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Pain, Depression and Coping Styles: Assessment and Evaluation in Cancer Pain Population

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Abstract

Cancer patients may suffer from a plethora of symptoms at all stages of their disease. Pain is one of the most feared and distressing symptoms experienced by people with cancer and may be the dominating symptom at time of diagnosis of cancer, a sign of disease relapse, a symptom of late toxicity and a key symptom in patients with advanced cancer. Pain is often associated with depression and impaired quality of life, consistent with a biopsychosocial model. The main goal of this study is to investigate the relation among pain, anxiety and depression in a population of oncological patients and the secondary objective is to analyse the association between cancer pain and coping styles.

Keywords: Pain; Depression; Cancer; Coping

Introduction

Cancer patients may suffer from a plethora of symptoms at all stages of their disease [1], one of the most feared and distressing symptoms experienced by people with cancer is pain [2] and may be the dominating symptom at time of diagnosis of cancer, a sign of disease relapse, a symptom of late toxicity and a key symptom in patients with advanced cancer [3]. An international survey of cancer pain demonstrated that approximately 90% of patients with cancer experienced pain [4]; it is often associated with depression and impaired quality of life, consistent with a biopsychosocial [2]. Recently a growing number of epidemiological and clinical data has shown the existence of complex relations between cancer pain and mood disorders [5]; depression is the most common psychiatric disorder in cancer patients: it occurs in about 10-25% of cancer patients, a rate to be estimated to be at least four times greater than in general population [6]. The presence of pain has found to increase the prevalence of major depression in cancer population [7], patient with high pain were four time less likely to respond to depression treatment, as pain decreased to response to treatment, for depression increase. Furthermore pain severity and frequency, pain related functional impairment, and diffuse pain are all associated with more depressive symptoms and more severe depression [7], symptoms are more common in those who have more advanced disease, are hospitalized, or have greater disability, or physical distress [8]. When cancer pain persists and worsens, it can serve as a sign of the progression of disease and can create a sense of hopelessness, in fact patients' fears that their lives are not worth continuing or patients lose the meaning of living if they must live in pain. So cancer pain has a significant impact on quality of cancer patient's life influencing physical, psychological and spiritual aspects [9]. The relation between physical symptoms mood disorder is complex because physical symptoms can be integrated in diagnostic clusters of mood depression in cancer patients such diagnostic criteria may be unreliable and of low specificity [10]. Several authors have proposed, in the specific context of cancer, excluding somatic symptoms such as anorexia, fatigue and weight loss and taking in account psychological features for depression diagnosis criteria [11]. Possible mechanisms for this relationship span the biopsychosocial spectrum and include neurophysiological, cognitive, environmental, personological and predispositional factors [2]. Aminergic hypothesis posits that mood depression is the result of a neurochemical imbalance or a functional deficiency of key neurotransmitters, the monoamines: serotonin, norepinephrine and dopamine [12]. According to this theory some authors state that an aminergic reduction is involved both in mood modulation, in the limbic system, and in pain control, through the descending inhibitory system [13]. In fact more recently mood depression is considered a systemic disease, involving not only peculiar circuits of the central nervous system (CNS) but the entire body, so other pathogenetic hypotheses, complementary to the neurotransmitter-related hypothesis, must be considered [14]. Undoubtedly the reduction of neurotransmitters (the so called aminergic hypothesis of mood depression) remains the main hypothesis used to explain the background of several clusters of symptoms (anhedonic, somatic, cognitive manifestations) that can be assumed to be linked to differentiated serotonergic (5-HT), dopaminergic (DA) or noradrenergic (NA) deficits. Moreover, depression can also be related to hormonal, immunological and trophic alterations. In the hormonal hypothesis of depression, several circuits are involved: the hypothalamus–pituitary–adrenocortical axis (HPA), hypothalamus–pituitary–gonadic axis (HPG) and hypothalamus–pituitary–thyroid axis (HPT). Moreover, the chronic release of glucocorticoids, during prolonged HPA activation, can induce hippocampal neuronal death and a consequent shrinkage of this area, as found in several neuroimaging studies of depression and other psychiatric pathologies that may be associated with chronic stress [15]. Of major importance in oncology is the immunological hypothesis of depression, which refers to the fact that chronic stress can induce 'neuroinflammation', through an increased release of pro-inflammatory cytokines [16]. Particularly at the CNS level, the activation of microglia causes several responses including, on one hand, an increase of pro-inflammatory cytokines, a reduction of glutamate reuptake and an increase of glutamate release (increasing excitotoxicity) and, on the other, an induction of indoleamine-pyrrole 2,3-dioxygenase (IDO), an enzyme that can divert tryptophan from the pathway of serotonin production (causing depression) to the pathway of kynurenines [16]. Related to this broad concept of mood depression pathogenesis is the consideration that antidepressants (ADs) exert not only a brain activity, but also influence total body functioning , acting not only on neurotransmitters, but also on HPA axis (for example reducing CRF level and normalizing the glucocorticoid receptors

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systems). Moreover antidepressants, increasing anti-inflammatory cytokines, counteract the increase of pro-inflammatory ones. On the other hand it is well known that ADs can induce an increase production of neurotropic factors (such as BDNF), favouring neurogenesis [14]. Another aspect that confirms the close relation between cancer pain and mood depression is the treatment. It is well known that ADs with a broad spectrum of action on norepinephrine (NE) and serotonin (5HT) demonstrate a larger efficacy as compared to selective noradrenergic (NARIs) or selective serotoninergic antidepressants (SSRIs) both on depression and on chronic pain [17]. ADs demonstrate both a fast direct and a late indirect pain-mitigating effect, this latter related to the improvement of mood depression. Direct and prompt pain reduction produced by ADs is related to the synaptic increase of neurotransmitters, mainly due to reuptake inhibition. Moreover NE and 5HT increase induces a potentiation of endogenous opioid system and an enhancement of the pain inhibitory descending pathways. In the spinal cord NE and 5HT directly inhibit the spino-thalamic tract, as well as opiates do, and, at the same time, reduce the synthesis and release of pain-promoting neurotransmitters [2]. The main goal of this study is to investigate the relation among pain, anxiety and depression in a population of oncological patients and the secondary objective is to analyse the association between cancer pain and coping styles.

Patients and Methods

Patients

Patients diagnosed with mood depression and pain was evaluated from the Psycho-Oncology Unit, Department of Neuroscience and Oncology, University of Turin. Main baseline demographic and clinical characteristics are summarized in Table 1.

Inclusion criteria: Patients of both sex, aged 18 years or more, diagnosed within the last 12 months, with a mood disorder according to DSM-IV-TR (Fourth Edition, Text Revision of the American Psychiatric Association APA, 2000) criteria, and concomitant oncological uncontrolled pain. The entire sample had a concomitant opioid and an antidepressant therapy.

Exclusion criteria: Patients were excluded if without mood depression concomitant with pain or if were physically or mentally unable to complete study procedures. Mental competence was evaluated using The Mini-Mental State Examination (MMSE), in which individuals scoring 20 or less on the MMSE would be excluded. However, no subjects were excluded due to this criterion [18]. This trial was carried out according to "Declaration of Helsinki" (2002) and it was approved by the Città della Salute e della Scienza Hospital and University International Ethic Committee. Nature of the study and all procedures were fully explained to the patients and written informed consent to treatment was obtained by each patient.

Procedure and instruments

462 patients included in the study were assessed at baseline visit (T0) with the following rating scales, where all their demographic and clinical data were recorded. The sample is heterogeneous in sex variable due to the site disease prevalence of breast and uterus-ovary in our centre population. 173 patients were under psychotherapeutic treatment. The psychotherapy is performed using the Brief Adlerian psychodynamic psychotherapy (B-APP) model [19]. The current intensity of pain was assessed using a 0-10 visual analogue scale (VAS) [20], ranging from no pain to extreme pain. Patients were requested to show which point on the line best represented their pain intensity of the last week. Depression and anxiety symptoms were assessed with the Hospital Anxiety and Depression Scale (HADS) [21], a self-rating scale for anxiety and mood depression. The HADS has been validated from our group for fast screening of mood depression in cancer patients [22]. Scores of 8 or more are considered to be a significant case of psychological morbidity [23]. Pain quality was measured with the "Questionario Italiano del Dolore" (QUID) [24], Italian homologous of McGill Pain Questionnaire, estimating the different pain clusters (sensory, affective, cognitive and mixed) according to verbal pain descriptors selected by patients. Some terms refer to the sensory-discriminative aspects of pain; other items correspond to affective-emotional components of pain, and other descriptors are referred to the cognitive components of pain. In this way it is possible to presume for each patient, a degree of somatic, affective and cognitive component of his/her pain. Cancer-related coping styles were assessed with the Mini-Mental Adjustment to Cancer Scale (Mini-MAC) [25], assessing coping with cancer. It is 29-item instrument that examines the cognitive and behavioral responses to cancer using a 4-point Likert scale, the scores is on the five sub-scales: fighting spirit, hopelessness, anxious preoccupation, fatalism and denial/avoidance [26].

Statistical analyses

Data were analysed using SPSS for Windows version 16.0 (SPSS Inc., Chicago, IL, USA). The relationships between the psychological aspects and pain were examined using Pearson's correlation coefficient. We divided the sample in two groups according to VAS scores (see below) and we used the Independent – Simple t Test to evaluate significant differences between the two groups as for depression, anxiety and coping style. The significance threshold was set at p=0.05.

Results

VAS scores evidenced that 200 patients out of 462 (43,29%) experience relevant pain (more than cut-off of 5) [20]. On this basis,

Subjects	N	462	
Sex	Male Female	130 332	28% 72%
Mean Age (Range)	5677 ± 12,07 (21-82)		
Antidepressant therapy	Citalopram Sertraline Venlafaxine Mirtazapine Paroxetine Escitalopram	99 78 90 69 53 73	21.4% 16.9% 19.5% 14.9% 11.5% 15.8%
Psychotherapy	No Yes	289 173	62.6% 37.4%
Site Disease	Colon-rectum Breast (no mastectomy) Breast (with mastectomy) Lung Prostate Epathic Gastric Dermatologic Uterus-ovary 0sseous Head and neck	83 87 85 44 11 40 33 40 21 8 9	18% 19% 18.4% 9.5% 2.4% 8.7% 7.1% 8.7% 4.5% 1.7% 2%
Stage of Illness (TNM)	I II III	185 220 57	40% 48% 12%
Diagnosis (DSM-IV-TR)	Adjustment Disorder with Depression Depressive Disorder not otherwise specified Major Depressive Disorder – single episode Major Depressive Disorder– recurrent episode Dystimic Disorder	292 41 80 11 38	63.2% 8.9% 17.3% 2.4% 8.2%

Table 1: Baseline demographic and clinical characteristics.

further analyses were conducted in order to highlight differences between the two groups as for depression, anxiety and coping styles.

Pain, depression and anxiety

We divided the sample in two groups (group LP [low pain]: VAS < 5; group HP [high pain]: VAS ≥ 5) to investigate the difference between patients with high and low pain as for depression and anxiety. The Independent – Sample t Test showed a significant difference between the two clusters for anxiety and depression subscales of HADS. This result was agreed with correlation analysis that emphasized a positive correlation between both subscales of HADS and VAS (Table 2).

Analysing the Mini MAC subscales we found a significant difference between the two groups for anxious preoccupation, denial/avoidance, fighting spirit and hopelessness coping scale. The Pearson's coefficient showed a positive correlation between VAS, anxious preoccupation and hopelessness subscales and a negative correlation between VAS and denial/avoidance coping style (Table 3).

Finally, we observed a significant difference for quality of pain. The independence Sample t Test highlighted a difference in sensorial, affective and mixed subscales. This date was confirmed by correlation analysis where we found a positive correlation among VAS and sensorial, affective and mixed QUID subscales (Table 4).

Discussion

The purposes of this analysis were to examine the relationship of cancer pain with depression and with coping styles. These findings indicated that pain and depression are both highly prevalent in cancer patients and suggested that pain showed a positive correlation with depression and anxiety ($p<0.001$). Moreover there was a statistically significant difference in prevalence of depression between those with high level and those with low level of pain perception. Group comparisons suggested that the participants who suffered from high level of pain were more depressed than those who suffered with low level of pain. This finding was supported in other studies, showing that patients with pain had a higher prevalence of depression [2]. It is argued that pain might play a causal role in producing depression and in addition that pain can add greatly to the debilitating effects of the disease and foster hopelessness and fear. Cancer threatens patients' existence and cancer pain may cause suffering which leads to emotional distress for cancer patients and worsened quality of life [27]. Moreover our data highlighted significantly differences ($p<0.001$) at QUID sensorial, affective and mixed subscales between patients with high pain and low level of pain. High cancer pain patients compared to low cancer pain patients were significantly more likely to choose descriptors from QUID emotional and sensory adjective list. Data were in agreement with the literature that supported the studies which demonstrated the relationship between pain and depression [28]. Besides our study showed that the relationship between depression and the affective dimension of pain, was mediated by negative cognitive appraisal of pain, whereas the impact of sensory dimension of pain on depression is mediated by a focus on somatic symptoms [29]. The finding of high levels of pain sensation/intensity might emphasize cancer pain variability over time with the severity of the disease, while the finding of high affect might be related to a perception of their pain as health or life threatening. Moreover this sample highlighted positive correlations for quality of pain. Greater pain intensity was significantly correlated with higher level of affective, mixed ($p<0.001$) and sensory pain ($p<0.01$). Worsening pain leads to increased psychological distress and the effect is evident across the cancer disease spectrum [2]. Coping may further impact the pain experience associated with cancer. The present study found significantly differences between groups for anxious preoccupation, denial/avoidance, fighting spirit and hopelessness. In fact, in accordance with previous studies [30], low pain patients showed a significant higher presence of fighting spirit, a strategy that had been defined by optimism and determination to beat the illness [31]. In fact fighting spirit was predictor of perceived control over pain. In a study Vallerand et al. found that the perception of control over pain, would mediate the relationship between pain level and functional status. It was based on clinical experiences of pain that were more willing to function and had higher functional status when they believed they had the ability to control their pain. Perception of

HADS	Group LP		Group HP		Independent t Test		Pearson's Correlation	
	Mean	*SD*	*Mean*	*SD*	*t(df)*	*p*	*r*	*p*
Anxiety	11.65	4.42	14.02	3.31	6.34(460)	0.000*	0.31	0.000*
Depression	8.45	4.26	12.37	4.94	9.15(460)	0.000*	0.35	0.000*

HADS Mean Scores and Statistical Analysis (* p<0.05)

Table 2: Pain and copying strategies.

Mini MAC	Group LP		Group HP		Independent t Test		Pearson's Correlation	
	Mean	*SD*	*Mean*	*SD*	*t(df)*	*p*	*r*	*P*
Fatalism	2.72	0.57	2.64	0.64	-1.93 (460)	0.171	0.03	0.574
Fighting Spirit	2.65	0.64	2.45	0.71	-3.17 (460)	0.002*	-0.06	0.178
Hopelessness	2.67	0.66	2.88	0.75	3.12 (460)	0.002*	0.11	0.021*
Anxious Preoccupation	3.09	0.62	3.30	0.61	3.61 (460)	0.000*	0.10	0.036*
Denial/ Avoidance	2.73	0.61	2.49	0.67	-4.05 (460)	0.000*	-0.14	0.003*

Table 3: Mini MAC Mean Scores and Statistical Analysis (* p<0.05).

QUID	Group LP		Group HP		Independent t Test		Pearson's Correlation	
	Mean	*SD*	*Mean*	*SD*	*t(df)*	*p*	*r*	*P*
Sensorial Pain	0.28	0.36	0.46	0.54	4.05 (460)	0.000*	0.12	0.009*
Evaluative Pain	0.40	1.50	0.48	0.91	0.65 (460)	0.515	0.01	0.903
Affective Pain	0.19	0.38	0.49	1.03	4.37 (460)	0.000*	0.19	0.000*
Mixed Pain	0.09	0.15	0.25	0.46	5.12 (460)	0.000*	0.28	0.000*

Table 4: QUID Mean Scores and Statistical Analysis (* p<0.05).

control over pain decreases the pain related distress and subsequently leads to improved functional status [32]. In our study some coping styles were associated with pain intensity. Mini-Mac analysis showed significantly correlations among cancer pain for hopelessness and anxious preoccupation coping styles ($p<0.05$). These patients, when confronted with a painful situation, were characterized by negative self-statements, negative thoughts about future and exhibited greater level of cancer worries and higher level of perceived risk of recurrence of pain than the other group [33]. In studies of subjects with cancer pain, catastrophizing has been linked to increased pain intensity, anxiety and depression [34]. In addition, ineffective coping mechanisms and inability to control pain have been found to relate to functional interference [35]. Interestingly was also the negative correlation between pain intensity and denial/avoidance coping style ($p<0.005$). An interpretation of these findings might be that psychological response to cancer pain such as denial/avoidance have been found to prolong disease-free when was integrated with personality factors [36]. In fact denial or other form of avoidance coping could be prominent in the early phase of the illness experience and may be adaptive, allowing the individual the opportunity to integrate the illness in their lives. On the other hand it might be very difficult deny the role that pain has played in the chronic phase, in the patient' life a cause of the long experience and continuing effects of cancer and treatments.

Conclusions

This research confirmed that pain and depression are highly prevalent in a large sample of cancer patients. Mood disorders are more prevalent in oncological patients with pain than those without pain. Our data confirmed data of literature concerning the relationship between the presence of depression and pain [29]. Our study had some limitations. This sample included subjects with different cancer localizations and stages, who underwent different cancer treatments such as analgesic drugs that could influence the assessment of depression. Despite these limitations, a significant strength of the study is the wide number of the sample analysed, in which was very prevalent the presence of pain and depression. The study findings could have implications for assessment and management of pain associated with cancer treatment. Unrelieved cancer pain may lead to a more negative pain experience to include psychological impact and catastrophizing about pain experiences. Negative cognitions about pain have been identified as important factors influencing patients' adjustment to disease [13]. Consequently, health care practitioners should include assessment of pain, psychological factors and coping into their routine patient assessment prior to cancer treatment to provide appropriate care and make multidisciplinary referrals. Tailored treatments that meet cancer patients' psychosocial as well as medical needs may result in improvement pain management and functional ability. In fact various types of psychotherapeutic approaches have been developed over several decades, and cancer patients may benefit from many of these interventions [2]. The kind of management may depend on the severity of depression, stage of disease, functional status of the patient, patient motivation to participate in psychotherapy and patient interest in self-reflection. In our experience the Brief Adlerian focused psychotherapy approach is the most efficacies in term of compliance and timing in case of cancer's patients.

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