

The impact of anxiety disorders on the quality of compliance among patients with co-morbid psychiatric or medical conditions: there are many questions but where can we find the answers?

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SUMMARY

High comorbidity rates with various psychiatric and medical disorders are an important feature of anxiety disorders. The authors of this article focus on the impact of co-existence of other medical problems on the quality of compliance in patients with anxiety disorders. They scrutinised up-to-date evidence on the discussed issue with relation to patients with prominent mental health problems (major depressive disorder, bipolar disorder, schizophrenia) or medical disorders.

anxiety disorders / comorbidity / compliance

INTRODUCTION

In any discussion around anxiety disorders the issue of comorbidity deserves special place. There is a growing body of evidence implicating significant differences between ‘isolated’ psychiatric disorders (e.g. major depression, bipolar disorder or schizophrenia) and analogous mental health issues accompanied by anxiety disorders, in terms of neurobiology, epidemiology, treatment effectiveness and outcomes [1]. Accordingly – even though anxiety disorders themselves may seem to be relatively ‘irrelevant’ against the background of potentially severely debilitating major psychiatric illnesses –

this pattern of co-occurrence must be a matter of concern for every mental health professional.

Given the fact that comorbidity of various mental disorders or medical illnesses is rather a rule than an exception in patients with anxiety disorders (epidemiological data regarding this issue have been summarised in Tab. 1), an in-depth analysis of all the possible interrelations between the discussed disorders and other health problems is far beyond the scope of this article. Nevertheless, as those ‘nosological pairs’ certainly exert huge impact on compliance, the most important aspects of this problem are presented below. (Tab. 1 – *next page*).

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PSYCHIATRIC COMORBIDITIES

Depression

As presented in Tab. 1, anxiety disorders are commonly accompanied with other mental health problems. This fact implies multiple definitional and conceptual difficulties. The widespread discussion about actual relations between

Table 1. Prevalence rates of comorbid psychiatric or somatic conditions and anxiety disorders (adapted from: [1–9]).

	Any anxiety disorder	GAD	SAD	OCD	PTSD	PD
Mental disorders						
Major depressive disorder	47–58%*	39–62%*	37%	67%*	37%	21.6–55.6%*
Bipolar I disorder (epidemiological trials/clinical trials)	no data	10.5–34%* / 20.8–26.1%*	4.2–16%* / 12.5–26.1%*	2.0%* / 10.9%*	6.0%* / 18.8%	7.4–24.0%* / 18.3%*
Bipolar II disorder (epidemiological trials/clinical trials)	no data	20.8–26.1%* / 16.5%*	12.5–26.1%* / 18.3%*	8.7%* / 7%*	insufficient data / 12.2%*	4.3–12.5%* / 13.9%*
Schizophrenia (mean prevalence rates)	38.3%	10.9%	14.9%	12.1%	12.4%	9.8%
Alcohol abuse	4.7–13.2%	4.3%	4.41%	14.9%	lifetime substance abuse: 21.6–43.0%	6.38%
Alcohol dependence	3.8–7.9%	10.52%	8.64%	23.7%		12.42%
Any drug abuse	1.4–7.9%	2.82%	2.13%	7.8%		4.65%
Any drug dependence	0.6–3.5%	5.24%	2.94%	13.9%		5.94%
Medical illnesses						
Asthma	nonsevere: OR: 1.51 (95% CI: 1.00–2.32); severe: OR: 2.09 (95% CI: 1.30–3.36)	5–26%	3–10%	3%	life-threatening asthmatic attack group: 20%; asthma controls: 11%	1–15%
Cancer	6–33%	1–13%	2%	no data	2–22%	6–9%
Cardiovascular disease	OR: 1.43 (95% CI: 1.20–1.71)	OR: 1.48 (95% CI: 1.09–2.01)	no data	no data	no data	OR: 1.29 (1.04–1.59)
Chronic pain	17–35.1%	0–9.1%	8.3–11.8%	0–8.2%	1–10.7%	2.1–11.2%
Chronic obstructive pulmonary disease	no data	0.9–5.6%	no data	no data	no data	0.5–7.7%
* lifetime prevalence CI – confidence interval; OR – odds ratio						

co-occurring psychiatric disorders (whether they should be considered to be separate or joint) is still under way [1].

It is particularly difficult to consider anxiety and depressive disorders separately, mainly because of the fact that although anxiety has not been included in descriptions of depression formulated in the widely recognised psychiatric classifications (ICD-10 and DSM-IV-TR), anxiety indeed is one of the most frequent element of clinical outlook of depressive disorders. According to Malhi et al. and Schoevers et al. the symptom of anxiety is – along with the syndromes of substance abuse and personality disorders – one

of the most common psychopathological components of depressive disorders. [10, 11]

In general, patients with comorbid anxiety and depressive disorders are considered to be more compliant than those who suffer because of a 'single' anxiety disorder. Stein et al. hint at two possible explanations of a disproportion in compliance rates between patients belonging to those two groups. The first one says that people belonging to the former population are heavier burdened with symptoms and therefore are more likely to seek mental health specialist. They may also need more aggressive treatment. As far as patients without depression are concerned,

they seem to be more likely to visit general practitioners and (consequently) receive insufficient therapy. Physicians treating patients with anxiety disorders without depressive components (or patients themselves) might also believe that such a 'mild' health problem does not require long therapy with high doses of antidepressant drugs. The fact that those patients often receive a diagnosis of 'other anxiety disorders' (including apparently vague category of 'anxiety not otherwise specified') further contributes to the relative inattention of doctors to those mental health problems. [12]

Given the fact that pharmacotherapy of co-occurring anxiety and depressive disorders hardly ever brings an instant benefit, the outcome largely depends on the quality of compliance. A physician should remember that compliance to a long-term treatment among those patients is directly proportionate to both simplicity of drug use and lack of side effects. For this reason the usage of compounds characterised by a broad-spectrum efficacy (sertraline or paroxetine), wide therapeutic windows and favourable pharmacokinetic and drug-interaction profiles (sertraline, citalopram or escitalopram), as well as relatively comfortable profile of side effects (e.g. weight gain; at this point bupropion should be mentioned as an antidepressant drug of weight-reducing properties [13]), seems to be particularly profitable. [14]

Bipolar disorder

Although the problem of co-occurrence of bipolar disorder (BD) and anxiety disorders seem to be relatively well analysed epidemiologically, a number of clinical questions remain unanswered.

Epidemiological data suggest that there are some specific patterns of comorbidity among those patients. Anxiety disorders are more frequent in the population of patients with BD (in comparison to major depression) and they seem to be more common among patients with mixed episodes of BD. High rates of comorbidity with panic disorder gained special attention of researchers, leading to the concept of so-called 'bipolar disorder-panic disorder' (BD-PD) as a distinct subtype of BD (theoretical model of BD-PD

has been discussed in: [15]). The fact that anxiety disorders are particularly frequent in the group of patients with bipolar II disorder requires attention, as this category of BD is commonly misdiagnosed as unipolar depression. [16] It is very important to differentiate comorbid major depressive disorder from BD in patient with an anxiety disorder, because using antidepressant drugs in persons with BD might precipitate mania or cycle acceleration (although data on this issue are inconsistent; see: [17]).

It is difficult to discuss the specific problems of compliance among patients with co-occurring anxiety disorders and BD, as data on treatment of this pattern of comorbidity are extremely scarce. For the time being we have no other option but to assume that general rules of improving compliance in patients with BD apply also to people with a combination of the problems discussed.

Nowadays, the structured psychoeducation is considered to be the best way of empowering treatment adherence in patients with BD. The most widely recognised algorithm of BD psychoeducation – so called Barcelona Psychoeducation Program, developed by Vieta and Colom – is a very effective therapeutic tool in terms of treatment compliance enhancement and relapse prevention. [18, 19, 20] Scott defined the main assumptions of the Program in the following words: '(1) the intervention had to emphasise a psychobio-social model so that all treatment interventions, whether pharmacological or psychological, made sense (i.e. appeared rational) to the patient; (2) the program had to target the core psychosocial issues, and the intervention used must be evidence based (hence in common with the other approaches the core elements target adjustment, treatment adherence and reduction of substance misuse, regularisation of social rhythms, and relapse prevention strategies); and (3) the program should give individuals specific and selected information about their disorder in a user-friendly format and also teach and allow practice to effective coping skills.' [21] The Program consists of 21 sessions, divided into three units, focusing on the major classes of problems in course of BD treatment (awareness of the disease, drug adherence and avoiding substance abuse). [19, 22]

One should also be aware of the fact that the important problem in therapy of bipolar disorder can be differences between physicians' and patients' convictions about the disorder and its treatment. As it has been shown in the study performed by Mączka et al. a number of patients were convinced that physicians consider improving their life quality to be much less important than alleviating symptom severity. The hierarchy of problems proposed by the patients as the main obstacles in taking drugs appeared to be the exact antithesis of physicians' beliefs on this issue. [20]

Schizophrenia

Just as in the case of BD, there are very few consistent data about comorbidity of schizophrenia and anxiety disorders. [1] This is the reason why we assume that obstacles to compliance among those patients would be a combination of problems met in both classes of mentioned disorders.

Non-adherence with antipsychotic drugs is the major form of poor compliance in patients with schizophrenia. The meta-analysis of 24 studies, performed by Cramer and Rosenheck, has shown that the mean adherence rate with those medications is 58% (range: 24–90%). This figure seems to be quite low, comparing with 65% with antidepressant and 76% with treatments for non-psychiatric disorders [23, 24]. Goff claims that in reality this outlook may be even more pessimistic, as in the trials included in the cited meta-analysis the quality of adherence was estimated mainly by the results of patient self-reports and clinician judgment (both of which tend to overestimate the adherence rates). Poor compliance among patients with schizophrenia or schizoaffective disorder leads to as serious repercussions as increased risk of relapse, higher rates of emergency room visits, hospitalisations, and suicide. [24]

The general reasons for either good or bad compliance among people with psychotic disorders are not much different from those characteristic for other mental health problems. It is no secret that the patient's satisfaction with treatment, continuity of care, and insight regarding the need for treatment will improve the quality of adherence. On the contrary, chronicity of

a disorder, complicated treatment regimens, drug side effects, and poor social functioning would lead to deterioration of compliance. [24, 25]. Among specific problems worsening adherence in patients with schizophrenia the following should be noticed: cognitive impairment, depression, substance abuse, inadequate discharge planning or aftercare environment, and lack of family. [24]

Given all those factors, Goff recommended the certain set of interventions aimed to improve treatment adherence among people with schizophrenia or schizoaffective disorders: 1) usage of multiple sources of information to estimate the patient's degree of adherence; 2) working on the treatment alliance as a key determinant of adherence, 3) assessment of the patient for risk factors associated with non-adherence; 4) appreciation of a fluctuating nature of adherence and flexibility in adjusting interventions; 5) incorporating the patient's point of view and preferences; 6) simplification of the drug regimen; 7) education and involvement of family members; 8) matching the interventions to factors contributing to non-adherence. [24]

Deterioration of psychotic symptoms subsequently to a trial of fluvoxamine (or – perhaps – other selective serotonin reuptake inhibitors as well) may be yet another source of non-compliance among people with co-occurring schizophrenia and anxiety disorders who presented with impulsive or aggressive behaviours. [26]

Substance use disorders

Relatively high proportions of substance use disorders among patients with anxiety disorders can be possibly explained in a threefold way: '1) the presence of one disorder leads directly to the development of the other (direct casual model); 2) presence of one disorder increases an individual's risk of developing the second disorder via some third variable (indirect casual model); and 3) common factors may account for an individual's increased risk for developing both disorders (no causal relationship between disorders).' [27, 28]. Data gathered in National Comorbidity Survey suggest that this kind of self-medication is not equally common among different anxiety disorder. Such behaviours were the most prev-

alent in patients with generalised anxiety disorder (GAD), while the rarest – among people with speaking subtype of social anxiety disorder (SAD). [29] Those rates were significantly lower than figures frequently reported from clinical samples. In a recently published study Robinson et al. evidenced that there is a substantial relationship between self-medication and substance use disorders in this population. [28]

It is widely recognised that a possibility of easing anxiety with a fast-acting compound (such as alcohol or benzodiazepines) may be the more attractive option patients than using slow-acting drugs (such as antidepressants). This seems to be the key obstacle in course of therapy of anxiety disorders among people with substance use disorders. Another problem is that prescribing anxiolytics is habit-forming and (in a mechanism of 'vicious circle') causes exacerbation of anxiety upon withdrawal. [30] In such cases implementation of a proper pharmacotherapy can be a serious challenge.

MEDICAL COMORBIDITIES

Although there is a great deal of various aspects of interrelationships between anxiety and course of medical illnesses (such as highly elevated risk of coronary heart disease among patients who recently underwent panic attacks [8]), the relation between anxiety and noncompliance with medical treatment (in a wide sense) remains unclear. DiMatteo et al. found substantial variation in effects of anxiety on the quality of adherence (ranging from -0.64 to 0.39). One of possible explanations of this result is the notice that there is no 'universal model of anxiety'. Anxiety disorders range from panic disorder (PD; which possibly does not exert much effect on compliance) to obsessive-compulsive disorder (OCD) or GAD which might improve compliance activities. [31]

CONCLUSIONS

Patients with comorbid anxiety and depressive disorders are considered to be more compliant than those who suffer because of an isolated anxiety disorder. This may be due to either a greater expression of symptoms or a need for

a more aggressive treatment in the former population. Isolated anxiety disorders tend to receive relatively little attention both from physicians and patients themselves, further contributing to a lenient attitude towards treatment. The quality of compliance to a long-term treatment among patients with comorbid anxiety and depressive disorders seems to be directly proportionate to both simplicity of drug use and lack of side effects.

As for now, data concerning treatment of co-existence of bipolar disorder and anxiety disorders are extremely scarce. Therefore we need to assume that the general approaches towards empowering compliance in bipolar disorder (particularly the implementation of Barcelona Psychoeducation Program) should also be suitable for the patients with dual diagnosis. The discussion about improving compliance among people with schizophrenia and anxiety disorders meets similar obstacles.

Anxiety disorders are quite commonly seen in the population of patients with substance use disorders. However, the nature of the relationship between those classes of disorders is not clear. Substances of abuse are the most frequently used as self-medication among people with GAD; this kind of behaviour is the rarest in patients with SAD. The risk of the intake of fast-acting anxiolytics (such as alcohol or benzodiazepines) is one of the major obstacles to proper compliance in treatment of anxiety disorders in this clinical population.

The relation between anxiety and noncompliance with treatment among patients with medical illness remains vague. Various anxiety disorders seem to exert different influence on the quality of adherence. In this respect, anxiety disorders range from PD (which possibly does not exert much effect on compliance) to OCD or GAD which might improve compliance activities.

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