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ORIGINAL ARTICLE

"Don´t tell me that I am hysterical": Unmet needs of patients with panic disorder

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Abstract

OBJECTIVES: In the new millennium, a growing focus on human rights and preserving individual autonomy urges the promotion of needs of the psychiatric patients. The topic of human needs takes its place also in patients with panic disorder. This review intended to explore current facts concerning the needs of the patients and present a broader understanding of patients' needs, due to the complexity of problems of patients with panic disorder. The text also focuses on psychosocial well-being and the quality of life of patients with panic disorder.

METHODS: The PubMed was used to search for articles published between January 2000 and February 2020 using the following keywords: "panic disorder" or "agoraphobia" and "unmet needs" in combination with "pharmacotherapy" or "psychotherapy" or "cognitive behavioural therapy" or "family" or "quality of life." A total of 264 articles were selected by primary keyword picking in different combinations. Altogether 182 articles were reviewed.

RESULTS: We identified the most important unmet needs of patients with panic disorder connected to symptoms, treatment and help-seeking, stigma and self-stigma, family and quality of life. To help the patients to improve the unmet needs connected with:

(1) *symptoms* is to increase the awareness of treatment steps for patients and their families, good cooperation with therapists, and management of persistent symptoms, alleviation or elimination of anxiety symptoms, avoidance and safety behaviour.

(2) *treatment* is the quick approach, effective one, not too difficult, without side effects and harmless, not requiring hospitalization and not disturbing the daily routine, increasing treatment compliance, improving patient self-confidence and an active social network, affordable health and social services and more suitable information for families;

(3) *stigma* is to change of public opinion about people with mental health problems and to create effective antistigma programs;

(4) *family* is to include the support for a functional and independent life,

helping to manage everyday tasks and stop excessive protection, while reducing the stigmatization of the whole family.
(5) *the quality of life* is to help to integrate into the community and improve the factors that affect the quality of life; like esteem, self-acceptance, social acceptance etc.
CONCLUSIONS: This review aimed to explore the unmet needs in patients with panic disorder or agoraphobia. In selected articles we identified 5 basic unmet needs and described the basic strategies to cope with them. It is essential for every clinician to understand those needs as it can substantially help to alleviate patients' symptoms and improve their quality of life. The importance of this understanding further highlights that unmet needs described for panic disorder overlap with unmet needs of other psychiatric disorder and thus have broader utility.

INTRODUCTION

Panic disorder is characterized by sudden episodes of intense fear and horror that appear without an apparent external cause (Hoppe *et al.* 2012, APA 2013). The unpleasant symptoms of this disorder come unexpectedly, and they are not tied to a specific situation. A sudden attack of intense fear occurs, together with feelings that something terrible happens, that a person loses control and may faint or die without any somatic reason (Fleet & Beitman 1998, Sandin *et al.* 2015). A typical panic attack lasts several minutes but sometimes it can return in "waves" for up to two hours (Amami *et al.* 2010). Panic attacks are associated with severe somatic symptoms such as heart palpitations, chest pain, feeling of choking, dizziness, nausea, or tingling of the limbs. Anxious thoughts, states of depersonalization, and derealization can also appear (Drenckhan *et al.* 2015, Baker *et al.* 2019). A common response to a panic attack is to escape from the situation, where the attack has occurred (e.g. escaping from the subway), or to seek help and safety (medical emergency services) as quickly as possible (Rudaz *et al.* 2010, Riccardi *et al.* 2017). Since some symptoms of panic disorder imitate those of cardiovascular diseases, patients with panic disorder frequently turn to physicians with the fear of dying from a heart attack (Fleet & Beitman 1998, Teng *et al.* 2008, Coss-Adame & Rao 2015, Ohst & Tuschen-Caffier 2018) and often seek help from somatic specialists (internists, neurologists, gastroenterologists, etc.) and are unnecessarily subjected to a series of examinations that show no pathological condition (Greenslade *et al.* 2017). Subsequently, they tend to avoid situations where help is difficult to obtain (Helbig-Lang *et al.* 2014). Most individuals with panic disorder develop agoraphobia (Balaram & Marwaha 2020).

The lifetime prevalence of the panic disorder is 1-3% in the general population and 3.0 - 8.3% in clinical conditions (Roy-Byrne *et al.* 2000, Lepine 2001, Lepine 2002, Carta *et al.* 2015, de Jonge *et al.* 2016). Even in optimal treatment approach using clinical guidelines, more than half of patients continue to have suprathreshold or subthreshold symptoms (Chen & Tsai 2016). If left untreated, the panic disorder becomes a chronic and incapacitating condition associated with a higher risk of psychiatric co-morbidity, poor quality of life, reduced working ability, health problems, morbidity and mortality, high family burden, and significant consumption of health care (Batelaan *et al.* 2007, Batelaan *et al.* 2010).

The original model of panic disorder integrated biological and psychosocial findings because the panic disorder can be effectively treated by both pharmacotherapy and psychotherapy, cognitive behavioural therapy (CBT) in particular (Furukawa *et al.* 2006, Hamm *et al.* 2016, Imai *et al.* 2019, Lai 2019, Park & Kim 2019). According to the original concept (Gorman *et al.* 1989), the panic disorder has three main symptoms: (1) panic attacks and stress responses; (2) anticipatory anxiety; and (3) increased fear and phobic avoidance and impaired emotional regulation. Gorman *et al.* (1989) linked these symptom domains to nervous substrates: (1) brainstem and hypothalamus, (2) the limbic system, and (3) the prefrontal cortex. Antidepressants with serotonergic activity act on at the brainstem level. Benzodiazepines, relaxation and breathing techniques influence the anticipatory anxiety on the limbic system level, and cognitive behavioural therapy (CBT) is effective in treating avoidance behaviour (agoraphobia) at the prefrontal cortex level. In the revision of this hypothesis, Gorman *et al.* (2000) suggest that a necessary nerve substrate for panic disorder is a dysfunctional "cross-talk" between emotional drive (limbic structures) and cognitive inhibition (prefrontal cortex) (Santos *et al.* 2015, Dresler *et al.* 2013, Lai 2019).

In the new millennium, a growing focus on human rights and preserving individual urges the promotion of the needs of psychiatric patients. Both patients and their families initiate to identify their needs and focus more on their health care utilization (Hamer *et al.* 2009). Regardless of higher health care consumption, panic disorder patients report unmet needs (Katerndahl 2008). When patients with panic attacks seek care, they most frequently consult a general practitioner or hospital emergency department (Katerndahl & Realini 1995).

A recent debate focused on the necessity of respect and individual freedom and the need to live a meaningful life (Hamer *et al.* 2009). While these needs are essential for all individuals regardless of their health status, they are particularly significant in patients with psychiatric disorders. The topic of human needs encompasses also patients with panic disorder. This text intends to explore current facts concerning the needs of the patients with panic disorder. The purpose of this review is to present the complex needs of patients with panic disorder. The text also focuses on psychosocial well-being and quality of life.

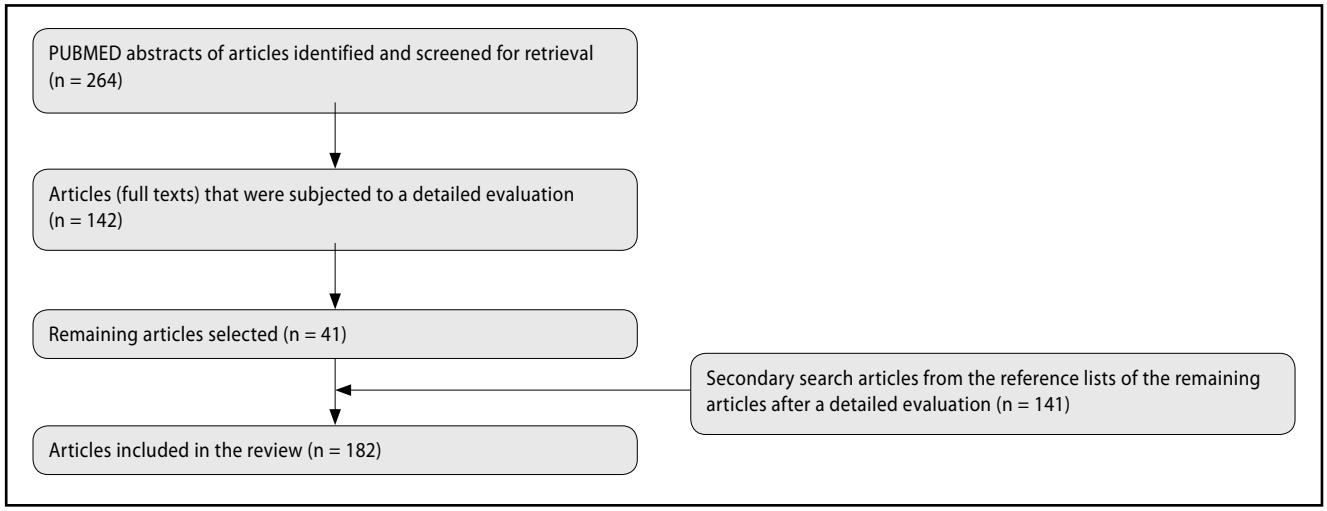

Fig. 1. Summary of the selection process

METHOD

PubMed was used to search for articles published between January 2000 and February 2020 using the following keywords: "panic disorder" or "agoraphobia" and "unmet needs" in combination with "pharmacotherapy" or "psychotherapy" or "cognitive behavioural therapy" or "family" or "quality of life." Studies that met these inclusion criteria (1) published in a peer-reviewed journal were included; (2) the articles could be prospective or retrospective original human studies; or (3) reviews on the topic; (4) subjects must be over 18 years of age; (5) contributions were published in English. The exclusion criteria were (1) conference abstracts; (2) comments and dissertations.

A flowchart (Figure 1) summarizes the total number of documents reviewed and the number of contributions included in the search process. A total of 264 articles were selected by primary keyword picking in different combinations of —142 articles selected according to inclusion criteria. After a thorough examination of the full texts, 41 articles remained. The secondary text was then searched from the reference lists of the original selected articles, and after being evaluated for suitability, added to the first list (n = 141). Altogether there are 182 articles reviewed. The flowchart (Figure 1) was created according to PRISMA recommendations (Moher *et al.* 2009).

This review aimed to explore the unmet needs in patients with panic disorder. Based on the background, the following research questions were formulated:

(1) What are the areas of unmet needs in patients with panic disorder?
(2) What are the unmet medical needs?
(3) What are the unmet needs for psychotherapy?
(4) What are the unmet needs for pharmacotherapy?
(5) What are the unmet needs for quality of life?
(6) What are the unmet needs for family and loved ones?

RESULTS

Due to the wide variety of patient's needs, the results were divided into four groups according to their common elements. There were needs associated with (1) symptoms; (2) treatment; (3) quality of life; and (4) a family. In these categories, we have described in particular the needs that present a significant problem or a significant life burden for patients with panic disorder in clinical practice.

Needs connected with the symptoms

Despite considerable progress in the therapy, many patients have persistent symptoms that limit daily functioning after acute treatment (Furukawa *et al.* 2006, Wendt *et al.* 2018). A significant number of patients experience only partial remission or recurrence of symptoms (Heldt *et al.* 2011, Dusseldorp *et al.* 2007). Patients need information about symptoms and their physiological background and learn the breath control technique to stop the development of symptoms in panic disorder (Fentz *et al.* 2013, Pompoli *et al.* 2018). They also need education in pharmacological treatment (Nordgreen *et al.* 2016, Grubbs *et al.* 2019).

The use of validated assessment tools, can improve the recognition of panic disorder in primary care population, thus empowering a recommendation for specialized therapy (Muñoz-Navarro *et al.* 2016, Sung *et al.* 2018). When assessing improvement in patients with panic disorder, it is necessary to consider both improving or worsening their panic conditions with a typical somatic and psychological component, as well as an overall improvement in adaptation. The current state can be assessed in five dimensions:

- Panic attacks (Sung *et al.* 2018)
- Anticipatory anxiety (Helbig-Lang *et al.* 2012)
- Phobias (including agoraphobia) (Greene & Eaton 2016)

- Disability in the roles (work/family/social) (Hendriks *et al.* 2016, Carmassi *et al.* 2018)
- General health (Löwe *et al.* 2003).

Up to date, there has been no valid, specific, or sensitive biomarkers, that have been recognized in patients with panic disorder, or the evaluation of the treatment response. Potential candidate biomarkers of panic disorders have been proposed, including respiratory patterns (Blechert *et al.* 2010, Blechert *et al.* 2013, Meuret *et al.* 2018), heart rate variability (Diveky *et al.* 2013, Kotianova *et al.* 2018, Mumm *et al.* 2019), peripheral blood markers (Cosci & Mansueto 2019), hypothalamic-pituitary-adrenal axis dysregulation (Abelson *et al.* 2008, Jakuszkowiak-Wojten *et al.* 2015), and), neuroimaging (Prasko *et al.* 2004, Sim *et al.* 2010, Kang *et al.* 2012, Kamaradova *et al.* 2013, Grambal *et al.* 2015); however, the clinical utility, sensitivity, specificity, and the predictive value of the biomarkers for panic disorder remain questionable (Kim YK 2019).

Selective serotonin reuptake inhibitors and benzodiazepines are among the most often prescribed drugs for panic disorder (Dusseldorp *et al.* 2007, Breilmann *et al.* 2019). Many patients with a low level of insight believe that benzodiazepines are the most helpful in avoidant, or safety behaviour. In these cases, it may be difficult to reach an agreement on the need to use exposures during the treatment (Beutel *et al.* 2013, Teismann *et al.* 2018). The habit of calming or avoiding anxiety can then be in contradiction to the common goals of treatment. Patients want to reduce their anxiety but not to give up on evasive or protective behaviour or the use anxiolytic medication (Laurito *et al.* 2018, Tanguay Bernard *et al.* 2018, Quagliato *et al.* 2018). In addition for lack of insight into the necessary treatment steps, some patients may not understand that avoidance and safety behaviour helps to maintain the disorder and gradually reduce their self-confidence and the chance to get rid of the symptoms. They are less willing to face situations where they feel discomfort, anxiety, or other negative emotions.

Cognitive models of panic disorder have stressed the part of catastrophic beliefs of physical signs as a fundamental intermediating factor of the efficiency of cognitive behavioural therapy (Fentz *et al.* 2014, El Amiri *et al.* 2018, Ohst & Tuschen-Caffier 2018). Perceived capability to control panic attacks has also been proposed to produce a crucial role in treatment change (Fentz *et al.* 2013, Sandin *et al.* 2015).

In short, the most significant unmet needs concerning symptoms are awareness about treatment steps for patients and their families, proper cooperation with therapists, and better management of persistent symptoms. Some patient´s wishes in this area may be counterproductive, for example, the need to feel good at all costs. When this happens, the therapist must collaboratively explore the patient's beliefs and schemas that underlie these wishes. Failure to do so will most likely not improve the patient's mental state and hinder treatment success.

Comorbidity with a personality disorder

A personality disorder is a frequent comorbidity in patients with panic disorder. About 50 % of panic patients meet the criteria for personality disorder diagnosis (Friborg *et al.* 2013, Kolek *et al.* 2019a). This comorbidity is frequently connected with childhood abuse (Kolek *et al.* 2019a). Personality disorder comorbidity predicts significantly more psychosocial impairment (Skodol *et al.* 2005, Ansell *et al.* 2007; Penner-Goeke *et al.* 2015) and is related to worse longitudinal results of the patients with anxiety disorders (Ansell *et al.* 2011; Skodol *et al.* 2014, Keefe *et al.* 2018). In studies of cognitive-behavioural therapy, panic disorder patients with a comorbid Cluster C personality disorder experience less panic symptom change (Porter & Chambless 2015). However, in our study (Prasko *et al.* 2005) which focused on the efficacy of a six-week CBT program in patients with panic disorder or agoraphobia and comorbid personality disorder and patients with panic disorder or agoraphobia without the comorbid personality disorder, results showed that treatment efficacy in the patients with panic disorder without personality disorder had been significantly better compared with the group with this comorbidity in CGI and specific inventory for panic disorder—PDSS. However, the groups did not differ in objective anxiety scale HAMA and subjective anxiety scale BAI. Also, in our last study (Kolek *et al.* 2019b), the presence of comorbid personality disorder predicted lesser improvement during the therapy.

In psychotherapy of patients with a comorbid personality disorder, it is necessary to address childhood adversities (Hoffart & Sexton 2002). Long-term psychotherapy is usually needed (Heldt *et al.* 2011, Beutel *et al.* 2013, Kolek *et al.* 2019b).

Needs connected with the treatment

The treatment of panic disorder includes psychotherapeutic and pharmacological approaches (Bandelow *et al.* 2015, Imai *et al.* 2016, Bighelli *et al.* 2018, Breilmann *et al.* 2019). Perceived unmet needs are linked to the severity of the disorder, avoidance, interference with functioning, comorbid depression, anticipation anxiety, and duration of worries (Chartier-Otis *et al.* 2010, Park & Kim 2019).

The findings of Marcs *et al.* (2009), who studied the characteristics of treatment received by patients with panic disorder and explored barriers to the treatment, suggest a need for better distribution of treatment possibilities, in addition to create interventions more accessible or adjusting them to the specific needs of primary care patients. There is a great need for mental health services in the general population (Messias *et al.* 2007). According to Goodwin & Andersen (2002), factors other than the severity of panic disorder may influence

the use of services. In addition to perceived (perception of poor mental health) and objectively evaluated need (severity of panic attacks, psychiatric morbidity), or predisposing (being married, older, more educated, white) factors were independently associated with the use of treatment for panic attacks.

Other commonly unsatisfied treatment-related needs are adequate family support, social contact, early recognition of the disorder, and support for decisions to seek and receive treatment, and also reduced time elapsed between the appearance of first symptoms and first consultation (Johnson *et al.* 2009, Chartier-Otis *et al.* 2010, Green *et al.* 2012). According to Craske *et al.* (2005) study, the most common obstacles to the treatment were concern about the price of services (63.9 %), not knowing where to get the treatment (63.2 %), lack of health insurance coverage (52.4 %), and appointment waiting times (52.1 %).

Recent studies of pharmacological interventions in patients with panic disorder have led to substantial evidence supporting the efficacy of SSRIs, SNRIs, and clonazepam (Bighelli *et al.* 2016, Imai *et al.* 2016, Bighelli *et al.* 2018). Other drugs, such as mirtazapine, milnacipran, and inositol, have been shown to have antipanic properties (Breilmann *et al.* 2019). In addition to SSRIs and SNRIs, TCAs, MAOIs, benzodiazepines, and atypical antipsychotics have been accepted as validated alternative for a second-line pharmacological intervention (Bruce *et al.* 2003, Freire *et al.* 2014, Breilmann *et al.* 2019).

CBT, antidepressants, and self-help are considered the best treatment choices for patients with panic disorder, according to the National Institute for Health and Clinical Excellence guidelines for the treatment of anxiety disorders (NICE 2011). The first pharmacological option is to administer SSRI or TCA. In contrast, the administration of benzodiazepines or antipsychotics is not the first choice. According to NICE, the benzodiazepine administration is associated with "less good outcome in the long term". The usage of SNRIs has not been designated in the strategies despite the high-quality indication for its efficacy in panic disorder (Sheehan *et al.* 2005, Ferguson *et al.* 2007, Pollack *et al.* 2007). Not only SSRIs and TCAs, but also SNRIs and benzodiazepines are suggested by the American Psychiatric Association practical guidelines (APA 2009). Besides, SSRI and SNRI have been recommended by the World Federation of Biological Psychiatry Societies (WFSBP) (Bandelow *et al.* 2008). There is also evidence of modest efficacy of mirtazapine, milnacipran, duloxetine, and inositol, as well as the efficacy of augmentation of antidepressants using pindolol, olanzapine, aripiprazole and clonazepam. Nevertheless, the need for a more effective, better tolerated, and faster-acting medication is still unsatisfactorily met in clinical terms. Therefore, novel mechanism-based anti-panic drugs, like CRF1 receptor antagonists, orexin receptor antagonists, glutamatergic receptor modulators, angiotensin II receptor antagonists, and endocannabinoid system modulators have been proposed (Perna *et al.* 2015).

Numerous meta-analyses have been performed, it has been found that both CBT and pharmacotherapy alone or in combination provide a significant effect-size in acute treatment stage relative to a minimal treatment or no treatment, and medium effect size when compared to psychological or drug placebo (Furukawa *et al.* 2007, Hofmann & Smits 2008, APA 2009, Sánchez-Meca *et al.* 2010, Katzman *et al.* 2014, NICE 2015, Imai *et al.* 2016). The magnitude of the effect is reduced after 6 to 24 months of follow-up, especially in (mono) pharmacotherapy (Haby *et al.* 2005, Furukawa *et al.* 2007, Katzman *et al.* 2014, Sánchez-Meca *et al.* 2010). Short-term effectiveness of psychological and psychopharmacological treatments for patients with the panic disorder appear to be similar (Imai *et al.* 2016). The use of pharmacotherapy in monotherapy is also linked with a significantly amplified risk of loss of the effect during and after the drop out of continued treatment (Haby *et al.* 2006, Furukawa *et al.* 2007, Farach *et al.* 2012). It is a consensus that CBT should be offered to patients with panic disorder first and also to those who discontinue pharmacotherapy (Katzman *et al.* 2014, Sánchez-Meca *et al.* 2010). Whether other psychotherapies could be recommended remains uncertain, because very few studies have been conducted as well as those that would compare CBT and other psychotherapies (Arch & Craske 2009).

In addition to the drug therapy neuromodulation procedures, such as transcranial magnetic stimulation (TMS) have been tested in patients with panic disorder with variable outcomes (Prasko *et al.* 2007, Machado *et al.* 2014, Iannone *et al.* 2016, Zugliani *et al.* 2019).

Further integration of genetic, neurobiological, psychophysiological, and behavioural data is needed to validate the pathways of therapeutic change in pharmacotherapy and CBT in panic disorder or agoraphobia. The goal of pharmacotherapy of panic disorder may be to expand the learning process during treatment with CBT, which focuses on the plasticity of the cortical brain structures, as such intervention is effective in both animals and humans (Dresler *et al.* 2013, Santos *et al.* 2015). Also, the administrations of D-cycloserine has reduced the most prominent symptoms of agoraphobia in combination therapy (Choi KY & Kim 2016, Park & Kim 2019).

Physical movement has been debated as a therapeutic alternative or add-on for the treatment of the panic disorder. The study of Gaudlitz *et al.* (2015) showed that regular aerobic exercise adds benefits to CBT. Also, the study of Bischoff *et al.* (2018) showed an accelerating effect of moderate-intense exercise within an exposure-based CBT for patients with panic disorder or agoraphobia.

Very important long-term needs of patients with panic disorder are the alleviation or elimination of anxiety symptoms, avoidance, and safety behaviour (Imai *et al.*

2016). Primary needs are related to the correct timing of the treatment – a useful approach is a quick, effective one, not too difficult, without side effects and harmless, with no need for hospitalization, and no disturbance to the daily routine (Imai *et al.* 2016). These optimal properties are rarely achieved, but it is essential to do the best that can benefit and not harm the patient. However, the need for treatment, such as cognitive behavioural therapy with exposure therapy, is generally in conflict with the tension experienced and the desire not to have anxiety or physical symptoms. Some patients do not have sufficient insight and therefore, do not seek the treatment. The family sometimes has a higher need for treatment than the patient himself (Pompoli *et al.* 2016). The patient needs to start treatment early and select effective therapy (Nordgreen *et al.* 2016). To even start the treatment, patients with panic disorder/agoraphobia must have developed a satisfactory level of insight (to be aware of a psychiatric disorder that can be treated) and trust in their therapist (de Cort *et al.* 2017, Halaj *et al.* 2019). Although patients come to the therapist's office, many are not sure whether they actually want the treatment. Internet-based interventions have the potential to offer highly available low-threshold evidence-based treatment to individuals with panic disorder (Pompoli *et al.* 2016, Ebenfeld *et al.* 2019, HQO 2019).

Many individuals with panic disorder experience ambivalent feelings at the start of treatment and avoid visiting the specialist (Green *et al.* 2012). The therapist needs to discuss the advantages and disadvantages of panic disorder symptoms and avoidance or safety behaviours that provide a short-term feeling of calmness, as well as the advantages and disadvantages of "a life without panic disorder" (Praško *et al.* 2007, Imai *et al.* 2016).

In general, patients with panic disorder can be effectively treated psychotherapeutically and pharmacologically. Although pharmacological treatment is useful in the treatment of a panic disorder, their potential side effects may be a problem to adherence to treatment and long-term preservation of treatment results. Therefore, it is vital to deliver affordable and effective psychotherapeutic interventions for patients with panic disorder either as a separate or complementary treatment. Psychotherapeutic procedures, especially cognitive behavioural therapy and short psychodynamic therapy, are effective treatments for patients with panic disorder. However, they do not work in all patients, and further approaches to the treatment of resistant and co-morbid patients will also need to be developed in psychotherapy. Another problem is the relative unavailability of effective psychotherapy. Therefore, internet psychoeducational and psychotherapeutic self-guided programs could be efficient options for broach distribution in routine care.

Stigma

One of the essential needs of panic disorder patients and their families is to be a respected person, who is not labelled and is not looked down upon (Ociskova *et al.* 2014, Holubova *et al.* 2019). The patient's effort to avoid stigmatization is understandable but leads to delaying or avoiding adequate assistance (Camp *et al.* 2002; Cinculova *et al.* 2017). Mass media play a central role in building the image of psychiatry and patients with psychiatric disorders, thus worsens maladaptive coping responses of families with relatives suffering from panic disorder (Hoffmann-Richter 2000). The general public often learns about the panic disorder through popular magazines. Stereotypes and negative prejudices about the psychiatric patients, that media and society bring, are misleading (Gray 2002). This is partly due to still prevalent stereotype that people with mental disorders are dangerous, impulsive, and aggressive (Goffman 1986, Nawka *et al.* 2012, Nawkova *et al.* 2012).

Stigmatization affects patients as well as their family members. Part of the interpersonal rejection experienced by many patients may result from the avoidance and safety behaviour of individuals with panic disorder and agoraphobia, another part from misrepresentation of diagnosis information or erroneous knowledge of psychiatric treatment (Holubova *et al.* 2019). Refusal based on the patient's mental health problems may also occur in situations, where the patient is acting normally, and others only know that they are undergoing psychiatric treatment.

A simple "label" of having a psychiatric diagnosis can trigger stigmatization. Because of that, patients can be stigmatized and rejected in various social situations, including work and family relationships (Ociskova *et al.* 2018). Even patients, who have completed treatment, may continue to be subjected to stigmatization. People can act cautiously around the patient, overly focus and analyze their behaviour, and connect the behaviour with the unfavorable label. The fear of labelling is a reason why people with panic disorder, are often afraid of psychiatric diagnosis to the extent that they actively avoid seeking adequate help (Ociskova *et al.* 2015). When it comes to the panic disorder, the general population (including the patients themselves) are usually convinced, that flawed personality traits cause the panic disorder. They may assume that individuals with panic disorder behave in some way wrong, incorrectly, or strangely (Praško *et al.* 2007). These erroneous assumptions lead to avoidant or hostile behaviour, blaming and humiliating patients.

The authors conclude that the stigmatization of patients with panic disorder and their families can be reduced by the cooperation of patients, their families, and healthcare professionals in a way that is free from common prejudice and stereotypes (Cangas *et al.* 2017). Similarly, families can experience stigmatizing reactions in the health care system itself. The path to a diagnosis can be very tedious. Families may stigmatize the person, mostly after they have found it to be a mental disorder because they lack proper information about it (Borgo *et al.* 2017). They do not have enough

knowledge; they feel insecure and helpless. It can, therefore, be difficult for them to be continually supportive and empathetic, especially when their relative had lost hope because they are desperate or suicidal (Batinic *et al.* 2017, Teismann *et al.* 2018). Celebrity confessions about their experiences with panic disorder can reduce stigma and self-stigma, as the community gains more familiarity about the disorder and grow into higher awareness about it (Lee *et al.* 2019).

In short, the most critical unmet needs concerning for stigma are the change of public opinion about people with mental health problems and programs aimed at reducing stigma.

Barriers in help-seeking

Very often, the treatment is initiated with a considerable delay, which prolongs the patient's suffering. Patients and their caregivers may consider psychiatric or psychotherapeutic services unavailable, have a poor opinion of their functioning, have a terrible personal or substitute experience, or fear the negative consequences of treatment (Craske *et al.* 2005, Nordgreen *et al.* 2016). The treatment is sometimes initiated in a humiliating way (patients are brought to a psychiatrist under the family pressure) when relatives want treatment, but the patient does not want it or is ambivalent (Westra 2004, Wolf &, Goldfried 2014). The dominant behaviour of family members can also affect the atmosphere in the family and their view of the need for treatment. Many factors also influence attitudes to drug use: the patient's self-concept and a desire to cope without outside help, attitudes to psychopharmacs or psychotherapy, previous experiences and public myths about treating psychiatric disorders, as well as fear of stigmatization by psychiatric disorder or treatment (Cinculova *et al.* 2017).

In short, the most critical unmet needs linked to obstacles in seeking help are affordable health and social services and more suitable information for families.

Self-stigma

People with specific coping strategies, such as dissociation, are more disposed to feelings of shame and guilt. Such persons may be susceptible to developing self-stigma as well because the primary emotional source of self-stigma is the feeling of shame (Link *et al.* 2001, Alonso *et al.* 2008, Prasko *et al.* 2011). There is an association between self-stigma and the number of previous hospitalizations, antidepressant dosage, discontinuation of medication, the severity of the disorder, and the number of psychiatrists attended by the patient (Ociskova *et al.* 2014, Ociskova *et al.* 2017). Additionally, self-stigma lowers adherence to pharmacotherapy (Cinculova *et al.* 2017) and can present a significant problem in seeking therapeutic assistance (Barney *et al.* 2009, Ociskova *et al.* 2015, Cinculova *et al.* 2017). Patients' efforts to side-step stigma may lead to rejection of the fact that they have a mental disorder preferring physical explanation of the roots of the problems, and avoiding or delaying the search for proper psychiatric or psychotherapeutic management (Camp *et al.* 2002, Finney & DiStefano 2008, Barney *et al.* 2009). Additionally, self-stigmatization is associated with insufficient treatment cooperation (Sirey *et al.* 2001; Padurariu 2011; Cinculova *et al.* 2017). Some of our studies also show that self-stigma lowers treatment efficacy in patients with anxiety disorders (Ociskova *et al.* 2015; Ociskova *et al.* 2018).

Treatment options

Selective serotonin reuptake inhibitors (SSRIs) and CBT with exposures are a treatment of choice for panic disorder, but about 30 % of patients do not respond adequately (Bandelow *et al.* 2015, Pompoli *et al.* 2016, Zickgraf *et al.* 2016). Regardless of practicing the optimal approach, about 10 % of patients remain resistant to treatment (Perna & Caldirola 2017).

Despite the treatment, the most significant unmet need for panic patients and their families is the problem of finding adequate panic treatment with access to appropriate pharmacotherapy and cognitive behavioural therapy (Caldirola & Perna 2019). The availability of treatment, adequate doses of medication, and information on the possible response to treatment and the prevention of relapse may also be a problem (Rollman *et al.* 2005).

Many patients are being treated inappropriately because of an ineffective psychotherapeutic or pharmacotherapeutic approach, receiving inadequate doses of medication (Milrod & Busch 1996). However, adequate treatment may be unavailable (Reid *et al.* 2018). Patients who have been confronted with several complications associated with the use of drugs, including polypharmacy, inadeqate dosing, no access or money for the drugs or even the shoratage of the drug (Bhatara *et al.* 1998, Bystritsky 2006, Pary *et al.* 2019).

Many patients with panic disorder have experienced side effects of medication and sometimes do not believe in the effect of the drug. Others describe the ambivalence regarding the importance of psychopharmacs and the inability to remember how to use them, leading to non-adherence to treatment (Aoki *et al.* 2014, Chambless *et al.* 2017, Maiwald *et al.* 2019). Others find the side effects of the medication intolerable, and repeatedly stop the medication in the first week, forming a rejecting attitude towards medication. A partner or family can also oppose drugs. Unpleasant side effects include physical symptoms such as initiall tiredness, transient increases in tension, long-term sexual dysfunction, weight gain, and decreased pleasure (Craske *et al.* 1989, Daiuto *et al.* 1998, Chambless *et al.* 2017).

Unmet needs during outpatient treatment

In many patients with remission, it is necessary to increase self-esteem (Fentz *et al.* 2014, van Tuijl *et al.*

2016). Equally important is their adherence to treatment, regular use of medication, and regular check-up by the attending psychiatrist. Patients with panic disorder may face community difficulties, and their psychiatric management needs to take these problems into account. With the expansion and diversity of mental health services, the organization of treatment becomes a more service-oriented approach. Facilitating access to social contacts, employment, and housing in panic disorder treatment is essential, as many have lost their jobs due to the development of agoraphobia (Clark *et al.* 2012, Stansfeld *et al.* 2014, Asai *et al.* 2017). In short, the most critical unmet needs during treatment are increasing treatment compliance, more effective drugs without side effects, affordable psychotherapy, especially CBT, and a more extensive range of psychosocial interventions, improving patient self-confidence and active social network.

Quality of life needs

This type of needs could be defined as any anxiety or discomfort that patients have identified as not related to the treatment of panic disorder symptoms, but that negatively affect their ability to integrate into the treatment community and their quality of life. School, employment, the economic situation, family conflicts, and the desire for daily activities are examples of concerns expressed by patients (Fidry *et al.* 2019). Some individuals with panic disorder deal with abuse (physical, emotional and sexual), divorce, child loss, and a distance from offensive or critical family members. Alternatively, they can become too dependent on the family and pay for it with their freedom. Many patients have difficulty finding work, paying rent and other financial problems. It may be difficult for students to attend a school regularly; they may have issues at school, especially with concentration (Andersch & Hetta 2003, Fidry *et al.* 2019).

The disorder significantly disrupts the life experiences of many patients, who report a negative impact on their curricula, interpersonal relationships, careers, and the establishment of their own families (Praško *et al.* 2007, Fidry *et al.* 2019). Therefore, the most critical unmet needs concerning quality of life are ability to integrate into the community and improvement to the factors that affect the quality of life.

Family-related needs

The constraints that come with the symptoms of panic disorder increase the dependence of patients on their relatives. Some patients are increasingly unable to handle their daily tasks due to numerous anxious thoughts, reduced self-esteem, and evasive behaviour. In addition to assuming day-to-day responsibilities, patient's families usually participate in safety and avoidant behaviour and may be a decisive factor in maintaining treatment failure (Craske *et al.* 1989, Daiuto *et al.* 1998, Praško *et al.* 2007). In this respect, these families can be clearly distinguished from most families with relatives with other psychiatric disorders. In particular, family members living in the same household with the patient (such as partners, parents, children, and other relatives) enter into daily avoidant behaviour (Zaider *et al.* 2010, Whisman *et al.* 2019).

The most common stressors, preceded by panic disorder, are partner, family and work conflicts, lack of adaptation to role changes (mother's role, relationship changes) and new roles in life, economic stressors (Praško *et al.* 2008, Borgo *et al.* 2017). Multiple minor psychosocial stressors, such as excessive criticism, rejection, overly competitive atmosphere, can also act as triggers (Manassis *et al.* 1994).

People, who have panic disorder, often depend on their loved ones (Praško *et al.* 2008). In more severe cases, a close person often must be present at all times in order to help the afflicted person. Whether the fear of abandoning precedes or is a consequence of panic is difficult to determine. However, in childhood, there is commonly a premature separation from parents that has been followed by anxiety or resignation. A partner of the patient often feels confined. Sometimes it may be convenient because it gives them a sense of domination and necessity in a relationship or a sense of value. Other times, however, it feels like a significant constraint and conflicts arise, which in turn aggravate panic disorder or lead to the development of comorbid depression.

Indeed, people with agoraphobia tend to be afraid of abandonment as well as fear of attachment to another person in adulthood (Bowlby 1973, Nemiah 1988, Manassis *et al.* 1994). Therefore, they have an excessive need to control relationships. Since a high degree of interpersonal control is unattainable, relationships suffer from tension. A patient with agoraphobia may have feelings of excessive commitment to their partner who gives them a sense of security. This can result in reduced ability to express his/her other needs openly but must submit and subside even in situations where they are not comfortable (e.g. always responding positively to their sexual needs), leading to deep dissatisfaction with the relationship. Very often, there is an intense ambivalence. The patient is dependent, therefore, subordinate, at the same time, they perceive a partner with considerable aversion (Borgo *et al.* 2017). The situation is a stalemate for them. They cannot be alone.

Agoraphobia can lead to partner and family conflicts e.g., requiring a partner to accompany the patient, restricting traveling for the whole family (e.g. on vacation), avoiding cinemas, theaters, concerts or avoiding shopping, and requiring someone else to shop - all these can limit the whole family. The typical signs of panic disorder, the avoidance of travelling, shopping of other places and situations due to the fear of panic, and the loss of autonomy, lead to increased dependence on family members (Detzel *et al.* 2015, Borgo *et al.* 2017).

Reinforcing the avoidant behaviour by relatives and dependence gradually dominates family life and leads

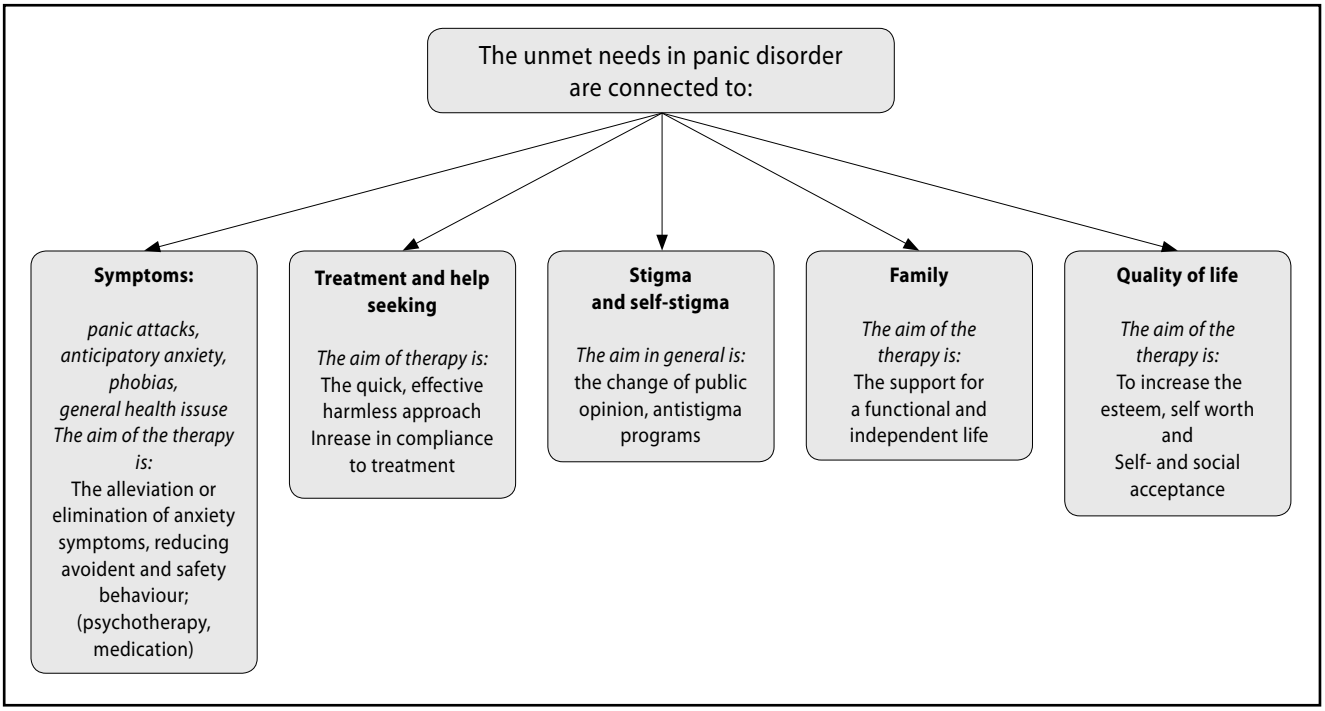

Fig. 2. Types of unmet needs in panic disorder patients

to a build-up of tension and disagreements on how to proceed further. Family relationships and functioning can also adversely affect the severity of symptoms as well as safety and evasive behaviour. Depression, guilt, grief, substance abuse, social stigma, and other secondary symptoms are also part of the picture. The fact that the family member has been identified as having a mental disorder can alter the family. Relatives begin dealing with stigmatization and the fear of being stigmatised.(Suresky *et al.* 2014). Not surprisingly, the family tends to keep the diagnosis of panic disorder in secrecy. A mental disorder becomes a secret that is not shared. The taboo also includes the unique burden of caring for a relative with panic disorder.

The existence of a psychiatric diagnosis further reinforces the fear of social degradation and exclusion (Detzel *et al.* 2015). All this poses considerable difficulties that families of panic disorder/agoraphobia patients must deal with. Developing acceptance and understanding attitudes towards a family member with panic disorder can be challenging, and is a long-term task rather than a matter of rapid adaptation. It is not uncommon for them to deal with relatives for the entire duration of treatment (Suresky *et al.* 2014).

Family members have become more important in psychiatric care in recent decades. It has been found that caregivers often carry a heavy burden; e.g. interference with domestic activities, leisure and career, tense family relationships and reduced social support, reduced mental health, subjective distress, and burnout (Detzel *et al.* 2015).

Patients also appreciate such support as a relaxing conversation with family members about their disorder. Most caregivers suffer from moderate stress. This burden is associated with characteristic behaviour, reduced performance in patient-related tasks, and negative family and household costs. It has been found that the conviction of people with panic disorder that they can control their psychological problems is related to a higher level of burden management and disappointment in the relationship (Detzel *et al.* 2015, Borgo *et al.* 2017).

In short, the most crucial unsatisfied family needs are support of a functional and independent life, help in managing everyday tasks and the stopping of excessive protection, while reducing the stigmatization of the whole family.

DISCUSSION

Implications for pharmacotherapy

The treatment adherence, including regular use of the medication for a sufficiently long period, is determined by many factors on the part of the therapist and the patient.

In most countries, it is stipulated by law, that patients have the freedom to choose their treatment. However, the availability and cost of treatment are often the decisive factors. Permitting patients to choose between evidence-based treatments would increase the patient's engagement and may lead to patient's significant feeling of safety and satisfaction. Similarly, the freedom of choice would likely increase compliance, thereby improve results, and reduce the overall cost and burden of the disorder (Brazier *et al.* 2009).

Adherence to drugs is related to the patient's insight. If they believe their problems are due to a physical illness, they usually tend to refuse psychotropic medication, and even if they accept the medication, they often discontinue it. Another reason for poor drug adherence is myths about psychopharmacs. Especially the patients and their family belief that the medication is harmful to health, washes out the brain, has intolerable side effects, changes the personality of the person, etc.

Implications for psychotherapy

CBT and psychodynamic therapy are evidence-based approaches that are usually offered to patients with panic disorder (Sandell *et al.* 2015). Some people fear psychotherapy. They are convinced that they will have to reveal secrets they never confessed to anyone before and that the psychotherapist will not like them or somehow will lure them (Prasko *et al.* 2011). They also often think that "just talking" cannot change the intense bodily symptoms. Sometimes they are disappointed with past unsuccessful psychotherapeutic attempts when they have the impression that they were just talking, but their panic attacks or agoraphobia were not treated. Cognitive behavioural therapy improves panic disorder treatment outcome relative to medication alone in the primary-care setting (Craske *et al.* 2005).

(1) What are the areas of unmet needs in patients with panic disorder?

We identified the most important unmet needs of patients with panic disorder connected to symptoms, treatment and help-seeking, stigma and self-stigma, family and quality of life.

(2) What are the unmet medical needs?

The most significant unmet needs concerning symptoms are increasing awareness about treatment steps for patients and their families, good cooperation with therapists, and better management of persistent symptoms. Primary needs related to treatment are faster and more effective approach, less complicated treatment, no side effects and harmlessness, no need for hospitalization and no disturbance to the daily routines. The long-term needs of patients are the alleviation or elimination of anxiety symptoms, avoidance and safety behaviour. The most critical unmet needs linked to obstacles in seeking help and during treatment are increasing treatment compliance, improving patient self-confidence and an active social network, affordable health and social services and more suitable information for families.

(3) What are the unmet needs for psychotherapy?

The essential unmet needs connected to psychotherapy are good cooperation with psychiatrists (in case of using psychiatric medication in combination) and psychotherapists, the need for affordable psychotherapy, especially CBT to treat panic disorder, and more extensive range of psychosocial interventions, improving patient self-confidence and active social network. Achieving insight through education, understanding barriers to medical collaboration, identifying maladaptive coping, and working to effectively reduce the panic problems that involve exposure to anxiety that patients often avoid is therefore crucial in meeting the need for symptom relief.

(4) What are the unmet needs for pharmacotherapy?

Equally important is adherence to treatment, regular use of medication and regular check-ups by the attending psychiatrist. Despite the level of treatment, the highest unmet need for patients and their families is the problem of finding adequate panic disorder treatment with access to appropriate pharmacotherapy. The availability of treatment, adequate doses of medication and information on the possible response to treatment and the prevention of relapse may also be a problem. Insight into the problem, the therapeutic cooperation of both the patient and the family, finding a right specialist and setting the medication to be of real benefit to patients are crucial for good cooperation in treatment.

(5) What are the unmet needs for quality of life?

The most critical unmet need for quality of life is ability to integrate into the community and improvment to factors that affect the quality of life.

(6) What are the unmet needs for family and loved ones?

Finally, the most crucial unsatisfied family needs are proper support in a functional and independent life, help in managing everyday tasks and stopping the excessive protection, while reducing the stigmatization of the whole family. The most critical unmet needs concerning stigma are the change of public opinion about people with mental health problems and more effective antistigma programs.

CONCLUSION

Panic disorder is a multifaceted heterogeneous multifactorial and polygenic disorder. The heterogeneity complicates the diagnosis treatment results and prognosis. Numerous psychopharmaceuticals are effective and accessible for the treatment of patients with panic disorder and agoraphobia. Nevertheless, the results have not been entirely satisfactory in many patients, emphasizing the need for growing the spectrum of anti-panic pharmaceuticals. Practically, there is a great need for more efficient, more tolerable, and fast-acting medical and psychotherapeutic interventions for panic disorder. Although the debate about obstacles in care has been conventionally focused on the stigma, health care network, and economic factors, there are also simple aspects, such as not knowing where or whom to call for help.

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