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PANIC DISORDER IN PRIMARY CARE

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The aim of this work is to analyze the prevalence and comorbidity of panic disorder (PD) in Primary Care (PC) settings, the percentage of patients correctly diagnosed and treated, and the efficacy and scientific adequacy of treatments applied in this context. Results show that in Spain, the one-year prevalence of PD is high in the PC setting (7%), while it is 0.6% in the general population, affecting more women than men (OR=1.63). PD is comorbid with other mental disorders in 70% of the cases, reducing patients' quality of life. Of all anxiety disorders, PD is the most incapacitating and that which results in most medical visits. In spite of this, 50% of PD patients are misdiagnosed and very few receive "minimally adequate treatment", which in the long term leads to high dropout and relapse rates. An active effort must be made to disseminate evidence-based prevention and treatment programmes that show greater efficacy than conventional treatment.
Key words: *Primary care, Panic disorder, Prevalence, Comorbidity, Cognitive-behavioural treatment.*

El objetivo de este trabajo es analizar la prevalencia y comorbilidad del trastorno de pánico (TP) en las consultas de Atención Primaria (AP), estudiar el porcentaje de pacientes diagnosticados y tratados, y revisar la eficacia y adecuación de los tratamientos a la evidencia científica en dicho contexto. Los resultados indican que en España la prevalencia año es elevada en las personas que acuden a AP (7%), mientras que en la población general es de 0,6%, siendo más frecuente en mujeres que en varones (OR=1,63). El TP suele cursar con otros trastornos mentales en el 70% de los casos, lo que suele deteriorar la calidad de vida de estos pacientes. A pesar de ser el trastorno de ansiedad que genera mayor incapacidad e hiperfrecuentación de los servicios médicos, no se diagnostica correctamente en la mitad de los casos y pocas veces recibe un tratamiento mínimamente adecuado, lo que a la larga produce más abandonos y recaídas. Se requieren esfuerzos por diseminar los tratamientos y los programas de prevención basados en la evidencia científica, que han demostrado ser más eficaces que la práctica habitual.
Palabras clave: *Atención primaria, Trastorno de pánico, Prevalencia, Comorbilidad, Tratamiento cognitivo conductual.*

According to the DSM-IV TR, a panic attack consists in the temporary and isolated appearance of intense fear or distress, accompanied by four (or more) of the following somatic and/or cognitive symptoms, which are of sudden onset and attain their maximum expression in the first 10 minutes: increased heart rate, sweating, trembling, sensations of smothering, feeling of choking, chest pain or discomfort, nausea or abdominal distress, dizziness or fainting, derealization or depersonalization, fear of losing control or going crazy, fear of dying, paresthesias, and shivering or hot flushes. PD, on the other hand, is characterized by a history of recurrent and unexpected panic attacks of which at least one has been accompanied (for a period of one month or more) by persistent worry about the possibility of having a new attack or concern about the possible consequences and/or a significant change in behaviour related to the panic attacks.

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The cognitive model of panic (Clark et al., 1997) holds that panic attacks result from interpreting in a catastrophic way certain body sensations, mostly related to anxiety responses (palpitations, sweating, breathlessness, dizziness, etc.). Such benign sensations are perceived as though they were much more dangerous than they actually are (for example, there is a tendency to think that increased heart rate can lead to a heart attack), and such catastrophic interpretations are responsible for bringing about the development of PD.

A meta-analysis of 12 studies with general population in Europe (Wittchen & Jacobi, 2005) revealed a one-year prevalence for PD of 1.8%, with a range of 0.7 to 3.1. This study takes into account the data from the ESEMeD (European Study of the Epidemiology of Mental Disorders) promoted by the WHO (Alonso et al., 2004a) in six European countries (Germany, Belgium, France, Holland, Italy and Spain), which found a one-year prevalence for PD of 0.8% (0.6-1.0), though the figure for Spain was somewhat lower (Haro et al., 2006): 0.6% (0.4-0.8). Life prevalence in Europe was 2.1% (1.9-2.3), and in Spain, 1.7% (1.3-2.1).

According to the National Comorbidity Survey-Replication (NCS-R), in the USA the prevalence of PD in the general population (N = 9282) over the previous 12 months was 2.7% (Kessler, Chiu, Demler, Merikangas, & Walters, 2005), that is, 3.4 times higher than the figure from the ESEMeD-Europe study and 4.5 times that for Spain. For life prevalence, the NCS-R found a figure of 3.7% (i.e., 1.8 times higher than the European rate and 2.2 times higher than the Spanish rate). Moreover, 22.7% of the population had had at least one panic attack in their life (Kessler et al., 2006). Furthermore, the Health Care for Communities study (Bystritsky et al., 2010), another survey in the US population (N = 9585), found a prevalence of 40% in subclinical panic. As it can be seen, there are substantial differences between the USA and Europe, but in any case panic widely affects people in general.

For decades now it has been well known that PD is much higher in the Primary Care (PC) context than in the general population (Katon, 1986). Even so, in PC, until fairly recently its actual prevalence was not known with much precision, and was estimated at about 4% on average, according to a review of 8 relevant studies carried out in the 1990s (Roy-Byrne, Wagner, & Schraufnagel, 2005b), being much higher in patients with cardiovascular (20% to 50%) or gastrointestinal problems (28% to 40%). In Spain, the PRIME-MD (Spitzer et al., 1994) revealed a prevalence of 2.2% (Baca-Baldomero et al., 1999). Currently, however, epidemiological studies on PD in PC are being published that need reviewing, with a view to clarifying the differences due to method (interviews, screening, detection by GPs, etc.), as well as other variables (such as countries). In turn, it is important to have access to data on the percentage of these patients that are detected, how many receive treatment, dropout rates, and so on.

It is also known that individuals with PD tend to present high comorbidity, especially with major depressive disorder (Dunner, 1998) and with chronic physical conditions; they also experience a clear deterioration in their quality of life and alterations in their social functioning and intimate partner relationships (Birchall, Brandon, & Taub, 2000). However, researchers do not yet have a clear idea of the extent to which such comorbidity persists or has changed, especially in Spain.

Within this context, cognitive-behavioural treatment (CBT) for PD has shown high efficacy and efficiency (Arntz, 2002; McHugh et al., 2007; NICE, 2011); nevertheless, in PC traditional pharmacological treatment continues to be used – a treatment approach that is not even in line with the guidelines based on the scientific evidence (Cano-Vindel, 2011; Fernandez et al., 2006). Given the scarcity of resources and high demand in the PC setting, on the one hand, and the special conditions under which CBT needs to be applied (i.e., group treatment, small number of sessions, etc.), on the other, it is necessary to review the efficacy and efficiency of this approach in this context.

The aim of this study is to carry out a review of the scientific literature with the following purposes: (1) to analyze the prevalence of PD in the PC context and its comorbidity with other disorders; (2) to study the percentages in PC of cases detected and treated, and the types of treatment given; and (3) to review the efficacy, efficiency and adequacy of the treatments in relation to the scientific evidence.

METHOD

The authors carried out a review of the scientific literature with data obtained from Web of Science, PsycInfo, Pubmed and ScienceDirect, and using the terms ("panic disorder") AND ("primary care" OR "primary health care" OR "family practice") in the keywords field (MeSH Major Topic) of the different databases.

RESULTS

Epidemiology: prevalence and comorbidity

The most recent epidemiological studies are generally more solid from a methodological perspective, and yield higher prevalences of PD in PC than in the general population, especially among patients with cardiovascular, respiratory or gastrointestinal conditions, with vestibular dysfunctions and with thyroid problems, versus physically healthy individuals (Gili et al., 2010; Simon & Fischmann, 2005). The PREDICT study, carried out at PC health centres in 6 European countries (including Spain), revealed a life prevalence, assessed through the Patient Health Questionnaire (PHQ; Spitzer, Kroenke, & Williams, 1999), of over 7%, being 5.6% in men and 9.2% in women, with higher values for Spain: close to 9%, the figures for men and women being 5.9% and 11.6%, respectively (King et al., 2008). Another study, focusing on the Catalonia region of Spain (Serrano-Blanco et al., 2010) and using a diagnostic interview, yielded a life prevalence for PD of 8.8% and a one-year prevalence of 7%, with 3.9% for men and 8.8% for women, while a study with a large sample of PC patients (N = 7936) distributed proportionally across

the whole of Spain and using the PRIME-MD instead of a diagnostic interview found a somewhat higher current prevalence, of 9.7%, with 6.8% for men and 11.5% for women (Roca et al., 2009). Although there have not been many studies to date and they are not always comparable, it may well be that the life prevalence of PD in PC in Spain (8.8%, with diagnostic interviews) is equal to or just slightly lower than that found in the USA, which was 6.8% (Kroenke, Spitzer, Williams, Monahan, & Lowe, 2007) measured with the PHQ and 9.5% (Kroenke, Spitzer, Williams, & Lowe, 2010; Marks, Wegelin, Bourgeois, & Perkins, 2010) assessed with the MINI (Mini-International Neuropsychiatric Interview). Moreover, it is likely that the prevalence of PD in Spain increased (2.2% vs. 9.7%) over a decade, if we compare the studies by Baca-Baldomero et al. (1999) and Roca et al. (2009) carried out with the same screening instrument (PRIME-MD).

As we have seen, the prevalence of PD in PC is always higher for women than for men, with no differences in this proportion (OR=1.63; CI 95%: 1.2-2.2) between the 15 countries from four continents in which the first research was carried out (almost 20 years ago) with over 26,000 patients, the "Psychological Problems in General Health Care" by the WHO (Sartorius et al., 1993); thus, it is highly probable that the greater prevalence among women (2.8%) compared to men (1.5%) is due to factors of a biological and psychological, more than cultural, nature (Gater et al., 1998).

Both in Spain and in other countries, research continues to find an association between panic and physical health problems (Gili et al., 2010). Thus, there is a relation between panic and digestive disorders (Lydiard et al., 1994), between panic and hypertension (Davies et al., 1999) and between panic and cardiovascular risk, as reflected in the results of a study with around 3500 women aged over 50, which reveals that one or several panic attacks are associated with a 3 to 4 times higher risk of myocardial infarction in the following 5 years (Smoller et al., 2007). The population surveys run by the WHO in different countries revealed an OR=2.7 between having a heart condition and panic (Ormel et al., 2007). In the PC context in Spain, Pascual et al. (2008) compared a sample of 130 patients with PD with/without agoraphobia and agoraphobia without panic attacks with other types of patients attended at a PC health centre, finding that the former presented greater risk of headaches (OR=4.2), heart disease (3.9), osteomuscular disorders (3.8) and digestive problems (2.0). In another study, an OR=2.0 was found between mental disorders (including PD) and gastrointestinal disorders; moreover, 14.5% of the patients with these physical problems met the criteria for PD (Roca et al., 2009).

There is also comorbidity between PD and other mental health problems. PD tends to be comorbid with other mental disorders in 70% of cases (Roy-Byrne et al., 1999), depression being the most common of these (OR=5.39), followed by social phobia (OR=5.15), in the PC context in Spain (Serrano-Blanco et al., 2010). According to the data from the NCS-R (Dunner, 1998), 56% of patients diagnosed with PD present a history of major depressive disorder, and 22% of depression patients have had panic attacks at some time in their life. Thus, the presence of comorbidity is associated with more severe anxiety and depression symptoms, a higher suicide rate (Pilowsky et al., 2006), greater frequency of different comorbid conditions, poorer response to and adherence to treatment (Lecrubier, 1998) and greater risk of somatoform disorders (Roca et al., 2009).

Patients detected and treated

People with mental disorders in the ESEMeD study used PC services 19.1 times more than those without disorders and without subclinical symptoms (Alonso et al., 2007). Also, patients with PD attend PC and Mental Health facilities more frequently than those with other anxiety disorders (Fernandez et al., 2006; Roy-Byrne et al., 2005b). In Spain, PD patients use psychiatry services around 4 times more than psychology services, and receive treatment from professionals more (49.3%) than those with other emotional disorders (Fernandez et al., 2006); furthermore, PD represents the major cause of referral from PC (46.3%) to mental health services (Martín et al., 2009). It should also be highlighted, as several studies point out, that approximately half of PD patients are incorrectly diagnosed in PC (Kroenke et al., 2007; Zajecka, 1997). At the same time, a controlled study revealed that only 64% of patients correctly diagnosed with PD receive some sort of pharmacological and/or psychological treatment (Roy-Byrne et al., 1999). Moreover, this figure falls considerably if we consider "adequate treatment", since another study found that less than a third of patients who met the criteria for various anxiety disorders received minimally adequate psychotherapy or pharmacotherapy (Stein et al., 2004). In Spain, the percentage of patients with PD who received minimally adequate treatment from their psychiatrist

(29.6%) and their psychologist (23.0%) was even lower (Fernandez et al., 2006). That is, not only are half of PD cases not correctly identified, but less than half of them receive treatment, regardless of whether it is in accordance with the scientific evidence. Possibly because of this, the outcome is over-use of PC services by these patients and the aggravation of PD.

Types of treatment received

Research on the state of this question in Europe reveal that 52.5% of patients affected by panic take anxiolytics, antidepressants or some other psychoactive substance, as against 10.1% without mental disorders (Alonso et al., 2004b). Moreover, 60-70% of people diagnosed with anxiety disorder at some time in their life have had active symptoms of anxiety in the last year (Kessler, 2007), despite the fact that there are solutions based on the scientific evidence (Richards & Suckling, 2009). Furthermore, the exclusive use of pharmacological treatment leads to higher rates of dropout (especially after the first three visits, according to the ESEMeD study) and relapse (Gould, Otto, & Pollack, 1995; Katon, 1986; Katschnig et al., 1995; Pinto-Meza et al., 2011). All of these data serve to highlight – as did Ehlers (1995) many years ago – the fact that conventional treatment leads to high chronicity of PD.

According to the APA, the only two well established treatments for PD are Panic Control Therapy (Barlow & Craske, 2007; Barlow, Craske, Cerny, &

Klosko, 1989) and Cognitive Behavioural Therapy for PD (Clark, 1986; Salkovskis, Clark, & Hackmann, 1991). A meta-analysis (Barlow, Raffa, & Cohen, 2002) showed that the results for both types of treatment are highly effective in the long term. The treatment of PD with CBT, which includes the most recent contributions on cognitive restructuring, succeeds in eliminating the disorder in just a few sessions, with an effectiveness of 85%, and maintaining the absence of panic attacks in the follow-up (National Institute of Mental Health, 1993; Otto, Smits, & Reese, 2004; Wood, 2008).

It has been demonstrated that adding 12 sessions of CBT to a pharmacological treatment programme produces clinically and statistically significant improvements, and which would otherwise not occur in the long term (Craske et al., 2005). Thus, Martín et al. (2009) applied a panic control treatment programme to a group of 201 PD patients with or without chronic agoraphobia, the majority in pharmacological treatment, and obtained a marked reduction in anxiety, down to levels which would be considered within the bounds of normality; another study found that the remission rate for PD in PC was approximately double when CBT was combined with medication (in 6 treatment sessions plus 6 of follow-up), compared to conventional treatment (Roy-Byrne et al., 2005a).

The guidelines manual of the UK's National Institute for Health and Clinical Excellence (NICE, 2011) recommends, with a high level of evidence, CBT alone, given its high long-term efficacy, followed by antidepressant medication (SSRIs); this approach is in line with the results of a systematic review of the scientific literature on therapeutic alternatives for PD in PC carried out relatively recently (Navarro-Mateu, Garriga-Puerto, & Sanchez-Sanchez, 2010).

However, in PC very few patients receive CBT as a first line of treatment. A controlled study carried out with 81 PD patients in the USA (Roy-Byrne et al., 1999) found that just 42% received medication and 36% psychotherapy. In the follow-up at 4-10 months, 85% still met the diagnostic criteria for PD, but just 22% had received adequate medication (type and/or dosage) and 12% the appropriate psychological treatment (i.e., CBT). If we add to this the demonstrated fact that patients with PD show low adherence to the treatment offered in PC – partly due to the lack of time for providing adequate psychoeducation and proper follow-up (Latorre, López-Torres, Montañés, & Parra, 2005; Roy-Byrne et al., 2005b) – it is easier to understand these results. Another study (N = 363 patients with different anxiety disorders, including PD), carried out at different PC centres, found that fewer than 10% of patients had received any type of CBT from a mental health professional in the last 3 months (Stein et al., 2004), and only 25% had received the appropriate medication.

In Spain, the situation is even more disheartening, since the use of adequate psychological treatment is considerably scarcer than in the USA. Added to the fact that just 30% of Spaniards with anxiety disorder seek medical attention, only 0.9% of these receive psychological treatment, 27.1% psychological treatment plus medication, and 33% medication only; 39% receive no treatment at all (Codony et al., 2007b).

In sum, the type of treatment provided is predominantly pharmacological, despite the fact that the scientific evidence recommends the application of CBT as a first line of treatment. The percentage of patients receiving the

treatment backed up by most empirical evidence (i.e., CBT) does not exceed 12% in the USA, and just 1% in Spain. As a result of this, the efficacy rates are considerably low.

CONCLUSIONS AND DISCUSSION

In Spain, the one-year prevalence of PD in PC measured via interview is very high (7%) – just 1.4 times lower than that of the USA (9.5%) –, when we might expect the Spanish rate to be considerably lower, given that in the general population it is 4.5 times lower than in the USA (0.6% vs. 2.7%). This discrepancy may be due to better PC coverage in Spain, but it could also be an indication of the problems of our system, which is not dealing adequately with the problems of PD; indeed, in this regard, there are some signs that the prevalence of this disorder has increased over the last 10 years.

Likewise, it is confirmed that in PC, for the most part, the first-choice treatment for PD continues to be medication, rather than CBT, despite scientific evidence showing that psychological techniques are more efficacious, even in group format (Telch et al., 1993), and more efficient than conventional treatment in the PC context (Roberge, Marchand, Reinharz, & Savard, 2008). Only 30% of Spanish people with an anxiety disorder seek medical attention (the majority for panic conditions or generalized anxiety disorder), and less than 1% of these receive exclusively psychological treatment (Codony et al., 2007b). At the same time, conventional treatment scarcely fulfils even the minimum criteria of concordance with the scientific evidence. Moreover, the percentage of detection of PD in the PC context remains low. All of this probably explains, over time, the high percentage of dropout (Pinto-Meza et al., 2011), relapse, aggravation and PC over-use (Alonso et al., 2007), increased healthcare and social costs (Batelaan et al., 2007), work days lost and greater health impairment rates (Alonso et al., 2010).

Thus, more than half of patients experiencing panic attacks (52.5%) have, over the last 12 months, taken anxiolytics (especially benzodiazepines, which in the medium term generate addiction), antidepressants, or some other psychoactive substance (Alonso et al., 2004b; Codony et al., 2007a). Such drug use is quite generalized, despite the fact that CBT has shown high efficacy and efficiency, according to the most recent and reliable clinical guidelines (NICE, 2011). Furthermore, there are no prevention programmes in this field, and in general there is little knowledge among healthcare personnel (Latorre et al., 2005) about protective and vulnerability factors (such as smoking) (Wood, Cano-Vindel, Iruarrizaga, Dongil, & Salguero, 2010) for PD. There continues to be, then, a serious gap between research and practice in the treatment of panic, which implies a need for much greater efforts to disseminate treatment and prevention programmes based on the scientific evidence.

Finally, it should be highlighted that although the efficacy rates of CBT programmes for patients with PD in group format, via computer or through Internet are not as high as when CBT is applied in individual, face-to-face mode, such programmes nevertheless tend to yield clinically and statistically significant improvement, and at a lower cost (Reger & Gahm, 2009). There are Internet-based CBT programmes with empirical support and which can be used as efficacious and cost-effective tools for helping to reduce the prevalence rates of PD (Kiropoulos et al., 2008; Reger & Gahm, 2009).

Among the limitations of this review we should highlight the heterogeneous nature of the studies considered, the lack of systematic reviews and meta-analyses, and the scarcity of controlled and randomized clinical trials. As an example, the prevalence data of the different studies included here have been obtained with different screening instruments (Roca et al., 2009) and diagnostic interviews (Serrano-Blanco et al., 2010), which is why these rates may vary from one study to another; moreover, there are no meta-analyses in relation to such data. At the same time, many of these studies have assessed PD without taking into account whether or not there was an existing comorbidity with other mental disorders or physical symptoms, and the wide range of sample sizes employed makes comparisons between studies and the generalization of the results quite difficult. Even so, and though there is clearly a need for considerable further research, the most important conclusions of the present study are quite closely in line with those of the classic reviews carried out previously, which had already identified the problems that still remain uncorrected.

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