Antidepressant-induced sexual dysfunction

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Abstract

Depression is a common mental disorder in the general population and confers a significant burden on the individual and his or her family. Although it is a condition that is viewed as highly treatable, with numerous available treatment options, many of the agents used, may, in themselves, impose a burden in terms of associated adverse effects. Antidepressant-induced sexual dysfunction is a complaint which, although it occurs with relative frequency, is often not discussed owing to the sensitive nature of the topic. It is imperative to address this issue with patients in order to ensure optimal treatment response, compliance and adherence to medication.

Introduction

Depression is one of the most common illnesses worldwide, affecting approximately 350 million people. At its worst, depression can lead to suicide, which leads to an estimated one million deaths every year. The World Health Organization predicts that by the year 2030, depression will be the foremost contributor to the worldwide burden of disease. Currently, depression accounts for 4.5% of the worldwide total burden of disease, as well as approximately 12% of total years lived with disability worldwide. Without treatment, depression has the tendency to assume a chronic course, to recur, and to be associated with increasing disability over time.

In addition to the personal suffering of individuals, depression imposes significant costs on society in terms of direct and indirect costs, including, but not limited to, actual treatment costs (healthcare provider, medication and hospitalisation costs) and lost productivity because of absenteeism.

Prevalence and risk factors

The lifetime prevalence of depression in South Africa has been estimated to be 9.8% across all age groups, with females being 1.75 times more likely to develop depression than males. In addition, the age of onset is difficult to predict because the first episode may be mild and go untreated, but in general, depression can begin at any age, even in childhood and adolescence. Trends show that there are two peaks of an increased incidence of depression, and these occur in the 20s and 40s, with a mean age of onset at 30.

As with most mental illnesses, there is a strong genetic predisposition to depression, and it is 1.5-3 times more common in the first-degree biological relatives of persons with this disorder than in the general population.

Risk factors include being of the female gender, having experienced previous episodes of depression and a family history in a first-degree relative, i.e. a mother, father, brother or sister.

Table I details the signs and symptoms of depression.

Table I: The signs and symptoms of depression

- A period of at least two weeks of a depressed mood
- Changes in appetite, weight and sleep
- Loss of energy and fatigue
- Loss of interest in activities once enjoyed
- Feelings of worthlessness, hopelessness or guilt
- Anxiety
- Suicidal ideation

Treatment

The guidelines differ on how depression should be managed, but generally, and in accordance with the South African Society of Psychiatrists guidelines, the first-line treatment of mild depression should consist of psychotherapy, either alone or in combination with antidepressant monotherapy.

Moderate depression should be treated with an antidepressant, preferably one from the selective serotonin reuptake inhibitor (SSRI) class, a serotonin noradrenaline reuptake inhibitor, a noradrenaline dopamine reuptake inhibitor or mirtazapine. The aforementioned classes are preferred over the older antidepressants from the tricyclic antidepressant and monoamine
oxidase inhibitor class, owing to superior tolerability and safety. Newer antidepressant classes can also be used, as well as psychotherapy.4

An antidepressant must always be considered as first-line therapy for severe depression, in combination with psychotherapy. Electroconvulsive therapy should be used, where appropriate. A combination of an antidepressant and an antipsychotic medication should be used if psychotic features are present.4

The choice of medication should be based on the patient profile, side-effect profile, availability, nature of prior response to the medication (if applicable), the co-morbid psychiatric and medical conditions, patient preference, and potential drug interactions and cost.4

There are side-effects with all medication, and antidepressants are no different. However, the side-effect of sexual dysfunction can be common, and is not often spoken about owing to the perceived sensitive nature of the topic. Patients may feel embarrassed to discuss this with their healthcare professional, and hence it goes undetected. This has serious implications for a patient’s quality of life and the functioning of the family unit.

It is estimated that approximately 34% of men, and 41% of women, experience some form of antidepressant- or depression-related sexual dysfunction.3 If this side-effect is particularly burdensome, the patient could become noncompliant with the treatment, which might lead to the relapse and recurrence of depression.

In order to identify this particular side-effect, a pharmacist could either broach the topic directly, or use a less intrusive approach. Discussing the frequency of these side-effects in general, or in relation to a particular medication, could lead to an open discussion. Alternatively, basic psychoeducation on the subject of sexual well-being and dysfunction could also work.6

It is also important to assess which phase of the sexual response cycle is involved. Sexual satisfaction could be affected by diminished function in a specific phase of the sexual response cycle, or by a global decrease in pleasure that is associated with depression and its treatment.6

The sexual response cycle consists of four phases, namely desire (also referred to as “interest” or “libido”), arousal (encompassing erectile functioning in men and lubrication in women), orgasm and resolution.8

Antidepressant-induced sexual dysfunction is most commonly seen with use of the SSRIs, and occurs in 30-70% of patients. Antidepressants can cause side-effects in any one of the four phases, and include decreased libido, erectile or vaginal dysfunction, delayed time to orgasm and anorgasmia. Painful ejaculation has been reported in some case studies. A further complication is that dysfunction can occur in more than one phase, and there can be varying degrees of it. Other risk factors include age, i.e. being 50 years or older; tobacco use, i.e. 6-20 cigarettes smoked a day; recreational drug use, including alcohol; a prior history of little or no sexual enjoyment, and loss of income and level of education attained.5,7,8

Antidepressants target the neurotransmitters involved in sexual functioning (Table II). Although all classes may cause dysfunction, the classes which are highly serotonergic (the SSRIs) are most likely to cause this type of side-effect.9

Table II: Neurotransmitters and sexual functioning9

<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotonin</td>
<td>Activation of this receptor can inhibit sexual response</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Enhances libido</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>Facilitates erection and lubrication</td>
</tr>
<tr>
<td>Noradrenaline</td>
<td>Regulates the process of erection and orgasm</td>
</tr>
</tbody>
</table>

Management

Once a problem with sexual function has been identified, and determined to be secondary to the effects of the treatment, numerous strategies can be used to manage the condition. These strategies can be divided into three categories, i.e. a conservative or nonpharmacological approach, a pharmacological approach (this includes dose adjustments and switching) and adjunctive strategies.4 Some aspects of the nonpharmacological approaches can be performed by the pharmacist, whereas the latter two categories fall within the realm of the treating clinician.

Nonpharmacological approaches

If it is expected that the duration of therapy will not be long and if the patient is agreeable, it is acceptable to adopt a wait-it-out approach. Spontaneous remission occurs in 10% of all cases, and a further 11% of patients achieve partial remission.6 Counselling patients on these figures can provide reassurance. Other counselling should include general information on the likelihood of sexual dysfunction, the signs and symptoms of dysfunction, what to do should it occur, and other management strategies.9

Furthermore, a group of patients may elect to live with the side-effect after consideration of the risk of sexual dysfunction versus the benefit of antidepressant treatment.

Table III: Benefit and risk analysis in patients presenting with antidepressant-induced sexual dysfunction9

<table>
<thead>
<tr>
<th>Factor</th>
<th>Risk Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>The sexual function could have been worse when the patient was depressed</td>
<td></td>
</tr>
<tr>
<td>There may be a general lack of interest in sexual activity</td>
<td></td>
</tr>
<tr>
<td>There could be a lack of opportunity for sexual activity</td>
<td></td>
</tr>
</tbody>
</table>

Other approaches include referring the patient for behavioural therapy, or cognitive behavioural techniques and relationship counselling, with the partner involved.
Pharmacological approaches

Dose reduction is a reasonable strategy to employ before considering switching medication. An appropriate length of time is needed to assess if the sexual side-effects have diminished following a reduction in dose. This period depends on the half-life of the antidepressant, but the literature suggests that this could be anywhere from a few days to a few weeks. ⁹

The American Psychiatric Association recommends substituting the antidepressant that is causing the sexual dysfunction in patients who complain about this potential side-effect with one of the newer agents not associated with sexual dysfunction. This strategy works in approximately 39% of patients. The switch can take place within the same class, or from one class to another. However, when changing an antidepressant, the possibility of risk of relapse or recurrence of the depression must always be taken into account. There is also no guarantee that the new antidepressant will be completely devoid of sexual side-effects, or that it will be efficacious in the management of the patient’s depression. ⁶, ⁸

Bupropion and mirtazapine are associated with lower rates of sexual dysfunction than the SSRIs, as the former does not inhibit serotonin reuptake, and the latter is a serotonin receptor antagonist. ⁹

It would be prudent to mention that the approach to temporary medication discontinuation or a drug “holiday” is controversial, and is generally not a strategy which is supported because of the potential risk of withdrawal syndrome and effects on mood and compliance. ⁸

Alternative strategies

The clinician could add an adjunctive agent, which would firstly augment the action of the first antidepressant (Table IV), and secondly modify the side-effect profile of the first drug.

Table IV: Potential augmenting agents ⁶, ⁸

- Bupropion 75-150 mg once daily: Bupropion is beneficial for disturbances in orgasm
- Amantadine 100 mg twice daily: Amantadine is useful for orgasmic dysfunction
- Methylphenidate 5-40 mg daily: Methylphenidate may be of value in augmenting the antidepressant effect and minimising the side-effect of sexual dysfunction. Other articles have cited 10-25 mg
- Venlafaxine: Venlafaxine has been shown to have positive effects on desire, arousal and orgasm
- Sildenafil 50-100 mg per day: Sildenafil can be used in men with desire, arousal and orgasm difficulties
- Mirtazapine 15-45 mg per day: Mirtazapine is associated with lower levels of antidepressant-induced sexual dysfunction

The advantages and disadvantages of various strategies in the management of antidepressant-induced sexual dysfunction are outlined in Table V.

Table V: The advantages and disadvantages of various strategies that may be considered in patients presenting with antidepressant-induced sexual dysfunction

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watchful waiting</td>
<td>Preserves the efficacy of the initial antidepressant</td>
<td>Efficacy is not high as the sexual dysfunction usually persists</td>
</tr>
<tr>
<td>Dosage reduction</td>
<td>Preserves antidepressant efficacy and decreases the side-effects of the sexual dysfunction</td>
<td>Can cause a relapse or recurrence</td>
</tr>
<tr>
<td>A drug “holiday”</td>
<td>Is effective if the antidepressant has a short half-life</td>
<td>There is an increased likelihood of relapse. It also sends conflicting messages to patient about compliance and adherence</td>
</tr>
<tr>
<td>Switching</td>
<td>The chances of alleviating the dysfunction are high</td>
<td>There could be a possible relapse, and there is no assurance of antidepressant efficacy from the second medication</td>
</tr>
<tr>
<td>Augmentation</td>
<td>Confers the additional benefit of a second medication</td>
<td>Can increase the adverse effects. The costs increase, and there is an enhanced possibility of a drug interaction</td>
</tr>
</tbody>
</table>

Conclusion

Antidepressant-induced sexual dysfunction can occur in one or more phases of the sexual response cycle. By increasing communication and education around this side-effect, pharmacists can decrease the associated stigma, provide reassurance to their patients and help to ensure optimal treatment. Treatment can take the form of a nonpharmacological approach, including education and counselling; and a pharmacological approach, which includes dose reduction, switching agents or augmentation.

References