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The relationship between panic disorder and hypertension. A review of literature

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Summary

About 1/4 of the world's adult population suffers from hypertension. Due to the high prevalence of the disease, its impact on mortality and socio-economic costs, it is important to search for modifiable causes of its development. This review analyses studies in order to answer the question: Is there a higher prevalence of panic disorder in adults (≥18 years of age) with hypertension, than in the normotensive group?

There have been found 10 cross-sectional studies describing the correlation between hypertension and panic disorder. Odds ratio for these two clinical entities ranged from OR = 3.31 (2.99–3.67) to OR = 1.19 (0.87–1.62). Moreover, the frequency of coincidence of those two clinical entities was found between 4.2% and 18.75%. In the prospective studies there have been found a positive association between panic disorder and subsequent life-long development of hypertension OR= 1.7 (1.4–2.0). On the other hand, association between hypertension and subsequent development of panic disorder in the 12-months observation was OR = 3.23 (1.51-6.93), but in 3 years of observation it was insignificant OR = 1.12 (0.80–1.57).

Based on the literature review, due to the differences in methodology and the small number of prospective studies, it can only be suggested to clinicians that in some cases they should search for panic disorder in patients with hypertension, especially paroxysmal one.

Key words: hypertension, panic disorder, anxiety disorders

Introduction

Hypertension is one of the most common diseases in the world. In 2015, WHO [1] estimated the number of patients at about 1/4 of the world's adult population. The prevalence of this disease varies from country to country. In Poland it is estimated at about 10 million adults, which is around 32% of the population [2]. Significant

prevalence of hypertension also affects the costs of treatment. The American Heart Association [3] calculated that in 2010 the treatment of hypertension had cost the US budget a total of approximately 46 billion dollars.

In its report, WHO [1] points out that hypertension is one of the main causes of death and the third most frequent cause of loss of years of life spent being healthy (DALY – disability-adjusted life years) in the world. This disease is responsible for about 40% of cardiovascular deaths [3]. In addition, Blacher et al. [4] demonstrated a linear relationship between each increase in blood pressure by 10 mmHg and the increase in the risk of severe cardiovascular disease complications and death by almost 20%. According to the American Heart Association [3], the total direct and indirect cost of cardiovascular disease treatment in the USA in 2010 was about 315 billion dollars. Due to the high prevalence of hypertension, its impact on mortality and socio-economic costs, it is important to search for modifiable causes of the development of this disease.

The assumption that hypertension is associated with psychological stress dates back to the beginning of the 20th century, when Moschcowitz [5] described the type of stress personality in patients with high blood pressure. Mental disorders, as well as hypertension, are also an epidemic of the 21st century. The probability of developing a mental disorder during an individual's lifetime is approximately 25%. The most common mental disorders include affective disorders and anxiety disorders. According to the report of the European Study of the Epidemiology of Mental Disorders [6], approximately 13.5% of people will experience anxiety disorders during their lifetime, and 13% will experience panic attacks, of which 12.8% will meet the criteria for a diagnosis of panic disorder.

Studies have already been published [7, 8] describing the relationship between depression or anxiety disorder and hypertension. However, the connection itself between panic disorder and hypertension seems to be not sufficiently researched yet. For this reason, the authors of this article, on the basis of a review of literature, are attempting to answer the question: 'Is there a higher prevalence of panic disorder in adult patients (≥ 18 years of age) with hypertension than in the normotensive population, and what is the risk of comorbidity of these two disease entities?'

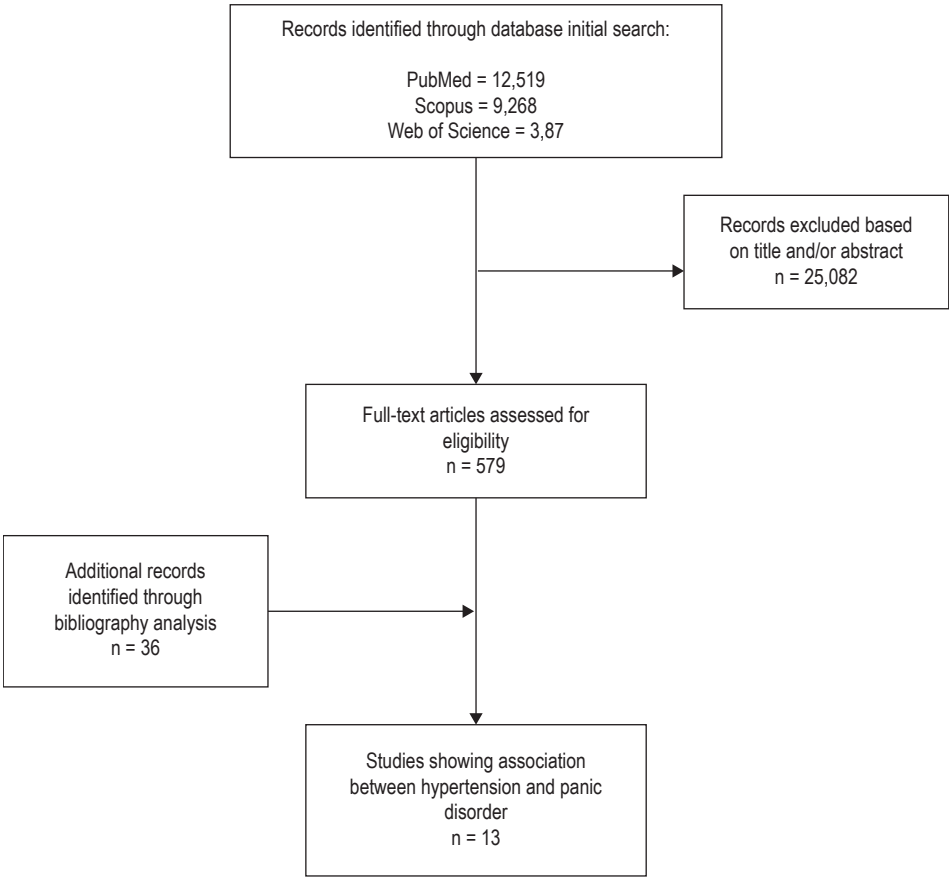
Methodology

Search strategy

Using the PubMed, Scopus and Web of Science databases, 25,661 articles were found until 14 September 2019. The research was made by entering the following key words: "panic attack" or "panic disorder" or "agoraphobia" or "anxiety disorders" and "hypertension" or "high blood pressure" or "ambulatory blood pressure monitoring" or "cardiovascular disease". Two independent researchers (a psychiatrist and internal

medicine doctor) manually selected the articles, analysing works written in English that described a population of adults (>18 years of age). As many as 25,082 records were excluded based on their title or abstract. Subsequently, 579 full-text articles with their bibliography were assessed for eligibility and ultimately, 13 articles were selected for this review of literature.

The main reason for the exclusion of articles from the research was a lack of distinction between panic disorder and anxiety disorders or an absence of separation between hypertension and cardiovascular disease in the studies on the relationship between mental disorders and somatic illness. Furthermore, articles without clear hypertension or panic disorder diagnostic criteria were also excluded. If more than one article was based on the same patient base, studies that were answering the research question similar



to the one in this literature review were selected [9, 21]. Any conflicts concerning the selection of articles were solved during the official meetings of all authors.

Results

The association between panic disorder and hypertension in cross-sectional and retrospective studies

Ten cross-sectional studies describing the comorbidity of panic disorder and hypertension were selected. Chen et al. [10] analysed the National Health Insurance Research Database in Taiwan, containing the data of 22,032 adults. Based on the International Classification of Diseases codes in the medical documentation, a total of 3,672 patients with a diagnosis of panic disorder and 3,001 patients with hypertension were found. The authors calculated the relative risk of comorbidity of panic disorder and hypertension as odds ratio (OR) = 3.31 (2.99 – 3.67). Weissman et al. [11] found the risk of comorbidity of hypertension and panic disorder as adjusted odds ratio (AOR) = 1.91 (1.04 – 3.51) in the database of a group of 5,034 randomly selected adults from the Epidemiologic Catchment Area programme. The diagnosis of panic disorder was based on the NIMH – DIS (National Institute of Mental Health – Diagnostic Interview Schedule), whereas the diagnosis of hypertension was based on self-declaration in a questionnaire: 'Has your doctor or health care professional ever told you that you had high blood pressure?'

In some studies, researchers discovered a positive relationship between panic disorder and hypertension, but it did not reach statistical significance. Tully et al. [12] found 121 patients with panic disorder and 770 hypertensive patients in the German National Health Interview and Examination Survey database of 4,181 adults. The authors used the CIDI (Composite International Diagnostic Interview) scale to diagnose panic disorder and performed three blood pressure measurements in the subjects. Patients were classified into the hypertension group if they had been using hypotensive drugs or if they had a blood pressure of >140/90 mmHg in three consecutive measurements. This study showed the risk of comorbidity of hypertension and panic disorder as OR = 2.04 (1.13 – 3.68). However, statistical significance was lost after the odds ratio was adjusted for age, sex, low income, education and any psychiatric disease diagnosed in the last 12 months, AOR = 1.69 (0.88 – 3.28). Davies et al. [9], in an analysis of the HUNT database (the Nord-Trøndelag Health Study) of 61,408 adults aged > 20, found that the association between panic disorder and systolic blood pressure was U-shaped. Panic disorder was diagnosed using HADS (Hospital Anxiety and Depression Scale) and had the lowest prevalence in subjects whose systolic blood pressure (SBP) was around 140 – 150 mmHg. At SBP ≥ 180 mmHg OR = 1.56 (0.86 – 2.84), while at SBP ≤ 108 mmHg OR = 1.14 (0.67 – 196). In the diagnosis of hypertension, three measurements

of blood pressure were taken at one minute intervals, and the average score from the second and third measurement was used for the analysis. Wiltink et al. [13] presented the risk of comorbidity of hypertension and panic disorder as AOR = 1.19 (0.87–1.62) in 4,661 randomly selected adults aged 35 to 74 from the Gutenberg Heart Study. The authors used the PHQ panic module (Patient Health Questionnaire) to diagnose panic disorder. Patients were classified as hypertensive if they had been using hypotensive drugs or their measurement of systolic blood pressure had been ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg after 8 and 11 minutes at rest.

The majority of the analysed studies have also shown a higher prevalence (in percentage) of panic disorder in hypertensive adults than in the control groups. Davies et al. [14] examined data from one primary care practice and reported that panic disorder was present in 13% out of 351 patients with hypertension, while this psychiatric disorder was diagnosed only in 8% of normotensive adults. In this study, the diagnostic criteria for panic disorder was based on the SCID scale (Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders). Patients were classified as hypertensive if they were undergoing treatment for hypertension or their last blood pressure measurement was >160/90 mmHg according to the medical documentation. Davies et al. [15], in a different study, showed that 12% out of 136 patients with resistant hypertension and 14% out of 136 patients with non-resistant hypertension treated at the Sheffield Hypertension Clinic were also diagnosed with panic disorder. The HADS was used to determine the presence of panic disorder, while patients with diagnosed hypertension were included in the study on the basis of their medical documentation. Po-Han Chou et al. [16], on the basis of a review of medical documentation of 630,492 randomly selected adults (≥20 years of age) from the National Health Insurance Research Database in Taiwan, found that in 13.4% of patients with panic disorder there was comorbid hypertension, while in the control group this percentage was only 6.3%. Neal et al. [17] analysed data from a hospital-affiliated family practice centre and showed that from 123 Afro-Americans with panic disorder diagnosed using ADIS-R (Anxiety Disorder Interview Schedule – Revised), 18.75% also had hypertension diagnosed by ABPM (ambulatory blood pressure monitoring) or by ≥ 2 measurements of blood pressure ≥ 140/90 mmHg. Batelaan et al. [18], as part of The Netherlands Health Survey and Incidence Study–2, conducted a prospective study on a group of 5,149 randomly selected adults from the general population, assessing the influence of anxiety disorders on the development of cardiovascular disease. The authors demonstrated that during the three-year observation period the risk of developing cardiovascular disease among the 257 patients with diagnosed panic disorder or with panic attacks was OR = 1.15 (0.45 – 2.93). In the study, the risk of developing hypertension as a separate variable among cardiovascular diseases was not analysed. At the time of entering the study, only 4.2% of patients with panic attacks

or panic disorder had comorbidity with hypertension, while in the general population this figure was 8.3% (somatic disease self-reported in a questionnaire, psychiatric diagnosis on the basis of the CIDI scale) [18].

The association between panic disorder and hypertension in prospective studies

In this review of literature, three prospective studies describing the association between panic disorder and hypertension were retrieved during the database search. Grimsrud et al. [19] found 767 persons with self-reported hypertension and 37 subjects with panic disorder diagnosed during the previous 12 months using the CIDI scale from a nationally-representative sample of South African adults database of 4,351 patients. The risk of developing panic disorder in hypertensive patients during the 12 months of observation was OR = 3.23 (1.51 – 6.93). Chou et al. [20] analysed data from the National Epidemiologic Survey on Alcohol and Related Conditions of 43,093 patients (≥18 years of age). The diagnosis of psychiatric disease was based on DSM-IV classification found in patients' medical documentation whereas in the case of hypertension, patients' self-declaration in a questionnaire (regarding whether a doctor or other health care professional had told them that they had high blood pressure during the previous 12 months). The authors showed that there was a risk of developing panic disorder in hypertensive patients during the three years of observation, but this relationship was not statistically significant: OR = 1.12 (0.80 – 1.57). Stein et al. [21] examined data from the World Mental Health Survey of 52,095 patients aged ≥ 21 with mental disorders. The diagnosis of panic disorder was made via the CIDI scale, and the diagnosis of hypertension through self-declaration in a questionnaire ('Has your doctor or health care professional ever told you that you had high blood pressure?', age ≥ 21 at diagnosis). The authors analysed a different relationship than in the prospective studies described above. They proved that there is a greater lifetime risk of developing hypertension in adults with a diagnosis of panic disorder OR = 1.7 (1.4 – 2.0).

Table 1. **Comparison of selected cross-sectional and retrospective studies describing the relationship between hypertension and panic disorder, including odds ratio**

Study	Diagnosis of panic disorder	Diagnosis of hypertension	Test group	Results
Chen et al. (2011) [10]	ICD-9, diagnosis repeated ≥ 3 times in medical records	Based on ICD-9 in the medical records	22,032 subjects >18 years of age from the TNHIRD: 3,672 patients with panic disorder, 3,001 with hypertension	Risk of comorbidity of hypertension and panic disorder OR = 3.31 (2.99-3.67)

table continued on the next page

Weissman et al. (1990) [11]	NIMH (DIS) based on DSM-III	Self-declaration in a questionnaire*	Random sample of 5,034 subjects ≥ 18 years of age from the Epidemiologic Catchment Area programme	Risk of comorbidity of hypertension and panic disorder AOR* = 1.91 (1.04-3.51)
Tully et al. (2013) [12]	CIDI based on DSM-IV, in the last 12 months	Three measurements >140/90 mmHg or taking hypotensive drugs	4,181 subjects aged ≥18 and ≤ 65 from the GNHIES: 770 patients with hypertension, 121 with panic disorder	Risk of comorbidity of hypertension and panic disorder OR = 2.04 (1.13-3.68); AOR**= 1.69 (0.88-3.28)
Davies et al. (2012) [9]	HADS	Three measurements of SBP at one minute intervals. The result is the average of the second and the third measurement	61,408 subjects aged ≥20: 15,717 patients had SBP >150 mmHg, 2,501 ≥2 HADS points	The relationship of panic disorder with SBP is U-shaped, with the least common comorbidity at SBP = 140-150 mmHg. At ≥180 mmHg OR = 1.56 (0.861-2.84); ≤108 mmHg OR = 1.14 (0.666-1.96)
Wiltink et al. (2011) [13]	≥2/4 Brief PHQ panic module questions are answered with 'yes'	Medical treatment of hypertension or measured SBP ≥140 mmHg and/or DBP ≥90 mmHg after 8 and 11 min at rest	Random sample of 4,661 participants (35–74 years) of a community-based observational cohort from the Gutenberg Heart Study, matched 1:1 for gender, age and residence	Risk of comorbidity of hypertension and panic disorder AOR**= 1.19 (0.87–1.62)

ICD-9: International Classification of Diseases-9; NIMH (DIS) – National Institute of Mental Health (Diagnostic Interview Schedule); CIDI – Composite International Diagnostic Interview; HADS – Hospital Anxiety and Depression Scale; PHQ panic module – Patient Health Questionnaire; Self-declaration in a questionnaire* – 'Has your doctor or health care professional ever told you that you had high blood pressure?'; TNHIRD – Taiwan National Health Insurance Research Database; GNHIES – German National Health Interview and Examination Survey; SBP – systolic blood pressure; DBP – diastolic blood pressure; OR – odds ratio; AOR* – odds ratio adjusted for age, gender, low income, education, and mental illness diagnosed in the last year; AOR** – odds ratio adjusted for age, gender, social status, marital status, smoking, obesity.

Table 2. **Comparison of selected cross-sectional and retrospective studies describing the relationship between hypertension and panic disorder, including percentage distribution**

Study	Diagnosis of panic disorder	Diagnosis of hypertension	Test group	Results
Davies et al. (1999) [14]	SCID based on DSM-III-R	Based on medical records. Patients undergoing treatment for hypertension or last ambulatory measurement >160/90 mmHg	351 subjects with hypertension aged 67 ±12 from one primary care practice	Panic disorder was more frequent in patients with hypertension (13%) than in normotensive patients (8%)
Davies et al. (1997) [15]	HADS	Based on medical records	136 subjects with resistant hypertension (SBP >160 and/or DBP >90 mmHg, despite taking >3 hypotensive drugs in full doses), 136 subjects with controlled hypertension from the Sheffield Hypertension Clinic	12% of patients with resistant and 14% with non-resistant hypertension had diagnosed panic disorder
Po-Han Chou et al. (2012) [16]	Based on medical records and ICD-9 codes	Based on medical records and ICD-9 codes	630,492 randomly selected patient data from the NHIRD in Taiwan, ≥20 years old. 1725 patients with panic disorder	Hypertension was more frequent in patients with panic disorder (13.4%) than in control group (6.3%)
Neal et al. (1994) [17]	Telephone interview, ADIS-R based on DSM-III-R	ABPM or ≥2 measurements of blood pressure ≥140/90 mmHg	123 Afro-Americans aged 18-72. Data from hospital-affiliated family practice centre	18.75% of patients with essential hypertension also had diagnosed panic disorder
Batelaan et al. (2014) [18]	CIDI based on DSM-IV, in the last 12 months	Self-declaration in a questionnaire*. Disease in the last 12 months	5,149 subjects aged 18-64, 257 patients with panic attacks or panic disorder from the NEMESIS-2 database with 3 years of observation	4.2% of patients with panic attacks or panic disorder also had hypertension diagnosed at baseline

SCID for DSM – Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders; HADS – Hospital Anxiety and Depression Scale; ADIS-R – Anxiety Disorder Interview Schedule-Revised; Self-declaration in a questionnaire* – 'Has your doctor or health care professional ever told you that you had high blood pressure?' ; ABPM – ambulatory blood pressure monitoring;

SBP – systolic blood pressure; DBP – diastolic blood pressure; NHIRD – National Health Insurance Research Database; NEMESIS-2 – Netherlands Health Survey and Incidence Study-2.

Table 3. **Comparison of selected prospective studies describing the relationship between hypertension and panic disorder, including odds ratio**

Study	Diagnosis of panic disorder	Diagnosis of hypertension	Test group	Results
Grimsrud et al. (2009) [19]	CIDI based on DSM-IV, in the last 12 months	Self-declaration in a questionnaire*	4,351 subjects >18 years of age from a nationally-representative sample of South African adults database: 767 patients with hypertension, 37 with panic disorder	Risk of developing panic disorder in patients with hypertension during 12 months OR = 3.23 (1.51-6.93)
Chou et al. (2013) [20]	Medical history, diagnosis on the basis of DSM-IV	Self-declaration in a questionnaire*. Disease in the last 12 months	43,093 patients aged ≥18. Data from NESARC with 3 years of observation	Risk of developing panic disorder in patients with hypertension during 3 years of observation OR = 1.12 (0.80–1.57)
Stein et al. (2014) [21]	CIDI 3.0 based on DSM-IV	Self-declaration in a questionnaire*	Data from the World Mental Health Survey, 52,095 patients (≥21years of age)	Lifetime risk of developing hypertension in adults with a diagnosis of panic disorder OR = 1.7 (1.4–2.0)

CIDI – Composite International Diagnostic Interview; DSM – Diagnostic and Statistical Manual of Mental Disorders; Self-declaration in a questionnaire* – 'Has your doctor or health care professional ever told you that you had high blood pressure?'; NESARC – National Epidemiologic Survey on Alcohol and Related Conditions; OR – odds ratio.

Discussion

Physiologic mechanisms connecting panic disorder and hypertension

In the animal model, the fight-or-flight response is the body's natural response to life-threatening external (predator attack) and internal (acidosis, trauma) situations [22]. Physiologically, this reaction is similar to a human panic attack. We consider it normal if it does not impair the individual's functioning and is adequate to the situation. Direct control over the fight-or-flight response is regulated by GABAergic and serotonergic systems, modulating the activity of the noradrenergic system in the locus coeruleus of the pons. Noradrenaline secreted in nerve synapses affects the sympathetic nerv-

ous system, causing an increase in the concentration of catecholamines in the blood serum. As a consequence, retention of water and sodium by the kidneys, reduction of renal blood flow, endothelial dysfunction, vasospasm, atherosclerosis, increased vascular stiffness, and increased heart rate and blood pressure are observed [22-27]. Autonomic dysfunction in patients with panic disorder is characterised not only by increased activity of the sympathetic nervous system, but also by decreased activity of the parasympathetic nervous system. Decreased parasympathicotonia suppresses the baroreceptor reflex and reduces heart rate variability, which could be a response that prepares the body for a fight-or-flight response [28, 29].

Hyperventilation is another factor that may be responsible for the coexistence of hypertension and panic disorder. In repeated panic attacks with hyperventilation, chronic CO_2 loss occurs in the lungs, which leads to compensatory removal of bicarbonate ions (HCO_{3^-}) by the kidneys. As the disease progresses, a panic attack can be triggered by a sudden increase in serum pCO_2 and acidosis. A decrease in blood pH results in the release of noradrenaline in the locus coeruleus of the pons, activation of the sympathetic nervous system and peripheral secretion of catecholamines. However, in the course of acidosis there is a decreased sensitivity of tissues to these substances and only sudden hyperventilation and hypocapnic alkalosis cause increased catecholamine activity and increased blood pressure [30]. Hypercapnic acidosis can occur especially at night when the respiratory rate is naturally reduced. A false alarm of dyspnoea then occurs, coordinated by the respiratory centre of the brain. Subsequently, this conditioned fear leads to hyperventilation, increased sympathetic system response, vasospasm, and temporary as well as chronic increase in blood pressure. The recovery of the acid–base homeostasis after a hyperventilation episode can take up to seven days. The fact that breathing exercises can help treat some patients with panic disorder or hypertension confirms, to a certain extent, the relationship between hyperventilation and hypertension [31, 32].

Patients with panic disorder experience panic attacks not only during the day but also during sleep. In 60-80% of them, various types of sleep disturbances can be diagnosed [33]. Meng et al. [34] demonstrated a correlation between sleep disturbances such as shortened sleep time, interrupted sleep, early morning awakening or insomnia and the development of hypertension. Li et al. [35] confirmed this observation by proving that benzodiazepines – drugs also used in anxiety disorders – cause a permanent decrease in systolic (10.5 ± 3.9 mmHg) and diastolic blood pressure (8.1 ± 3.6 mmHg) in patients treated for insomnia and hypertension.

Patients with panic disorder have increased cortisol levels in their blood, which may be partly related to their night-time panic attacks and sleep disturbances [36]. The association of hypercortisolaemia and sleep disturbances is confirmed by Holsboer et al. [37], who observed disturbances in nocturnal slow-wave sleep in healthy patients

during corticotropin-releasing hormone (CRH) infusion. In addition, Bandelow et al. [38] demonstrated a correlation between increased cortisol levels in overnight urine collection and aggravated symptoms of panic disorder. Hypercortisolaemia itself is associated with, among others, sodium and water retention in the kidneys, which can lead to an increase in blood pressure. A typical example of this phenomenon is Cushing's syndrome, one of the secondary causes of hypertension. In 2/3 of patients from this group, the occurrence of generalised anxiety disorder or panic disorder is also observed. Interestingly, the frequency of panic attacks in patients increases after elimination of hypercortisolaemia. This is most likely related to the relative cortisol deficiency and the subsequent uncontrolled increase in catecholamine concentration [39]. Similar fluctuations in cortisol concentration are also observed in patients with panic disorder. Shekhar et al. [40] demonstrated the complementary efficacy of corticotropin-releasing factor 1 (CRF1) and benzodiazepine receptor blockers in inhibiting anxiety-related symptoms [40]. What is more, Hamer and Steptoe [41] showed that 15.9% of the subjects who responded to stressful stimuli with an increase in cortisol levels will develop hypertension within three years (OR = 1.59 (1.17 – 2.17)). The development of hypertension in patients with panic disorder is influenced by both genetic and environmental factors. The naturally occurring gradual increase in blood pressure from adolescence, peak in working age and then decrease with age, coincides with the intensity of exposure to stress during human life [42]. It was proved on the animal model that feeling stressed is dependent on genetic factors, which may contribute to the manifestation of hyperresponsiveness to new environmental stimuli, and thus to the presence of dysfunctional behaviour, vulnerability to stress and fearfulness in an individual [43]. Korte et al. [44] suggest that hypertension, as well as other somatic diseases, are related to personality type and adaptation to stress, which is clearly disturbed in patients with panic disorder. While it seems that acute stress is not related to hypertension, data from the World Mental Health Survey [21] confirms such a relationship with chronic stress, abnormal stress responses and childhood adversities. In addition, patients with anxiety disorders leading an unhealthy lifestyle (little physical activity, and in men, nicotine dependence and improper diet) have a higher risk of developing hypertension [45]. Also, multiple visits of patients with mental disorders to physicians lead to an earlier diagnosis of coexisting somatic diseases in comparison to other patients [46].

In this article, the authors tried to describe some of potential mechanisms responsible for the association between hypertension and panic disorder, such as the theories of autonomic dysfunction, hyperventilation, sleep disturbances, hypercortisolaemia, or improper lifestyle. A panic attack itself is physiologically very similar to a natural fight-or-flight response. A temporary increase in catecholamines, cortisol, blood pressure and heightened senses help to overcome a real or fictional threat. As a result of repeated panic attacks, an anxiety approach is formed in the patient. Subsequent plastic changes

in the brain can predispose more strongly to further anxiety attacks in response to even mild somatic signals, which can lead to the development of hypertension [21, 44, 47].

Limitations of the studies conducted so far

In this review of literature, 10 cross-sectional and retrospective analyses describing comorbidity between panic disorder and hypertension were found [9-18]. Unfortunately, it is difficult to infer causality and/or directionality of the described relationship based on these types of studies.

In the three prospective studies [19-21] analysed in this article, the diagnosis of hypertension was made based on the patient's answer to the question: 'Has your doctor or health care professional ever told you that you had high blood pressure?' in the questionnaire. However, due to the high variability of blood pressure during 24 hours in patients with panic disorder, the diagnosis of hypertension is not always identical with the incidence of `having high blood pressure` [48]. The self-declaration of somatic disease by patients is not the only limitation of the presented studies. The assignment of subjects to the panic disorder study group using different psychiatric scales (CIDI, SCID, HADS, ADIS-R, PHQ panic module, NIMH) and medical classifications of diseases (DSM-III, DSM-IV, ICD-9) makes it difficult to compare the above studies. Moreover, some authors were analysing the risk of comorbidity of hypertension and panic disorder in patients for one or three years of observation, while other researchers did not use any time frames [12, 18, 19, 20].

Clinical implications and future directions of studies

In this review of literature, most of the cross-sectional and retrospective studies have shown a more frequent occurrence of panic disorder in adult patients (≥18 years of age) with hypertension than in the general population. Likewise, the prospective studies [19-21] largely point to a causal relationship between panic disorder and the development of hypertension. However, due to the differences in selection criteria of the study groups in the analysed publications, one should refrain from providing recommendations for an active investigation of every hypertensive patient for comorbidity with panic disorder until there are more prospective studies available, as well as studies in which the inclusion criteria of the study group have been unified. What is more, future studies should also concentrate on the influence of panic disorder treatment on control of hypertension treatment in patients diagnosed with both disease entities. Furthermore, it still remains inconclusive which screening test should be used in the diagnosis of panic disorder and which group of hypertensive patients would benefit the most from such a screening test.

On the other hand, due to the poor recognition and insufficient ambulatory treatment effectiveness of patients with anxiety disorders, general practitioners should pay particular attention to patients with paroxysmal hypertension, which is one of the features of panic disorder [48, 49]. Comorbidity of chronic psychiatric and somatic diseases impedes the proper treatment of both diseases. In the absence of detecting the associated mental disorder and thus suboptimal treatment of the somatic disease, progression of hypertensive complications and higher mortality among patients may ensue.

Conclusions

To summarise, in the above review of literature, the majority of studies suggest that there may be a positive association between panic disorder and hypertension in the study group of adults (≥18 years of age). In the cross-sectional/retrospective studies, the strongest correlation was found by Chen et al. [10]: OR = 3.31 (2.99 – 3.67), while the weakest correlation and statistically irrelevant by Wiltink et al. [13]: AOR = 1.19 (0.87 – 1.62). Moreover, the frequency of coexistence of hypertension and panic disorder in patients ranged between 4.2% and 18.75% [17, 18]. In the prospective studies, Stein et al. [21] have shown a positive association between panic disorder and subsequent risk of lifetime development of hypertension as OR = 1.7 (1.4 – 2.0). On the other hand, Grimsrud et al. [19] have shown the risk of developing panic disorder in hypertensive patients during 12 months of observation: OR = 3.23 (1.51 – 6.93), similarly to Chou et al. [20], who have also shown such a positive association in three years of observation, but it was statistically insignificant: OR = 1.12 (0.80 –1.57).

Finally, differences in the methodology of studies, the usage of different psychiatric scales to diagnose mental disorders and self-declaration questionnaires as a tool to classify somatic diseases prevents the authors from drawing unambiguous conclusions from this review of literature. Only two studies were found that used the international classification of diseases and medical history diagnoses to classify patients to the research group. These studies reported a higher frequency of hypertension in panic disorder patients than in the control group (13.4% vs 6.3%) [10] and a higher risk of comorbidity of hypertension and panic disorder: OR = 3.31 (2.99 – 3.67) [17]. Those publications, until more prospective studies and researches using international disease classification are made, can only suggest to clinicians that in some cases they should search for panic disorder in patients with hypertension, especially those with uncontrolled and paroxysmal episodes of increased blood pressure [48, 49].

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