PHARMACOTHERAPY VERSUS PSYCHOTHERAPY IN PANIC DISORDER. REVIEW

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(Abstract) Panic disorder is one of the most frequent psychiatric conditions and the incidence is increasing. More worrying than the number of patients is the major negative impact over personal, social and economic functioning. Due to the increasing risk of death, whether by suicide or by cardiovascular disease, in patients suffering of panic disorder a prompt, adequate intervention is essential. This condition has a chronic evolution, with low rates of remission and a significant negative impact over quality of life and over social and economic aspects. In this article we presented different aspects related to the therapeutic management of panic disorder, with special reference to pharmacotherapy and its specific classes and psychotherapy, particularly Cognitive-Behavioral Therapy. These two therapeutic categories proved to be the most efficient in both acute and long-term symptomatology, with improvement of anxiogenic rumination, avoidance behavior or agoraphobia. Pharmacotherapy, whether with antidepressants or benzodiazepines, is recommended to be followed by psychotherapy. SSRIs and SSNRs are recommended as first-line medication, while benzodiazepines are necessary only in acute phases or until the therapeutic effect of the above-mentioned medicines is obtained. In treatment-resistant patients at patients who do not respond sufficiently to any first-line treatments it is necessary to use other classes of medicines, such as atypical antipsychotics. Keywords: PANIC DISORDER, PSYCHOTHERAPY, COGNITIVE-BEHAVIOURAL THERAPY, PHARMACOTHERAPY.

Panic attack is one of the most important types of anxiety disorder. In Romania, due to the high level of risk, the acute episode of a panic disorder was included in the list of psychiatric emergencies, based on Order 488, point 159 of April 2016, from Mental Health Law. Since over 70% of the people who attempted suicide had an associated anxiety disorder, this Order is well justified. Panic attack is also independently associated with suicide risk, and comorbidity of panic attack with personality disorder is characterized by a higher risk of attempted suicide over either disorder alone (1, 2, 3, 4). Thus, anxiety associated with personality disorder was correlated with an increase in suicide attempt from 1.7 to 2.6 times (5).
Secondly, cardiorespiratory involvement in panic attack physiopathology can worsen its course or more, it can lead to death in population with the above-mentioned comorbidities (6,7,8). In the case of a cardiovascular disease, the anxiety symptoms in arrhythmic patients are associated with a higher severity of atrial fibrillation (9,10) and atrial fibrillation recurrence (10). Comparing the QT interval on electrocardiogram in a control group and patients suffering from panic disorder, Atmaca found that the QT in the latter group was significantly longer, prolonged QT being associated with arrhythmic events and sudden death (11).

In patients with panic disorders, the high risk of death, whether by suicide or cardiovascular disease, makes a prompt intervention mandatory.

Panic disorder has a chronic course and a low rate of remission with a significant negative impact not only on life quality but also on social and economic aspects (12,13).

Considering all these aspects, the main purpose of this article was to present data in the literature regarding different approaches of panic disorders, especially the adequate management of acute phase, which requires special emergency care. Therefore, the efficacy of pharmacological and psychological therapy, especially the cognitive behavioral therapy, used separately or combined will be analyzed.

To obtain the articles for this review, we searched PubMed using the following key words: “panic disorder”, “pharmacotherapy” and “psychotherapy”. The accepted studies were only those comparing pharmacological therapy with psychotherapy.

First line treatment

First line treatment of panic disorder is represented by selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs). According to meta-analyses and randomized clinical trials, Citalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline and Escitalopram are the first therapeutic option (5).

A study of Azhar (14) compared the efficacy of Fluvoxamine treatment alone and Fluvoxamine combined with Cognitive Behavioral Therapy (CBT) and CBT alone. The best results were obtained by combining the two therapeutic methods, with significant improvement of the following parameters tested before and after nine weeks of treatment: frequency of panic attacks reduced from 16.7 to 4.07 per week, catastrophic belief score from 100 to 31.79 and the scores from Hamilton Anxiety Rating Scale reduced from 37.14 to 22.86. The group that received only CBT obtained similar results, sometimes even better than the others for the above-mentioned variables. The Fluvoxamine alone group had the lowest scores for the mentioned parameters, therefore psychotherapy is essential for improving anxiety symptoms.

Venlafaxine, an SNRI, is also efficient in reducing the severity of panic disorder symptoms (5).

Treatment with Benzodiazepines

In the acute phase of a panic disorder, benzodiazepines are the most frequent recommended medicines. Their main advantage is represented by the short period of time necessary to achieve the therapeutic effects.

Watanabe et al. (15) presented the benefits of benzodiazepine therapy versus combined benzodiazepines and behavioral therapy. The conclusion is that the combination therapy might be superior to behavior therapy alone in terms of the global severity of symptoms, phobic avoidance behavior and social functioning.

In acute phase, combined therapy is ef-
Pharmacotherapy versus psychotherapy in panic disorder. Review

According to Mu-Hong and Shih-Jen (18) recommendations, CBT or pharmacotherapy should be the first option in panic disorder treatment, while combining the two of them should be indicated as second-line and administered to patients resistant to treatment. If favorable results are not obtained with any of these strategies, augmentation with atypical antipsychotics is an established drug treatment strategy. From this category Aripiprazole, Quetiapine and Olanzapine proved to increase the efficacy of baseline antidepressant treatment. The results with using other drugs, such as GABAergic antiepileptics, D-cycloserine and anti-inflammatories are inconsistent and need additional evidence to sustain their inclusion in the treatment of treatment-resistant panic disorders.

Management of treatment-resistant panic disorders

Panic disorder consists of recurrent paroxysmal panic attacks, along with the worry regarding future panic attacks and phobic avoidance behavior. Over 50% of patients on treatment continue to experience panic attacks symptoms and fail to obtain remission. Half of the cases that do remit will present relapses later in life (18).

Two types of criteria regarding remission of panic disorder have been proposed (19,20). The first criteria include: absence of panic attacks, absent or reduced agoraphobic avoidance behavior, Hamilton Anxiety Score (HAMAS) ≤ 7-10, absence of functional impairment, absent or reduced depressive symptoms, Hamilton Depression Scale (HAMDS) ≤ 7. The second criterion includes the following elements: Panic Disorder Severity Scale (PDSS) ≤ 3 and HAMDS ≤ 7. Treatment resistance is defined as the failure to meet any of the above-mentioned remission criterion after at least six months of optimal treatment (19,20).

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CBT or and pharmacotherapy

Even though some studies support the superiority of CBT over pharmacotherapy (21), it is generally accepted that their combination is more effective than CBT alone. A global improvement of symptoms but without an improvement on quality of life had been recorded. However, when long-term outcomes were examined combining CBT with pharmacotherapy proved unsatisfactory. The negative effects can be explained by the fact that the learning process during CBT is influenced by drug therapy (12), especially with benzodiazepines, which on long term had been associated with impairment of cognitive function (15,16). In the study by Krysta et al. (16) the anxiolytic agent is represented by Escitalopram and Duloxetine, which improve attention and executive function, Tianeptine, which improves attention and short-term memory, and Sertraline and Mirtazapine.

Meuldijk et al. (22) suggest that concise care with CBT and/or pharmacotherapy (three months) has similar outcomes as
classic therapy, which requires a longer period of treatment of three or six months to one year or even more. This approach involves 45-minute weekly CBT sessions for seven weeks consecutively. Following this method, the clinical results are obtained earlier, and patients are more satisfied with this type of care.

Treating panic disorders with CBT has certain advantages to pharmacotherapy: fewer side effects, lower relapse rate, and a higher rate of treatment adherence. Pharmacological treatment has many side effects and the risk of relapse is higher, resulting in discontinuation of treatment. In practice CBT is less used than pharmacotherapy especially due to the lower availability of specialized personnel (23, 24). Having patients repeatedly confront safe, but anxiogenic situations, as it happens in exposure therapy, results not only in a reduction in frequency of panic attacks but also a reduction of the fear of having another panic attack, compared to the administration of drugs alone which only reduces the frequency of attacks (21).

At the basis of these results stands the neurobiological change, which appears secondary to the psychotherapy. In panic disorder there is an improper cortical inhibition, for example from prefrontal cortex to an overactive limbic system, from amygdala and insular cortex and a poor modulation to the hippocampus (18). In the case of patients who followed CBT, exposure to anxiogenic situations did not over activate the amygdala. This deactivation represents a more efficient control over limbic system to the prefrontal cortex, which manages more efficiently anxiogenic triggers, by more rational analyze of the exposure (21).

Initiation of whichever therapy requires careful analysis of individual characteristics of patients with panic disorder. Therefore, CBT should be taken in consideration as first option in patient who, for example, worry excessively about or cannot tolerate the side effects of prescribed medicines. On the other hand, pharmacotherapy can be considered as first-line strategy for a patient who presents more somatic symptoms (palpitation, paresthesia, sweating etc.) than cognitive ones (persisting fear for not experiencing another panic attack) (18, 25, 26).

From our review and summing up all the studies above presented, in the treatment of panic disorder we can used pharmacotherapy, whether antidepressants or benzodiazepines, but it is recommended to be associated with psychotherapy. As first line treatment it is recommended selective serotonin reuptake inhibitors or serotonin and norepinephrine reuptake inhibitors, while benzodiazepines are necessary only in acute phase or until the first two treatment lines determined a therapeutic effect. For the resistant cases, it is required to use other group of drugs such as atypical antipsychotics.

REFERENCES

Pharmacotherapy versus psychotherapy in panic disorder. Review


