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Case Report

Probable Association Between Atomoxetine Exposure and Reversible Deterioration in Semen Parameters: A Case Report

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Abstract:

Although known to cause sexual dysfunction, atomoxetine has been considered safe regarding male fertility. Clinical evidence linking atomoxetine to impaired semen parameters is extremely limited. We report a case suggesting a probable association between atomoxetine use and reversible deterioration of sperm parameters in an adult male. A 40-year-old male with attention-deficit/hyperactivity disorder (ADHD) was treated with atomoxetine (25–50 mg/day). Serial semen analyses revealed progressive deterioration of sperm concentration, motility, morphology, and ejaculate volume temporally correlated with dose escalation. Normal parameters were documented prior to atomoxetine initiation, with full recovery following drug discontinuation. The patient concurrently experienced decreased libido that resolved after stopping the medication. Causality assessment using the Naranjo Adverse Drug Reaction Probability Scale yielded a score of 7 (probable). No alternative etiologies were identified. This case provides clinical evidence that atomoxetine may adversely affect semen parameters and male fertility through a reversible, functional mechanism. Clinicians prescribing atomoxetine to adult males should counsel patients regarding potential reproductive risks and consider fertility assessment when conception is desired.

Key words: atomoxetine; male infertility; sperm parameters; sexual dysfunction; naranjo scale

Introduction

Several factors can cause male infertility including illnesses, drugs, and environmental factors [1]. Several psychiatric medications have been associated with adverse effects on male reproductive health. Selective serotonin reuptake inhibitors (SSRIs), which are widely prescribed for the treatment of depression and anxiety disorders, have been shown to affect total sperm count, sperm motility, and increased DNA fragmentation [2, 3]. Several antipsychotics, although less well studied, have also been shown to impact male semen, such as risperidone, quetiapine, olanzapine, and aripiprazole [4, 5].

The use of medication for attention-deficit/hyperactivity disorder (ADHD) has been on the rise, with stimulants (amphetamine analogues and methylphenidate – MPH) prescribing rates reaching up to 8.4% in individuals aged 2 to 24 years [6] while a further 5.8% is misusing these medications without a prescription [7]. Albeit the alarming data from animal studies, the clinical evidence for stimulants' gonadotoxic effects is limited. A recent study in men seeking care for fertility purposes, failed to identify direct impact upon spermatogenic parameters but reported reduced semen volume and total motile sperm count, which could be clinically meaningful for patients with already impaired sperm parameters [8]. MPH specifically has inconclusive animal studies [3], while no negative effects on sperm parameters have been reported in a retrospective human study [9]. However, chronic MPH exposure was reported to increase testicular weight while decreasing serum testosterone, reduce Leydig cell numbers, and compromise fertility [10, 11].

On the other hand, non-stimulant ADHD medications, including atomoxetine and guanfacine have been thought to be fertility safe, as clinical evidence linking these drugs to infertility is scarce. Atomoxetine is a selective inhibitor of presynaptic norepinephrine reuptake in the central nervous system, while it also has low affinity for serotonin and dopamine. Pharmacovigilance analyses have indicated potential signals for reduced semen volume, sperm motility, and sperm concentration, suggesting further investigation is warranted [12], even though atomoxetine did not demonstrate any effects on fertility in animal studies [13]. However, atomoxetine is reported to cause sexual dysfunction with erectile dysfunction, decreased libido, ejaculation disorder, impotence and orgasm abnormalities [13, 14].

We present herein a case with atomoxetine-exposure-related severe sperm alterations, confirmed with multiple sperm analyses before, during and after the use of the medication.

Case Presentation

A married 40-year-old Middle Eastern male presented with ASD and ADHD-inattention type, and followed up at a specialized clinic.

In October 2024, he presented with bilateral scrotal pain and the scrotal ultrasonography revealed bilateral varicocele. He was treated with diosmin/hesperidin but the symptom persisted over 6 months, while semen analysis (according to WHO 2021 laboratory manual criteria [15] showing excellent parameters (Table 1). In April 2025, the patient underwent microscopic varicocele ligation.

In June 2025, he was prescribed atomoxetine 25mg/day and his dose was optimized to 40 and then to 50mg/day (Figure 1). The patient reported significant improvement in his attention and focus at work without getting irritable as before, reduced impulsivity, and improved mental clarity. He was not a systematic smoker, did not drink alcohol or take recreation drugs, did not take any other medication, supplements or testosterone/anabolic, and he was not exposed to heat (hot-tub/sauna). His BMI was 31 kg/m2, and had no fever or any illness around and during the atomoxetine introduction. He had no history of sexual transmitted infection and his wife was found with no fertility issues. He had no endocrine analysis during this period, except thyroid function testing which was normal in November 2024. No changes in these factors were reported in the observation period.

Due to the couple's difficulty conceiving a second child, serial fertility testing was performed, revealing a decline in semen parameters temporally correlated with dose escalation of atomoxetine, which reached its nadir four months prior (Table 1). Atomoxetine was tapered off which led to a significant rebound in sperm concentration, motility, morphology, and ejaculate volume (Figure 1). This pattern was consistent with functional suppression rather than structural impairment with testicular reserve appearing preserved with strong recovery trajectory. Rechallenging was not attempted due to ethical reasons, as the couple was still in pursuit of another child.

	Feb 25	Aug 25	Nov 25*	Dec 25	Feb 26
Volume (ml)	2.0	1.0	0.5	1.0	2.0
pH	8.0	8.0	--	7.0	8.5
Sperm concentration (M/ml)	53	52.7	33	22.5	65.7
Total sperm count (M/ejac)	106	52.7	16.5	22.5	131.4
Progressive motility (%)	47	44	0	34	44.7
Total motility (%)	57	54	36	43	76
Total motile sperm count (M/ejac)	60	28.6	6	9.7	99.2
Sperm motility index	81	71	--	45	--**
Normal forms (%)	8	7	2	5	13
Functional sperm (M/ejac)	9.4	3.9	--	1.0	12.6
Timeline summary	Varicocele ligation 4/25 Atomoxetine 25mg 6/25 Atomoxetine 40mg 8/25 Atomoxetine 50mg 10/25 Atomoxetine tapered off 11/25				

Table 1: Timeline of semen analysis parameters according to WHO 2021 laboratory manual criteria and atomoxetine exposure

** From a different hospital – see limitations* *** Not calculated*

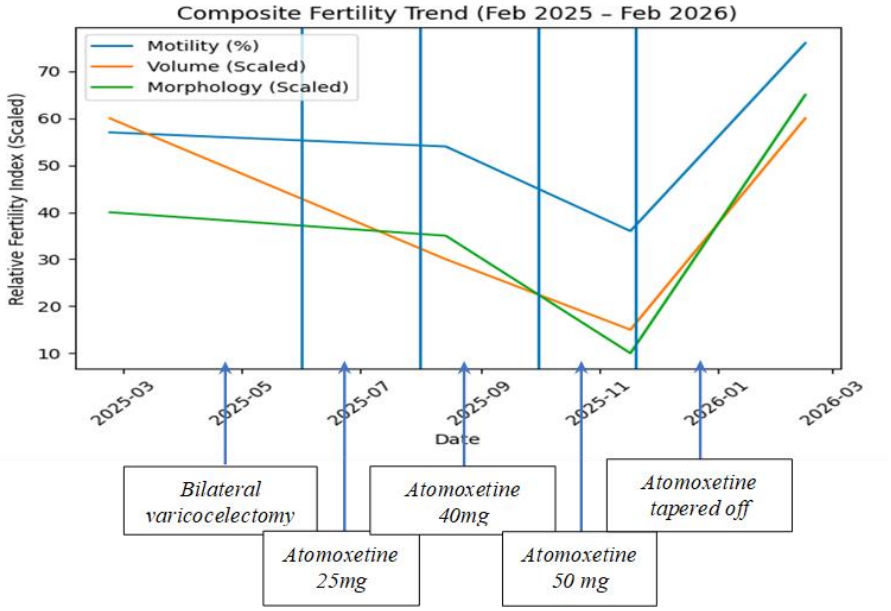

Figure 1: Composite fertility trend relative to medication exposure

The patient also reported a substantial decrease in libido within the first few weeks after atomoxetine initiation, which he defined as "a noticeable reduction in sexual desire and interest compared to his usual baseline, such as reduced spontaneous sexual thoughts, interest or responses, and lower motivation to initiate sexual activity". The reduction in libido became progressively worse, following the increase of atomoxetine. After stopping the medication, the patient reported that his libido gradually returned to his usual baseline over the following weeks.

Discussion

To our knowledge, reports directly linking atomoxetine to impaired sperm parameters are extremely limited. We presented a case of marked deterioration in semen quality temporally associated with atomoxetine exposure, documented on serial semen analyses during a period of difficulty conceiving. Atomoxetine exposure also led to substantial decrease in libido. Both issues were resolved following tapering off of the medication.

The patient had bilateral varicocele, which is a common causal factor for sperm parameters deterioration and male infertility [16]. However, his sperm parameters were not significantly affected (Table 1), which makes varicocele an unlikely primary explanation for the subsequent decline. Although varicocelectomy is generally associated with improvement in semen parameters, outcomes are heterogeneous, with several studies and meta-analyses demonstrating that most men experience increases in sperm count and motility after surgery, particularly when performed microsurgically [17]. A fluctuation could be expected in the early postoperative period due to the surgical stress, but by the first three months, after a full spermatogenic cycle (64-74 days), improvement is expected [18, 19]. In the present case, a documented decline was observed in sperm parameters 4 months after the surgery, when we would have expected improvement. The observed fluctuation is characterized by the rapid decline in sperm quality within weeks of initiating atomoxetine, which worsened with dose escalation and fully recovered upon discontinuation. These characteristics support a probable drug-related effect rather than a consequence of prior varicocele ligation, which is generally associated with gradual improvement or stable outcomes over time.

Causality was assessed using the Naranjo Adverse Drug Reaction Probability Scale [20]. The patient achieved a total score of 7, corresponding to a probable causal relationship between atomoxetine exposure and the observed deterioration in sperm parameters. This assessment was supported by a clear temporal association, marked improvement upon drug discontinuation, a dose–response relationship, and objective confirmation through serial semen analyses, while no other clear alternative etiologies were identified. Although rechallenge was not performed due to ethical considerations, the presence of objective laboratory evidence and dose-dependent worsening substantially strengthens the likelihood of a causal association.

The mechanism by which atomoxetine may affect sperm parameters is not well established; however, several biologically plausible pathways exist. As a selective norepinephrine reuptake inhibitor, atomoxetine increases central and peripheral norepinephrine levels, which may influence the Hypothalamic–Pituitary–Gonadal Axis and disrupt spermatogenesis. Experimental evidence suggests that elevated norepinephrine can impair male reproductive function through β-adrenergic signaling, inducing oxidative stress and ferroptosis in Sertoli cells, thereby disrupting spermatogenesis [21]. In addition, atomoxetine has been shown to induce oxidative stress and mitochondrial dysfunction in cellular models, with increased production of reactive oxygen species [22] Oxidative stress is a well-established mechanism of male infertility, leading to impaired sperm motility, membrane damage, and DNA fragmentation [23]. The observed dose–response relationship and reversibility in this case further support a functional, rather than structural, mechanism, likely mediated by neuroendocrine and oxidative pathways.

All classes of antidepressants are known to be associated with some degree of sexual dysfunction in both men and women, more with SSRIs and less so with SNRIs [3]. Atomoxetine, also an NRI, can cause sexual dysfunction [13, 14], and this was reported also in our case. Decreased libido began within a few weeks of atomoxetine initiation and was progressively resolved over the weeks following discontinuation.

Based on the negative animal studies [13] and the lack of clinical studies and reports, atomoxetine has been considered a medication without established adverse effects on male fertility. This was further supported by the lack of effect on sperm DNA integrity and semen quality in males exposed to a similar drug, duloxetine, a serotonin and norepinephrine reuptake inhibitor (SNRI) [24]. Another SNRI, venlafaxine, was found leading to better sperm morphology, non-progressive motility and viability in mice [25]. However, a recent pharmacovigilance study of drug-reduced male semen quality based on the Food and Drug Administration relevant database reported a risk signal for atomoxetine with an IC_{025} of 2.63 [12]. In the presented case, the impact of atomoxetine in the quality and quantity of the sperm was confirmed with serial sperm analyses and its temporal correlation with medication dose: normal sperm parameters before the introduction of atomoxetine, progressively declining levels as the dose was being optimized and a return to normal values after the discontinuation of the drug. Thus, prescription of atomoxetine for adults should be accompanied by properly counselling patients about the reproductive risks of the medication.

This case report raises awareness among clinicians regarding possible adverse effects on semen quality and quantity in adults exposed to atomoxetine, a medication that was previously considered without adverse fertility effects, and may inform patient counseling. The clinical importance of the report is further strengthened due to the progressive increase of the prevalence of adult ADHD to 2.58-6.76% [26] and the same trend in medicating ADHD, with higher prescribing rates in adult males [27].

The strength of this case report lies in the availability of serial semen analyses obtained independently of the medication and the clear temporal correlation between the exposure and the effect, supporting a plausible association. The main limitation is the absence of a rechallenge that was considered unethical, due to the continuing efforts of the couple to get another child. A further limitation is the absence of hormonal profiling (FSH, LH, testosterone, prolactin) during atomoxetine use, which would have helped elucidate the mechanism of spermatogenic suppression. Finally, one semen analysis (Nov 2025) was performed at a different hospital, which may introduce methodological variability in laboratory techniques and reference standards. However, it also followed the WHO 2021 criteria and a new analysis was performed couple weeks later (Dec 2025) with similar results.

Conclusion

This case raises concern that atomoxetine, apart from the possible sexual dysfunction, may be associated with reversible deterioration in semen parameters in some male adults. Further clinical study is needed before causal conclusions can be drawn. Relevant counseling should be offered to adults when proposing its use for the treatment of ADHD, and specific testing should be performed in cases where the couple is trying to conceive a child.

Ethical Statements

Authors declare no conflict of interest.

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Written informed consent for publication was obtained from the patient, and it is available if requested.

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