Management of generalised anxiety disorder

Generalised anxiety disorder is common and can present in older people, often in conjunction with depressive symptoms. Pharmacological treatments have included tricyclic antidepressants, benzodiazepines, and antipsychotics, but a selection of new drugs are now specifically licensed for this disorder. Psychological therapies such as cognitive behaviour therapy and changing lifestyle factors, such as substance misuse and exercise are also important to achieve therapeutic success.

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Generalised anxiety disorder is one of several anxiety disorders that can present in older people. It is common and estimates of prevalence vary according to the diagnostic criteria used. The prevalence is generally recognised as 2–6% with a male-to-female ratio of 1:2, but compared with younger patients, research in older people is limited. A recent Turkish study found a slightly higher prevalence rate of 6·9%, with only social phobia scoring higher at 11·5%.[1] Significant differences exist between the sexes in the prevalence, comorbidity pattern, and sociodemographic and clinical correlates. Patients also show different treatment-seeking behaviours.

Generalised anxiety disorder is a chronic condition characterised by exaggerated worry and tension, with no obvious precipitating factors. Having this disorder means always anticipating disaster, often worrying excessively about health, money, family, or work. It can be extremely disabling and usually worsens any underlying physical or mental health problems.

A recent study from a clinic in Pittsburgh, USA, focused on late-life depression and anxiety research, has provided evidence of the significant burden of this disorder in late life. These data confirmed again the high prevalence and chronicity of generalised anxiety disorder, as well as the importance of implementing effective management strategies for this frequently undiagnosed and untreated disorder.[2] The study found that older adults with generalised anxiety disorder were more disabled, had worse health-related quality of life, and used health-care services more frequently. Their social and role functions were also negatively affected.

When considering the management of generalised anxiety disorder, it is important to ensure a balanced, well considered, and consistent approach, confirming that a thorough assessment has been undertaken and that the diagnosis has been clearly established. Excluding and treating physical disorders, which can present with similar symptoms, is also important. Other psychiatric conditions, for example severe depression or psychosis, and also cognitive impairment should be excluded or appropriately investigated and treated, if present.

The evidence-base for the treatment of generalised anxiety disorder has grown substantially in recent years, and several modalities of treatment are now available. However, most of these have been studied in younger patients, so their applicability in older people should be evaluated carefully. This article focuses on the management of this disorder in older people, including specific drug treatments as well as psychological and social interventions, and education and support for patients and families.

Causes

Generalised anxiety disorder has many potential causes. An understanding of these is important since clearly identifying the cause might suggest the best treatment. Causes can be

divided into genetic or biological influences; psychological factors include predisposed personality types and traits, as well as neurobiological mechanisms. A stressful event can precipitate generalised anxiety disorder in a person with a predisposed personality type (especially anxious-avoidant), usually with additional help from genetic or biological and environmental factors. The disorder may persist and become chronic, especially if the stressor is perceived as threatening. It shows an increased prevalence amongst first-degree relatives suggesting a possible genetic link.

Bowlby's Attachment theory and Freud's Psychoanalytic theory, provide several explanations; either of generalised anxiety disorder being rooted in uncertain childhood attachment experiences, or where the ego has been overwhelmed by developmental failure in childhood and thus weakened. Cognitive behavioural theories propose that people who develop this condition will have an excessive response of the autonomic nervous system. Anxiety will then arise with conditioning to neutral stimuli and an alarm response will develop.

Several brain systems and neurotransmitters are involved from a neurobiological perspective and mediate normal anxiety. In generalised anxiety disorder, noradrenergic, serotonergic and gamma-aminobutyric acid (GABA) receptors are probably all involved. An abnormal mechanism or a normal mechanism responding to abnormal cognitive processes, underpins this concept.

In assessment of the causes of this condition, excluding and treating underlying physical conditions, which may present with symptoms of anxiety, is important. An episode of physical ill health can be a very frightening experience for older people, and can lead to a persistent state of anxiety. Cardiovascular, respiratory, and endocrine events happen frequently in this population and need to be diagnosed and treated accordingly.

General principles of management

Generalised anxiety disorder is one of the most common anxiety disorders seen in both community and acute hospital settings. The costs, to individuals and to society, associated with this disorder are high, and the level of impairment experienced by patients is reported to be equal to that of major depressive disorder. Severe anxiety can coexist with major depression. If present, major depression should be diagnosed and treated first, especially because of the risk of suicide. Furthermore, in older patients, generalised anxiety disorder itself (perhaps with some depressive symptoms) can be associated with significant risk of self-harm and suicide. It is a serious and chronic disorder that requires appropriate long-term treatment. In the acute phase of treatment, the focus will be on resolution of symptoms. The primary goal of longer-term treatment is remission (ie, total resolution of symptoms and functional impairment).

In December of 2004, NICE published clinical guidelines for the management of anxiety,[3] which includes panic disorder and generalised anxiety disorder. It recommends that a shared decision-making process should take place between the individual and health-care professionals during the process of diagnosis and also in all phases of management and ongoing support and care. Patients and their families should receive appropriate information on all aspects of the illness, including the nature, course, and available treatment options. They should be told of the predicted response to treatment and the most likely effects and side-effects, including the possibility of withdrawal symptoms, especially with abrupt cessation of medication.

Box 1: Interventions recommended by NICE[3]

- Benzodiazepines should not be used for longer than 2–4 weeks
- Interventions, such as psychological therapies, pharmacotherapy, and self-help modules should be offered in the long-term treatment of individuals with this disorder
- If the first intervention fails, then alternative interventions should be offered after reassessment of the individual's needs and symptoms, also exploring ongoing precipitating and perpetuating factors
- If two interventions have been tried with no improvement in symptoms, referral to specialist mental health services should then be offered

The process of diagnosis should include eliciting information about the individual's personal history, past history of successful or failed treatments and self medication, including use or misuse of recreational drugs or alcohol. Primary-care treatment options should be offered and made available to the patient as these services are often preferred by individuals, and are known to have lower drop-out rates. Individual and cultural preferences should always be considered. A summary of interventions recommended by NICE is shown in box 1.

A stepped-care treatment pathway provides a framework in which services can be organised. NICE recommends that the least intrusive, most effective treatment should be offered at any given time (figure).

The care and management will be based on:

- Treating comorbid conditions;
- Cognitive behavioural therapy with an experienced therapist, at home if needed (and if available);
- Structured problem solving;
- Full exploration of drug therapy (box 2);
- Day support to relieve carer stress;
- Referral for advice, assessment or management.

Antidepressants

An article by Katzman[4] of the Stress, Trauma, Anxiety, Rehabilitation, and Treatment (START) Clinic in Canada, summarised the current considerations for drug management of generalised anxiety disorder. The consensus across treatment guidelines suggests that first-line treatment should consist of an antidepressant including SSRIs and SNRIs. Patients can take 2–4 weeks to experience some relief of symptoms, and full remission of symptoms may take longer in older people.

Carter and McCormack wrote a review[5] of duloxetine for the treatment of generalised anxiety disorder. This treatment is effective in patients with at least moderately severe disease, and improves several clinical endpoints such as functional impairment and levels of anxiety. Longer-term treatment with duloxetine also demonstrated efficacy in preventing or delaying relapse in responders. It was generally well tolerated and the most common side-effect was nausea. Serious adverse events with both short-term and long-term treatment were relatively uncommon. The usual starting dose is 30 mg increasing to 60 mg if necessary and a maximum dose of 120 mg.

A reasonable amount of research has also been published on escitalopram, but most of this has studied younger patients. One study[6] pooled data for 856 patients from several randomised controlled trials and included patients up to 80 years of age. Escitalopram was significantly superior to placebo over 8 weeks. The dose was 10 mg daily for the first 4 weeks increasing to 20 mg daily if clinically indicated. A relapse prevention study lasting up to 76 weeks involving 375 responders to escitalopram 20 mg daily[7] showed that the risk of relapse was more than four times higher in the placebo group. However, all patients in this study were younger than 65 years of age. Pelissolo, in his recent review indicated that escitalopram was more effective than placebo and at least as effective as paroxetine for reducing the symptoms of generalised anxiety disorder.[8]

Several studies have compared paroxetine and escitalopram. Jorgensen and others[9] used a decision-analytic model with a 9-month horizon and adapted it for the UK. Inputs for the model included drug and non-drug specific probabilities from data for head-to-head trials, other publications, and expert opinion. The main outcome measures were success (response after 12 weeks' treatment and no relapse during the following 24 weeks) and costs. Escitalopram-treated patients had a 14·4% higher first-line treatment success and significantly lower discontinuation rates due to adverse events than had those treated with paroxetine. Additionally, treatment with escitalopram yielded lower expected costs with greater effectiveness compared with paroxetine. Two further studies found similar results. Baldwin and colleagues[10] found better efficacy with escitalopram 10 mg daily compared with paroxetine 20 mg daily over 12 weeks, and Bielski et al[11] reported similar efficacy for escitalopram (10–20 mg daily) and paroxetine (20–50 mg daily) over 24 weeks but escitalopram was better tolerated and fewer patients withdrew from the study compared with those on paroxetine.

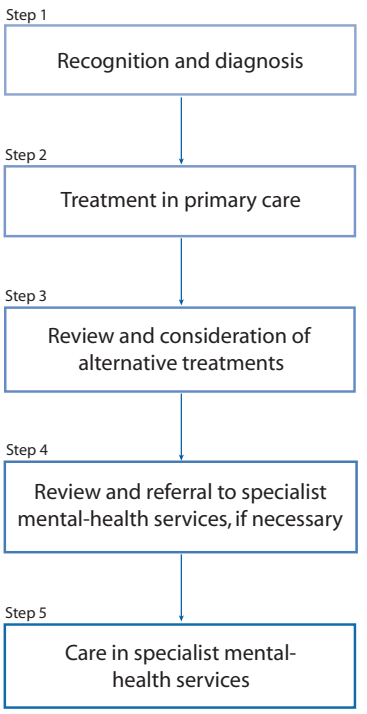

Figure: Stepped approach to care in patients with general anxiety disorder

New anxiolytics

Pregabalin is a new anxiolytic for the treatment of generalised anxiety disorder with a mechanism of action different from benzodiazepines and other anxiolytic agents. Pregabalin binds to the α2-δ subunit of calcium channels and acts as a presynaptic inhibitor of calcium release in stimulated neurons of various excitatory neurotransmitters.

Several studies have shown positive benefit in patients with generalised anxiety disorder including short-term[12,13] and longer-term studies.[14] The two short-term

Box 2: Drug treatments for generalised anxiety disorder

Selective serotonin reuptake inhibitors (SSRIs)
- Paroxetine*
- Escitalopram*
- Sertraline

Serotonin and norepinephrine reuptake inhibitors (SNRIs)
- Venlafaxine*
- Duloxetine*

Tricyclic antidepressants
- Imipramine

Benzodiazepines
- Alprazolam
- Chlordiazepoxide
- Clonazepam
- Diazepam
- Lorazepam

Anticonvulsants
- Pregabalin*

Antipsychotics
- Quetiapine
- Amisulpiride
- Risperidone

*Licensed specifically for treatment of generalised anxiety disorder

studies did not include older people. Feltner and colleagues[14] reported a randomised, placebo-controlled study in 339 pregabalin responders, including older patients, treated for 6 months. At the end of the study 65% of patients in the placebo group had relapsed compared with 42% in the pregabalin group.

One study has looked at pregabalin specifically in older people. This double-blind, randomised, placebo-controlled study of pregabalin 150–600 mg daily over 8 weeks involved 273 patients. Pregabalin was well tolerated and was significantly superior to placebo after 2 weeks.[15] Additionally, a review[16] from the USA outlines the benefits of pregabalin for generalised anxiety disorder. The recommended dose is initially 150 mg daily in two or three doses increasing over weekly intervals to 600 mg daily.

Antipsychotics

Antipsychotic drugs such as quetiapine, risperidone, and amisulpiride are commonly used for anxiety symptoms but are not licensed for generalised anxiety disorder. They should not be used as first-line treatment, and when used, small doses should be used and for short periods. Routine laboratory investigations should be done before and during treatment depending on which antipsychotic is prescribed. Quetiapine is commonly used and Baune[17] showed that a dose of 50–300 mg daily, as monotherapy or in combination with an antidepressant can be an effective for short-term treatment and maintenance treatment of generalised anxiety disorder.[17]

Other drugs

Sodium valproate has also been used in the management of generalised anxiety disorder, but again is not licensed for this indication. A randomised, double-blind placebo-controlled study by Aliyev et al[18] showed that significantly more patients in the treatment group responded. However, side-effects such as dizziness and nausea were more problematic in older people. Drugs such as buspirone, β-blockers, and antihistamines have also been used to alleviate symptoms. These drugs are not consistently efficacious and are not recommended for general use. In older patients, the cardiac side-effects of β-blockers should be considered carefully.

Psychological therapies

Cognitive-behavioural techniques involve cognitive restructuring (changing the way a person thinks), relaxation, worry exposure, behaviour modification, and problem solving. It can be effective for late-life generalised anxiety, but only pilot studies have been conducted in primary care, where older adults most often seek treatment. In a randomised clinical trial in Houston, Texas, USA, Stanley and others[19] showed that cognitive-behavioural therapy for older adults in primary care resulted in greater improvement in anxiety and depressive symptoms as well as in general mental-health of older patients compared with enhanced usual care.

A 2006 Cochrane review of psychological therapies for generalised anxiety disorder, examined the effectiveness of cognitive-behavioural therapy, psychodynamic therapy, and supportive therapy compared this with usual treatment. Because numbers were small the reviewers could not draw firm conclusions about which therapy was more effective. It was suggested that more non-cognitive-behavioural models were required to inform health-care policy on the most appropriate forms of psychological therapy.[20]

Lifestyle and education

Lifestyle and mental health is increasingly being recognised as an important area for research. More focus is given to lifestyle choices and the effect that this can have on a patient's physical and mental health. This is important for generalised anxiety disorder in older people. In particular, patients should be given appropriate guidance on issues such

as smoking, drinking, diet, fluid intake, and exercise. Self-medicating with alcohol to control symptoms can be problematic causing disturbed sleep, depression, and increased anxiety, as well as negative physical outcomes. Patients should also be advised to limit their intake of stimulants, since excess intake of caffeine and nicotine can worsen underlying symptoms of anxiety.

Despite the high prevalence of generalised anxiety disorder, only 30% of sufferers are diagnosed. Very few patients are prescribed medication or referred to psychiatric services. The key aim is to ensure early detection and management of these patients through better integration of services involving primary care. The use of simple diagnostic tools would also aid the early detection of patients with generalised anxiety disorder. By achieving early diagnosis and treatment of generalised anxiety disorder, we will be able to improve the quality of life of patients with this disorder.[21]

Conclusion

Generalised anxiety disorder is common in older people but is frequently missed. A mixture of anxiety and depressive symptoms is not uncommon and can be accommodated in the treatment plan since antidepressants (especially SSRIs) and cognitive behavioural therapy are effective in both conditions. A detailed assessment might identify specific aetiological factors (eg, stress due to poverty) and if these are appropriately managed, symptoms may improve or resolve completely. Several drugs are specifically licensed for and are effective for the treatment of generalised anxiety disorder including paroxetine, escitalopram, duloxetine, venlafaxine and pregabalin. However, most research has been undertaken in younger patients so these data need to interpreted with caution. Evidence exists for the benefit of psychological treatments and lifestyle factors are important.

Finding a treatment package that is relatively easy to follow and comply with is essential. Many patients will never receive a formal diagnosis; others might give up hope of successful treatment. However, modern treatments, can be both clinically and cost effective, emphasising the importance of assessment, diagnosis, and treatment.

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