

A clinical review of antidepressants, their sexual side-effects, post-SSRI sexual dysfunction, and serotonin syndrome

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ABSTRACT

Depression and anxiety are common, with one in six people experiencing symptoms in any given week. Of these people, 8.32 million are prescribed antidepressants. People living with HIV are likely to experience psychiatric disorder, with one in three experiencing depression and anxiety, and being at greater risk of developing post-traumatic stress disorder. Sexual side-effects of psychotropic medication are very common, cause distress, and can persist even after the medication has been withdrawn. Antidepressants are powerful drugs and can have severe interactions with many other substances. This article seeks to raise awareness of sexual side-effects of psychotropic medications and draw attention to ethical issues related to post selective serotonin reuptake inhibitor sexual dysfunction (PSSD). Additional risk factors and interactions between psychotropic medications and recreational drugs are identified. Recommendations are made to improve care and clinical outcomes through the development of therapeutic alliances.

Key words: Mental health/illness ■ HIV ■ Depression ■ Sexual dysfunction ■ PSSD ■ Chemsex ■ Recreational drugs ■ SSRIs ■ Antidepressants ■ Erectile dysfunction ■ Serotonin ■ Serotonin syndrome

Statistics indicate that one in six people over the age of 16 experience symptoms of common psychiatric disorders such as anxiety or depression in any given week (Baker, 2023). According to the annual report by the NHS Business Services Authority (2022) 8.32 million people have been prescribed antidepressants. This represents a significant proportion of the UK population. These figures undoubtedly impact on people with HIV: according to statistics from the Terrence Higgins Trust (2022), people living with HIV are twice as likely to experience depression as the general population. It is estimated that one in three people living with HIV experience depression (Terrence Higgins Trust, 2022), and the approximate global prevalence of post-traumatic stress disorder (PTSD) in people living with HIV is 28% (Tang et al, 2020).

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Sexual side-effects overview

Antidepressant medications such as selective serotonin reuptake inhibitors (SSRIs), come with a risk of causing sexual side-effects. The *British National Formulary (BNF)* (Joint Formulary Committee, 2022a; 2022b) categorises the prevalence of sexual side-effects with antidepressants as 'very common' to 'common', meaning that it will affect more than one in ten people. Specific side-effects include anorgasmia, reduced libido, vaginal dryness, and erectile dysfunction (Joint Formulary Committee, 2022a). These side-effects can be very distressing for the people who are experiencing them (Bala et al, 2018). There is a growing body of research into the phenomenon known as post-SSRI sexual dysfunction (PSSD); with De Luca et al (2022), for example, conducting a study to look at the treatment options available for PSSD. They acknowledged that the exact incidence and prevalence are unknown due to a lack of studies on the subject. Bala et al (2018) were also unable to determine prevalence in their literature review.

A number of patient-led advocacy groups, such as the PSSD Network and the UK PSSD Association, seek to raise awareness and funding for research into PSSD (UK PSSD Association, 2023). Investigation into PSSD reveals that, for many people, sexual side-effects can persist long after the SSRI is stopped. Reported symptoms include genital numbing, pleasureless or absent orgasm, and persistent suppression of libido, months or years after the medication is stopped (Bala et al, 2018; De Luca, 2022). The *BNF* warns that 'symptoms of sexual dysfunction may persist after treatment has stopped'. This warning is shown as a further comment on the drug information monographs for sertraline (Joint Formulary Committee, 2022a), fluoxetine (Joint Formulary Committee, 2022b), paroxetine (Joint Formulary Committee, 2022c), and citalopram (Joint Formulary Committee, 2022d), all of which are commonly prescribed SSRIs.

This issue raises significant concerns about informed consent when prescribing psychotropic medication. The doctrine of informed consent underpins every healthcare intervention. For consent to be informed, an individual needs to know what their condition is, what the prognosis is (with or without treatment), what the available treatments are, and what are the advantages and disadvantages (Selinger, 2009). The General Medical Council (GMC) (2020) gives some guidance on this subject:

it states that 'it wouldn't be reasonable' to share every possible risk of harm or side-effect and advises that the consultation should be tailored to each individual, depending on what is important to that person. The GMC (2020) further advises that any risk of serious harm, however unlikely, 'should usually' be disclosed. Given that antidepressant medication labels carry a warning that PSSD is a possible long-lasting consequence (Joint Formulary Committee, 2022a) and not just a side-effect, there is a strong case for necessary disclosure under the GMC (2023) guidance.

Literature review

There is very little literature exploring the prevalence of clinicians discussing sexual side-effects with patients, either before prescribing a psychotropic medication, or as part of monitoring response to treatment. A literature search on the sexual side-effects of psychotropic drugs returns a litany of papers which confirm that they do indeed exist, but there are far fewer studies available on how we manage and discuss sexual dysfunction.

A study by Boa (2014) found that patients wanted to discuss sexual problems but felt embarrassed to do so. Patients typically waited until the health professional brought up the subject. This study looked at sexual health more generally, not specifically sexual dysfunction secondary to psychotropic use. Krouwel et al (2020) looked at the barriers to discussing sex, sexuality and treatment-related sexual dysfunction, but the study focused on oncologists and their willingness to discuss sex with their patients. Bahrack and Harris (2009) concluded that health professionals need to do more to ensure that patients are made aware of potential sexual side-effects prior to starting an antidepressant.

Higgins et al (2006) found that mental health nurses felt that discussing sexual side-effects was a low priority, and they feared that being truthful about sexual side-effects could encourage non-adherence. This approach is problematic because it places the burden of disclosure back on the individual, who may feel too embarrassed to raise the subject, a concern supported by the Boa (2014) study.

In addition, if we, as health professionals, forewarn people about sexual side-effects, we can simultaneously offer hope that solutions are available. Management of sexual dysfunction is possible by switching medication, reducing dose, taking phosphodiesterase type-5 inhibitors or undergoing psychosexual therapy (Atmaca, 2020). This approach could potentially improve concordance if the individual is well informed, understands that there are solutions, and feels comfortable to discuss any sexual side-effects should they occur. Furthermore, non-disclosure of potential sexual side-effects could be seen as an ethical breach of the doctrine of informed consent, particularly if a patient develops PSSD after the medication is discontinued. This could be seen a breach of the ethical principle of non-maleficence.

Ideally, a mental health assessment should incorporate some consideration of pre-morbid sexual function and activity, especially if the patient is presenting to mental health services for the first time. Loss of libido and erectile dysfunction are

common symptoms of depression (Gonçalves et al, 2023). It is therefore important to ascertain the presence and severity of any sexual dysfunction before starting anyone on psychotropic medication. This helps us to understand if the sexual dysfunction is a symptom of mental illness or a side-effect of the treatment. Sexual dysfunction is also common in conditions such as hypertension, menopause, high cholesterol, cardiovascular disease, cancer, obesity and diabetes (Chen et al, 2019), so a comprehensive psychosexual history can assist in the early identification and treatment of various physical health problems.

Relevance to HIV care

Gooden et al (2022) and the Terrence Higgins Trust (2022) report that people living with HIV are twice as likely to experience depression than the general population, and one in three people living with HIV will experience comorbid depression. People with HIV also experience higher rates of anxiety and PTSD (Tang et al, 2020).

The National AIDS Trust (NAT) (2021) found that people living with HIV felt let down by mental health services, with many saying that mental health staff do not fully understand how HIV affects mental health. The NAT highlighted that many people living with HIV feel like they are treated differently or discriminated against because of their HIV status. According to the National Institute for Health and Care Excellence (NICE) (2021) men who have sex with men (MSM), trans women, people who inject drugs and sex workers are all at higher risk of contracting HIV: these groups are potentially more likely to face discrimination, barriers to health care, violence, abuse and trauma. Black people, especially those who are gay, trans or sex workers, are similarly at risk of racism, abuse and marginalisation.

Multifactorial discrimination has been shown to positively predict high depression scores, damaged psychological wellbeing, and increased substance misuse (Khan et al, 2017). Gokhale et al (2019) estimated that 27% of people living with HIV are diagnosed with depression and, within this group, 65% are prescribed antidepressants.

Recreational and over-the-counter drugs

The importance of a good history

Knowing about an individual's recreational drug use is important before commencing antidepressants due to the risk of serotonin syndrome. This syndrome is a rare but potentially life-threatening consequence of antidepressant treatment (Volpi-Abadie et al, 2013). The list of symptoms, as defined by Sternbach (1991), are still used today and include: diarrhoea, restlessness, sweating, muscle twitching, hypertension, tachycardia, pyrexia and seizures. It is a medical emergency and, if left untreated, can result in death.

Serotonin syndrome is precipitated by use of multiple serotonergic drugs, resulting in the overactivation of 5HT-1A and 5HT-2A receptors in the brain (Volpi-Abadie et al, 2013). Most antidepressants work by increasing the concentration of serotonin in the synapse, and are therefore serotonergic agents (Volpi-Abadie et al, 2013). Most stimulant recreational drugs increase the release of serotonin in the brain (Ellahi, 2015). Examples of stimulants include cocaine, MDMA and ecstasy,

crystal meth, amphetamines, as well as the almost infinite variation of novel psychoactive substances (Ellahi, 2015). The combination of two or more agents can cause serotonin syndrome (Volpi-Abadie et al, 2013); therefore, it is essential to know about recreational drug use before prescribing an antidepressant.

Prescribers are required to take a full medication history in any consultation, and this should include recreational drugs, and any non-prescribed medication (Royal Pharmaceutical Society, 2021). Failing to enquire about recreational drug use in a mental health review can result in unsafe and potentially deadly prescribing decisions. Due to the cumulative effects of serotonergic agents (Volpi-Abadie et al, 2013), people who regularly consume and/or mix multiple types of stimulant recreational drugs, would be at much higher risk of developing serotonin syndrome.

It is vital that health professionals take a comprehensive medication and drug history before prescribing any new serotonergic drug (Simon and Keenaghan, 2022). If an individual does not make a disclosure of recreational drug misuse, it is still important to counsel the person on the risk of serotonin syndrome. Khalili et al (2021) highlighted that some individuals under-report their drug use to health professionals. In addition, an individual may not be using recreational drugs at the point that an SSRI is prescribed, but they may go on to use drugs in the future. For this reason, health professionals must warn individuals about the interactions between SSRIs and recreational drugs, to enable them to make informed choices about any future drug use.

St John's wort is available over the counter and is used as a herbal remedy to improve low mood. However, it can have severe interactions with many medications (Joint Formulary Committee, 2023), and is a serotonergic agent, which means that it can therefore contribute to the development of serotonin syndrome (Ellahi, 2015).

Chemsex

Chemsex refers to the use of stimulant drugs with sexual partners, in sessions that can last for hours or days. Drugs typically used include mephedrone (or MKAT), methamphetamine, GHB and GBL. It is not uncommon for participants to consume multiple different drugs during a session (McCall et al, 2015). It is an ongoing public health issue, predominantly occurring in the MSM community, and participants often have sex with multiple partners during these prolonged sessions. (Macfarlane, 2016). People who participate in chemsex are recognised as being at higher risk of HIV infection (NICE, 2021).

The drugs commonly used in chemsex sessions are stimulants which, as established, can significantly increase the risk of developing serotonin syndrome. Íncera-Fernández et al (2021) found that MSM who participate in chemsex are more likely to experience depression, anxiety and substance addiction. They may seek mental health care, so it is imperative that health professionals ask about chemsex and sexual practices during mental health consultations. If a healthcare practitioner prescribes an SSRI without enquiring about chemsex and the associated recreational drug use, this could exacerbate the risk of serotonin syndrome due to the addition of another serotonergic agent (Ellahi, 2015).

Suggestions for practice

Nurses should endeavour to establish therapeutic alliances with the individuals they care for, as a strong therapeutic relationship has been shown to be linked to positive outcomes (Hartley et al, 2020). Pratt et al (2021) highlighted that individuals value openness and authenticity in nursing staff, and this approach fosters a non-judgemental relationship. A non-judgemental approach is key if individuals are to feel comfortable discussing subjects such as sexual activity, HIV, homosexuality, mental health and drug use, all of which can come with stigma. The work of Boa (2014) suggested that health professionals need to be more confident in instigating conversations about sex and sexual function because patients often feel embarrassed to bring up the topic themselves. Conversations about sex should be led by the clinician to establish a safe environment where the patient feels they have permission to discuss this without judgement or embarrassment.

Mental health assessments should enquire about pre-morbid sexual function because this can help identify potential differential diagnoses for physical health conditions (Chen et al, 2019). Furthermore, if we fail to ascertain sexual function and libido prior to starting an SSRI, it becomes difficult to distinguish whether any dysfunction is attributable to depression or is a side-effect of the treatment. Informed consent when prescribing psychotropics, particularly SSRIs, should include discussion about PSSD in order to be considered valid (GMC, 2020). People with HIV are more likely to develop depression, anxiety (Terrence Higgins Trust, 2022) and PTSD (Tang et al, 2020), so may present to services seeking treatment for these conditions. Integrating mental health screening tools into HIV services could improve health outcomes and improve access to mental health care for those living with HIV (Remien et al, 2019). It would also be important to not exclude single people from these conversations: the symptoms of PSSD, as outlined by Bala et al (2018), would be relevant to masturbation, not simply sexual intercourse.

Prescribers must also ask about any over-the-counter medication or recreational drug use (Royal Pharmaceutical Society (RPS), 2021) the individual may be taking before commencing an SSRI. People who are prescribed SSRIs should be warned about serotonin syndrome and counselled to avoid stimulants and St John's wort, because multiple serotonergic agents will exponentially increase the risk (Ellahi, 2015). All nursing staff have a responsibility to monitor the response to medication, and have knowledge of the adverse reactions and contraindications (Nursing and Midwifery Council, 2018). Independent nurse prescribers have additional responsibility in ensuring that prescriptions are safe (RPS, 2021).

Nurse and healthcare educators could endeavour to audit existing curricula and consider developing teaching material where gaps are identified.

Future research

Given the lack of literature on the subject, future research should explore clinician attitudes and knowledge regarding sex, sex and SSRIs, and PSSD, and informed consent in the context of sexual side-effects. The perspective of those prescribed SSRIs

is vital. Quantitative and qualitative research would also help to ascertain how often prescribers of psychotropic medication are instigating conversations about sex, sexual side-effects and PSSD. Research is warranted to ascertain the prevalence of PSSD.

Conclusion

Antidepressants are powerful drugs, with significant interactions, which are prescribed to over 8 million people in the UK alone. People living with HIV are more likely to experience depression, anxiety or PTSD, and are likely to be offered SSRIs as treatment for these conditions. Clinicians have a duty of care to ensure that all medications are prescribed safely, and this is paramount with regard to the prescription of SSRIs due to the propensity for severe interactions with recreational drugs, and over-the-counter medicine. PSSD is a rare, but potentially long-lasting, consequence of SSRI use, and healthcare ethics dictate that those being offered antidepressants must be made aware of the risks.

Chemsex is associated with a higher incidence of mental illness, and care must be taken to ensure that individuals seeking mental health care are not prescribed antidepressants if they are consuming recreational stimulant drugs. Nurses play a key role in forging supportive and non-judgemental therapeutic alliances, so that the individuals they support feel safe to discuss aspects of their life that have historically been associated with stigma. **BJN**

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KEY POINTS

- People living with HIV are more likely to experience mental illness and may be prescribed psychotropic medications
- There may be an informed accountability gap when discussing the sexual side-effects of this medication. This is particularly important given the long-lasting impact of post-SSRI sexual dysfunction
- Clinicians should enquire about sexual function and recreational drug use as part of a comprehensive history taking. A positive, non-judgemental attitude will support patients to discuss these issues
- Clinicians must ensure that individuals are aware of the risks of serotonin syndrome and be mindful of the interactions between serotonergic agents that can cause this

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CPD reflective questions

- Reflect on your own knowledge of the sexual side-effects of psychotropic medications. Is this something you currently discuss with the patients you work with?
- Thinking about post-SSRI sexual dysfunction, do you think there are any moral or ethical issues in not disclosing this as a possible long-term consequence of taking antidepressants?
- Consider your service. Are you familiar with the local referral pathways into mental health or chemsex support services? If not, do you think a mapping exercise would be useful?
- Would you feel comfortable initiating conversations about sex, drugs or psychiatry with the patients you work with? If not, how might you raise your confidence in doing so, given the risks outlined in this article?