Izhodišča: Depresivni simptomi so pri bolnikih s kronično bolečino pogosti in dobro poznani. Raziskave o bolečinskih simptomih in soobolevnosti z depresijo so bile večinoma opravljene zunaj psihiatričnega področja. Raziskav znotraj psihiatrije o telesnih bolečinskih simptomih (TBS) pri bolnikih z depresijo, posebno z akutno depresivno epizodo (ADE), je malo. Z raziskavo smo želeli ugotoviti pojavnost TBS pri bolnikih z ADE ter primerjati klinične dejavnike bolnikov z depresijo s TBS in brez nje.

Metode: Pri 150 telesno zdravih bolnikih, hospitaliziranih z diagnozo ADE, smo ugotavljali prisotnost TBS. Zbrali smo podatke o mestu in jakosti TBS, osnovnih socialno-demografskih značilnostih, izraženosti depresije, zdravljenju, samomorilnosti in morebitni odvisnosti od alkohola.

Rezultati: 71 % bolnikov je navajalo vsaj en bolečinski simptom, med katerimi je bila najpogostejša pritožba glavobol. Bolniki s TBS so imeli bolj izražene simptome depresije in so imeli predpisanih več protibolečinskih zdravil. Med bolniki z ADE in s TBS ter bolniki z ADE brez TBS nismo ugotovili razlik glede na socialno-demografske značilnosti, antidepresivno zdravljenje, samomorilnost in odvisnost od alkohola.

Zaključki: Rezultati raziskave so pokazali visoko pojavnost TBS pri telesno zdravih bolnikih, hospitaliziranih zaradi ADE, kar se delno ujema z izsledki podobnih tujih raziskav. Ugotovili smo pogosto in intenzivno uporabo protibolečinskih zdravil pri bolnikih z depresijo in TBS, kar odpira vprašanje racionalne farmakoterapije.

Introduction

People with organic or functional painful conditions become depressed in up to 80 %.[1] On the other hand, about 50 % of depressed patients report pain.[2]

There is a large body of evidence that patients with depression often complain of different somatic symptoms, among them poorly defined painful conditions.[3] However there is still a lack of consistent terminology which probably reflects conceptual issues about the nature of pain and depression.[2] To define pain symptoms in depressed patients different expressions appear in the literature. Terms like "functional", "medically unexplained", "unexplained painful physical symptoms" or "psychosomatic" are the most commonly used.[4,5]

The published data show that clinicians meet patients with painful physical symptoms (PPS) with or without depression in different clinical settings, often non-psychiatric. There is a paucity of data on depression with pain in patients treated in psychiatry, and in most of the studies the population of patients is diverse while the origin of pain (functional vs. organic) is poorly defined. However, the co-occurrence of pain and depression might be attributed to common neurobiological and psychological causes. [6] The presence of PPS complicates the recognition and treatment of depression and is associated with worse depression outcomes.[7-9] PPS often represent residual symptoms and are a risk factor for relapse of depression.[10] Opioid analgesics are an effective treatment option for pain control although there are safety concerns about abuse and dependence risk. Tramadol was shown to have antidepressant efficacy[11] while antidepressants and anticonvulsants might be adjuvant analgesic agents alone or in combination with psychotherapy for treatment of depression with PPS.[12-15]

The primary objective of our study was to identify the prevalence of PPS in otherwise somatically healthy patients hospitalized in Psychiatric intensive care unit due to acute depressive episode (ADE), and to me-

Table 1: Comparison of patients with depression and PPS and with depression without PPS (N=150)

	DEP with PPS (N=107)	DEP without PPS (N=43)	χ2, U	p
Gender (%)	M 35 (32.72) F 72 (67.28)	M 17 (39.53) F 26 (60.47)	0.631*	0.427
Age (years, SD)	50.14 (± 11.44)	50.77 (± 12.59)	2262.500**	0.874
No. of previous hospitalizations (SD)	4.81 (± 5.92)	4.56 (± 6.11)	2160.500**	0.553
HAM-D score (SD)	32.91 (± 5.76)	28.79 (± 5,98)	1424.000**	< 0.001
ZUNG score (SD)	60.90 (± 8.24)	56.14 (± 9.98)	1588.000**	0.003
CGI-S (SD)	5.55 (± 0.75)	4.72 (± 0.76)	1073.000**	< 0.001
GAS (SD)	33.10 (± 12.57)	47.40 (± 10.69)	899.500**	< 0.001
Alcohol use disorder N (%)	17 (15.88)	5 (11.62)	0.879*	0.644
Analgesic use N (%) ► parcetamol and NSAIDs N (%) ► tramadol N (%)	35 (32.71) 32 (29.90) 3 (2.80)	2 (4.65) 2 (4.65) 0 (0.00)	13.026*	0.001
Previous anxiolytic use N (%)	57 (53.27)	13 (30.23)	6.541*	0.011
SNRIs prescribed N (%)	86 (80.37)	37 (86.04)	0.669*	0.413
Anticonvulsants prescribed N (%)	33 (30.80)	14 (32.57)	0.459*	0.795
History of attempted suicide N (%)	63 (58.87)	24 (55.81)	2.202*	0.821

** = χ2 (chi square test)*
*** = U (Mann-Whitney test)*

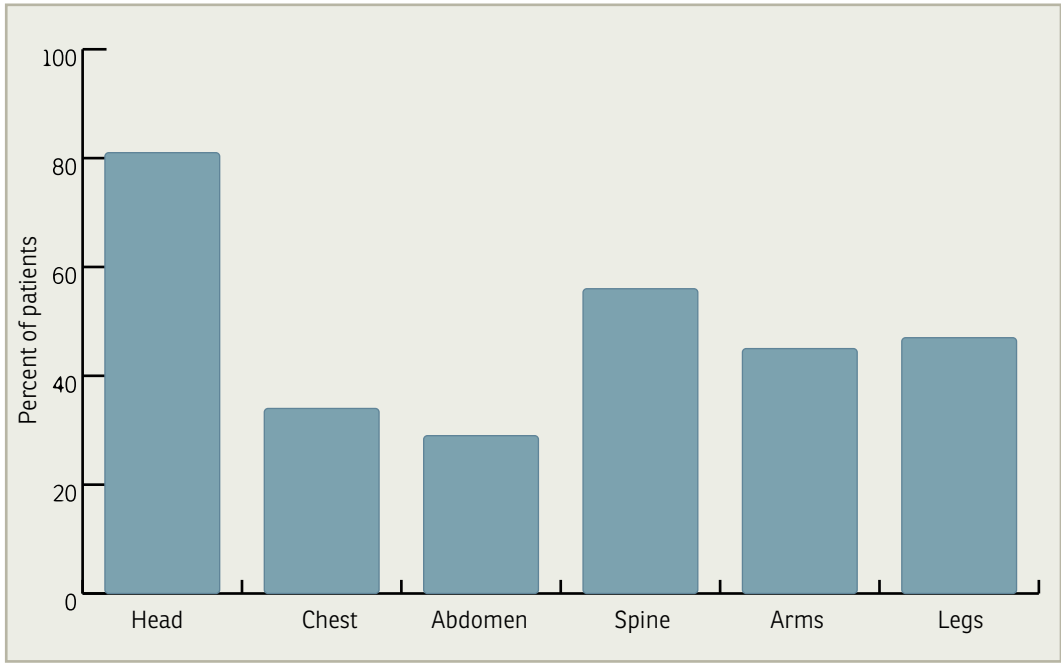

Figure 1: Distribution of painful physical symptoms by location (n=107)

asure the intensity and location of painful symptoms. The secondary objective was to evaluate the possible differences in socio-demographic and illness related variables, including pharmacotherapy, in patients with and without PPS. We hypothesized that there was a difference in socio-demographic and illness-related factors between patients with depression with and without PPS. The study was conducted in naturalistic conditions.

Patients and Methods

Patients, hospitalized in the Psychiatric Intensive Care Unit of the University Psychiatric Hospital in Ljubljana, Slovenia, under the diagnosis of ADE (ICD – 10 criteria for recurrent severe depressive episode, with or without psychotic symptoms) were consecutively recruited over a two-year period. The inclusion criteria were both genders, age 18 to 65 years, and the absence of co-morbid somatic illness that would require diagnostics or somatic treatment. Patients with chronic conditions like diabetes mellitus, chronic organic pain due to orthopedic or neurological condition or pathological laboratory findings were excluded. Patients were interviewed in the first week after admission. Depression was evaluated with 21-item Hamilton Depression Scale (HAM-D), Clinical Global Impression-Severity (CGI-S), General Assessment Scale (GAS) and Zung Questionnaire.[16-19] Painful symptoms were checked for location (head, chest, abdomen, spine, arms and legs) and severity with Visual Analogue Scale (VAS: 1–10). Data on basic socio-demographic characteristics, history of suicide attempt, co-morbid alcohol abuse, and prescribed pharmacotherapy were also collected.

All participants gave informed consent.

Statistical analysis

Patients were divided into two groups: one with and the other without PPS, and compared. $\chi 2$ test for categorical variables was used. Due to the non-Gaussian distribution of variables on age, VAS, CGI-S, HAM-D and Zung Questionnaire, non-parametric Mann-Whitney U test was used. $P < 0.05$ was considered statistically significant. Data were analyzed with SPSS version 17.0.

Results

Data from 150 patients were collected (47 (32 %) male). 107 (71 %) patients reported painful symptoms: 26.1 % had one painful symptom, 34.6 % two, and 39.3 % three or more. The mean severity of PPS was between 6 to 7 on VAS for all locations with headache

being the most common. The distribution of PPS is presented in Figure 1.

There were no statistical differences in socio-demographic characteristics between both groups (p> 0.05). 52.3 % of patients with depression and PPS were employed (41.9 % of patients with depression without PPS) and 50.5 % had high school education vs. 48.8 %, respectively. 65.4 % of depressed patients with PPS were married vs. 51.2 % in the group of patients without PPS. However, differences in illness related variables were found. Patients with depression and PPS scored higher on all clinical scales, and were more often prescribed anxiolytics before hospitalization while one third of these patients received analgesics (29.9 % recived paracetamol and non steroid anti-inflammatory drugs (NSAID), while 2.8 % received tramadol, respectively). The results are presented in Table 1.

Discussion

There is not much data on hospitalized patients with ADE and PPS in the literature. The majority of studies recruited non-acute outpatients, often in primary care or in other settings and did not explicitly exclude somatically ill patients.

In our study patients were carefully selected and only somatically healthy patients with ADE were included. Without other medical explanation, PPS were considered to be part of somatic syndrome of depression.

In comparison to other studies, high prevalence of PPS was found in our patients. In other studies in psychiatric setting the prevalence of PPS was between 30.4 % to 69 % in patients with major depressive disorder.[20-22] In a study by Arnow, patients with major depression reported significantly higher proportion of chronic pain than those without depression (66 % versus 43 %).[23] Patients with PPS were generally older and of female gender. In our sample, patients were almost the same age in both groups, with two thirds of females among patients with depression and PPS.

Among PPS headache was the most common complaint. Our results concur with a recent study where 68 % of outpatients with major depression reported PPS, 43 % had one or two symptoms with headache being the most common.[22]

In a multicenter international study STAR*D (Sequenced Treatment Alternatives to Relieve Depression) patients with PPS had more severe depressive symptoms and poor treatment outcome correlated also with gender, ethnicity and comorbidity.[24] In our sample, patients with ADE and PPS were more ill according to CGI-S. They had more depressive symptoms on HAM-D as well as on Zung Questionnaire and were functionally more disabled as measured with GAS. The same higher depression severity was found in out-patients with major depressive disorder with PPS.[11] In contrast to a recent study where suicidality was higher in patients with PPS, the history of suicide attempt was common in all patients reflecting the high suicide risk in Slovenian population.[20,25]

More than 80 % of the patients in both groups were prescribed serotonin and norepinephrine reuptake inhibitors (SNRIs), which might reflect the influence of reported efficacy of novel dual acting antidepressants and local effect. One third of the patients received mood stabilizers (antiepileptics) for augmentation of antidepressant efficacy in severe depression, as recommended in therapeutic guidelines. [26] High proportion of analgesic use was found in patients with PPS, which raises the question of rational pharmacotherapy, since these patients had no clear somatic co-morbidity. Most of the patients were treated with paracetamol and NSAIDs. Although not as dangerous as opioids, these drugs can still cause dependence, hepatotoxicity, renal failure and cardiovascular complications. [27] Rational therapy for co-morbid depression and PPS based on literature recommendations would be double-acting agents (duloxetine, venlafaxine, mirtazapine, bupropion, nefazodon and triclycic antidepressants) and antiepileptics (carbamazepine, lamotrigine, pregabalin and neurontin). [12,28-30]

Conclusions

There is a vast body of literature on pain and depression, with most of the studies conducted in primary care, in other specialties and focusing primarily on pain. The growing interest of properly diagnosing PPS in depression is also influenced by literature reports on the therapeutic efficacy of SNRIs on pain. However, there is still a lack of studies on epidemiology of pain in depression in psychiatric settings, especially in acute and severe episode of depression. The sample in our study was relatively small but pure, excluding patients with a co-morbid somatic illness. The results are partly in concordance with findings in other studies: the high prevalence of PPS, which is associated with more severe symptoms of depression. The results confirm that patients with ADE should be carefully examined and treated for all symptoms, and that the pharmacotherapy should be rational, not forgetting the potentially harmful over-prescribing of painkillers.

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