

What our patients want and need to know about generalized anxiety disorder?

O que nossos pacientes querem e necessitam saber sobre transtorno de ansiedade generalizada?

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Abstract

Persons with generalized anxiety disorder often do not seek treatment, and if they do, it is more often for the somatic symptoms (muscle tension, insomnia) or for a secondary depression than because of the cardinal feature of generalized anxiety disorder: worry. The worry aspect becomes apparent when the patient is proposed to try anxiolytic medication. The physician will then need to be prepared to answer many questions regarding the potential hazards and benefits of such medication. These patients tend to have a sceptical attitude, having informed themselves on websites that display claims that are based on anything from evidence-based scientific guidelines to distorted, erroneous and unfounded allegations. Which are the frequent questions that worried patients pose to the physician before accepting anxiolytic pharmacotherapy? Having seen anxious patients in my practice during 25 years, and having conducted several clinical trials of anxiolytics I have put together evidence-based answers in plain language to these questions in this paper.

Descriptors: Anxiety disorders; Social isolation; Evaluation of results of therapeutic interventions; Drug therapy; Psychotherapy

Resumo

Pessoas com transtorno de ansiedade generalizada geralmente não procuram tratamento e, se o fazem, é mais devido aos sintomas somáticos (tensão muscular, insônia) ou a uma depressão secundária do que por causa da característica central do transtorno de ansiedade generalizada: preocupação. O aspecto da preocupação torna-se aparente quando se propõe que o paciente tome uma medicação ansiolítica. O clínico terá então que estar preparado para responder a muitas perguntas sobre os riscos e benefícios potenciais de tal medicação. Esses pacientes tendem a ter uma atitude cética, por terem obtido informações em websites que apresentam afirmações que não têm nenhum embasamento científico ou alegações distorcidas, equivocadas e infundadas. Quais são as perguntas freqüentes que os pacientes preocupados colocam ao clínico antes de aceitarem a farmacoterapia ansiolítica? Tendo atendido pacientes ansiosos em minha prática por 25 anos, e tendo realizado vários ensaios clínicos com ansiolíticos, reuni neste artigo, em linguagem simples, as respostas baseadas em evidências a essas perguntas.

Descritores: Transtornos de ansiedade; Isolamento social; Avaliação de resultados de intervenções terapêuticas; Quimioterapia; Psicoterapia

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Introduction

This is a 52-year old woman, separated and living with a 22-year old daughter. She works as a civil servant in a government agency. She holds a doctorate in mathematics, does not smoke, drinks alcohol only occasionally, and does not drink high amounts of caffeine beverages. She exercises regularly and has passed her health check-ups.

She responds to an advertisement in the newspaper to find symptomatic volunteers for a study of a new anxiolytic. The advertisement describes some of the typical features of generalized anxiety disorder (GAD), including excessive worry, tension, cognitive dysfunction and insomnia. In a telephone conversation with an experienced research nurse she describes, for the first time and anonymously, worries regarding her daughter's future that impair her ability to relax and to focus on important job matters. Although she has an excellent work record and a good income, she worries both about her commitments as a mother and about the prospects of her daughter in a world of uncertainty. Subsequent to being unable to stop worrying she has developed difficulties concentrating, become irritable, restless, and unable to sleep well. She goes to work without feeling rested. Her dentist has remarked about her tense jaws and that she grinds her teeth. A tendency to dyspepsia has been aggravated by her worries. In spite of regular exercises she feels tense, particularly in her shoulders, and experiences palpitations when in meetings. She is now at a point when her functioning at work and at leisure is impaired due to her excessive worries.

Her attitude to accepting pharmacotherapy is sceptical. She has a strong opinion about drugs being addictive, and her daughter tells her "pull yourself together", and do not medicalize your problems.

Patients usually find relief when they receive a diagnosis. In respect to GAD, however, one question that often appears is what are the limits between the normal anxiety reactions and the psychiatric diagnosis.

A remarkable study of New Zealand newborn that were monitored till age 26 show that genes that regulate the turnover of serotonin in the brain play a role in protecting a person from developing a depression related to social adversity, or putting the person at risk.¹ Twin studies similarly indicate that some people have an inborn risk of developing morbid anxiety, including GAD, regardless of social adversity.²⁻³

Serotonin is a key player in regulating mood and anxiety. In experiments with healthy volunteers in the United Kingdom, medications that modulate serotonin turnover (serotonin specific reuptake inhibitors - SSRIs) had a direct impact on how threatening cues were perceived.⁴ This finding indicates that the medication firstly affects how we perceive danger and thus our emotional reactivity in terms of anxiety. Genes that regulate the transport of serotonin and its forerunner tryptophan in the brain were shown to have a different configuration in a study of Chinese patients with GAD.⁵

The worry that is typical of generalized anxiety is conducive to poor decision making, disrupted relations, lowers work performance, and promotes social isolation. GAD increases the risk of subsequent depression and alcohol abuse and possibly cardiovascular disease.⁶⁻⁷ Thus, there is no doubt that GAD ought to be treated with medications, or psychotherapy or both.

GAD that justifies treatment was found in 3% of adults in the USA.⁸ Survey participants with Hispanic and Black ethnicity had lower rates of both GAD and other psychiatric disorders than non-Hispanic Whites in the USA.⁹ A study of Swedish twins ranging from 55 to 74 years old found that 3% had had GAD sometime in their life, and that about one fourth of the risk for GAD was inborn.¹⁰ The lifetime prevalence of GAD with the WHO ICD-10 criteria, that are somewhat less restrictive than the American DSM-IV criteria for GAD, was found to be 4.2% in a São Paulo community sample.¹¹

Another question made by patients is regarding the best treatment for anxiety disorder: psychopharmacology and/or psychotherapy. It is important to discuss the options with the patients, explaining the evidences of benefit for each treatment.

Psychotherapy that stood scientific scrutiny has emerged in the 1960s through the development of cognitive-behavioral therapy (CBT). An interesting experiment showed that both CBT and a medication work: In Swedish subjects with social phobia, it was shown with brain imaging of amygdala that the anxiety provoked by a social stimulus could be blocked by either CBT or an SSRI medication.¹²

CBT can improve one's way of thinking about problems and unknown issues.¹³ Adrian Wells at the University of Manchester has developed a promising kind of CBT targeted at the kind of worries that are typical of GAD.¹⁴⁻¹⁵ The patients in my practice usually prefer to try medication first and then go on to a few sessions of CBT if need be, and it seems to work very well.

Anxiolytic medications benefit most patients with GAD and have been approved by regulatory authorities and academic psychiatrists.¹⁶ The primary drugs of choice today are the SSRIs and SNRIs (serotonin and noradrenaline reuptake inhibitor) because of their combined anxiolytic and antidepressant properties and sustained long-term efficacy. The benzodiazepines are useful for an occasional exacerbation of anxiety, and are sometimes taken together with SSRIs/SNRIs during the first 1 to 4 weeks of treatment, to alleviate muscle tension or insomnia. A new medication was recently approved by the regulatory authority in Europe: pregabalin. It has proven effective in patients with GAD.¹⁷

Patients are exposed to a variety of information about the side effects of psychiatric medications. One issue frequently raised by patients refers to the potential addictive effect of some drugs.

Media presentations about psychoactive medications rarely are positive, and the *stigma* of having a psychiatric problem is still evident, although less so today. In contrast, journalists and new age advocates do not question the utility of insulin for diabetes or vitamin B12 for pernicious anemia, yet they tend to depict psychoactive medications as immoral and hazardous.

Doctors who treat anxious patients know that one can expect anxiolytic benefits with SSRI/SNRI treatment in 3 out of 4 patients within 2 to 4 months. Following this symptom relief, patients report improved decision-making, prioritizing, risk management, and socializing with peers and family.¹⁸ Within 4 to 12 months, patients generally report notably improved relations and work functioning.

Street drug addicts or alcohol-dependent individuals with drug-seeking behaviour to experience euphoriant or stimulant effects have no use for SSRIs/SNRIs. These medications have no addictive potential.

Potential side-effects, specially the common ones, should also be discussed with the patients.

In the first 1 to 2 weeks of treatment, patients may experience some nausea, sweating or drowsiness, and rarely some increased anxiety. One should start with a low dose that is increased at a rate decided by the patient, usually with dose increases every 3 to 5 days. The patient should be in control of the medication. The physician should explain to the patient not to expect immediate reduced anxiety, suggesting to the patient to wait at least two months of treatment before deciding whether about continuing or not.

Nurses can be trained on how to manage anxiety patients, and they should help answering patients' questions and making sure that they get a re-appointment and follow-up. Patients should also receive brochures and other information sources describing the typical features of GAD, treatment options and typical cases. Another important strategy might be patient groups with weekly sessions where patients can share their experiences. Studies show that this kind of comprehensive care-taking increases the chances of improving.¹⁹

Patients may experience some continued adverse effects also when their anxiety has been reduced. They can present with a decreased (sometimes increased) sex drive, and orgasms may be delayed or not attainable. Men are sometimes better off not drinking alcohol prior to having sex, and may find sildenafil drugs beneficial. Sweating occurs. Some experience weight loss and others weight gain, probably due to different activity levels. Rarely, a patient experiences *lassitude*, i.e. restricted emotions in general. If that happens the physician should have to reassess the patient's symptoms and change the medication, or go for CBT.

If patients forget to take their daily dose, some medications (paroxetine and venlafaxine in particular) are known to cause nausea and dizziness, symptoms that vanish in 2 to 3 hours after renewed dosing.

Issues to consider with serotonergic medications are teratogenicity and behavioral effects acutely and long-term on the child. A review of such studies was published in 2005.²⁰ According to the Swedish Medical Birth Registry with 4000 mothers exposed to SSRIs/SNRIs during pregnancy, and according to 15 studies of another 2600 mothers, there is no apparent risk of teratogenic effects in therapeutic doses. Cases of acute adaptation disturbances in the newborn due to serotonin overactivity have been reported, and it is advisable that a baby exposed to SSRIs/SNRIs *in utero* be monitored for 48 hours for such symptoms: increased muscle tone, irritability, jitteriness, hypothermia, abnormal breathing and petechia.²¹

All SSRIs/SNRIs are excreted in the milk, but no adverse reactions in the baby have been reported. According to a prospective long-term study of children exposed *in utero* to psychotropic medications, levels of depression, anxiety, social withdrawal did not differ significantly between exposed children and those not exposed.²²

On the other hand, it is also known that the mother's anxiety during pregnancy adversely affects both maternal and fetal well-being. A number of studies conclude that pregnant mothers with anxiety and depression should be vigorously screened and treated to reduce the risk to mother and offspring.²³⁻²⁵

An additional question posited by patients is for how long they will have to take the medication.

"Rejuvenated" is actually the word patients sometimes use to describe the effects of the medication; others express that they have been suffering from a "deficiency" for years that has been corrected with treatment. Some patients take the risk of relapsing into anxiety rather than putting up with long-term medication, not because of adverse effects but because they object to the concept of mind-altering medications. Others insist on life-long treatment, not wanting to risk ever having to be miserable again.

Psychiatric experts advise to take the medication for at least a year given that there is notable anxiolytic relief in the first couple of months, because the patient's functioning keeps improving and a majority of patients then report having been completely restored.²⁶ Furthermore, there is no data that indicate an accumulation of adverse events; e.g. getting Alzheimer or cancer. On the contrary, the major risks in GAD (secondary depression, alcohol abuse, cardiovascular disease, work disability, social isolation) are consequential to untreated anxiety.

If any patient chooses to discontinue the medication, this should be done by tapering the dose during at least three weeks. In spite of tapering, patients may experience dizziness, nausea and sometimes tingling sensations in the skin. This may go on for 1 to 2 weeks. Many other medications (cortisone, antihypertensive, antiasthma) can also cause discontinuation symptoms.

A relapse into anxiety comes usually after 3 to 4 months. The risk of such a relapse in ordinary patients is hard to

estimate. In controlled studies of relapse prevention, there is a fourfold increased risk in patients who are switched to placebo after having first responded to an SSRI.²⁷

Attention should be given to specific subgroups with GAD.

In population surveys, in general and psychiatric practice, and in clinical trials of anxiolytic drugs there is twice as many women as men with generalized anxiety disorder. The reasons for this are unknown. Men apparently have a higher "social threshold" in seeking treatment than women, and men tend to be in a worse condition once they make an appointment. Studies of anxiolytic medications are beginning to look at differences in response to treatment; according to one such study there is no measurable difference in treatment efficacy and safety between men and women.²⁸

Elderly people are different in many respects, in that they have survived "competing hazards" of many kinds into old age. Then they are exposed to somatic diseases, loneliness, loss, restricted mobility, and neurodegenerative changes due to stroke and dementia that confound the assessment of anxiety. Perhaps we need geriatric diagnostic criteria and focus on current rather than past symptoms.²⁹ Current anxiolytic medications appear as safe and effective in the elderly as in the younger according to subgroup analyses of controlled studies, but there is no solid ground for guidelines. Also, it seems reasonable to assume that mental health in the elderly can be maintained by prevention (e.g. combating loneliness, engaging in stimulating activities, physical activity, and maintaining good nutrition).

Finally, it is essential to express to the patient that all the questions and concerns he or she may have should be discussed with the physician. Issues should be discussed thoroughly as the patients' beliefs about medication and psychotherapy have substantial impact on the chances of getting well.³⁰ Doctors need to set aside time for this. Patients are entitled to make informed choices about the utility of different treatments.

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