Sexual Dysfunction Related to Psychotropic Drugs: A Critical Review Part II: Antipsychotics

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Key words

- antipsychotic drugs
- sexual dysfunction
- sexual side effects
- treatment-emergent sexual dysfunction

Abstract

Sexual dysfunction is a potential side effect of antipsychotic drugs: this article presents a critical review of the current literature. Although many studies have been published on the subject, only some used a validated sexual function rating scale and most lacked either a baseline or placebo control or both. In addition, many of the studies on sexual dysfunction associated with antipsychotic medication are limited by other methodological flaws. However, there is consistent evidence to suggest that a large number of antipsychotic drugs adversely affect one or

more of the 3 phases of sexual response (desire, arousal and orgasm). Among the antipsychotics, the so called "prolactin-raising" are probably most associated with sexual dysfunction, even if further studies to confirm this are needed: the reviewed literature shows no consistent evidence that any one antipsychotic drug has a significantly superior side effect profile over another and current information on this topic is often based on methodologically weak research. Clinicians must be aware of drug-induced sexual dysfunction, since its presence can have important consequences for clinical management and compliance.

Introduction and Methods

This study was conducted using the paper and electronic resources of the library of the Azienda Provinciale per i Servizi Sanitari (APSS) in Trento, Italy (<http://atoz.ebsco.com/Titles/2793>). The library has access to a wide range of databases including (DYNAMED, MEDLINE Full Text, CINAHL Plus Full Text), The Cochrane Library, Micromedex healthcare series, BMJ Clinical Evidence. The full list of available journals can be viewed at <http://atoz.ebsco.com/Titles/2793>, or at the APSS web site (<http://www.apss.tn.it>). In completing this review, a literature search was conducted using the key words "antipsychotic drugs", "psychotropic drugs", "sexual dysfunctions", "sexual side effects", "treatment-emergent sexual dysfunction". All resulting listed articles were reviewed.

Sexual Dysfunction Induced by Antipsychotics

Epidemiology

Increasing evidence indicates that sexual dysfunction is common among patients prescribed

antipsychotic medication: until a few years ago, this problem was largely neglected by research teams [1–4], and sexual side effects induced by antipsychotic medication received only modest attention [5,6].

The reasons for this are several. Firstly, previous research tended to focus mainly on the effects of the underlying disease on the patient's sexuality, describing sexual disorders and behaviour associated with psychotic symptoms [7–9]. Secondly, patients, especially those suffering from schizophrenia, rarely spontaneously report sexual dysfunction [10]. In addition, similar to patients taking antidepressants, patients with psychosis are more likely to report sexual side effects if directly questioned about them. Studies that relied only on spontaneous reporting of side effects, report low rates of sexual dysfunction, while studies using structured interviews or questionnaires show higher rates of sexual dysfunction [3,11,12]. Despite this finding, in clinical practice psychiatrists often continue to underestimate the importance of formally enquiring about sexual dysfunction among their patients. It should be noted that some researchers [13–18] included iatrogenic endocrine disorders (amenorrhea, galactorrhea and gynec-

received 21.10.2012
revised 03.04.2013
accepted 24.04.2013

Bibliography

DOI <http://dx.doi.org/10.1055/s-0033-1347177>
Published online ahead of print:
4 June 2013
Pharmacopsychiatry 2013;
46: 201–208
© Georg Thieme Verlag KG
Stuttgart · New York
ISSN 0176-3679

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Table 1 Classification of sexual dysfunctions in DSM IV TR.

Sexual Desire Disorders	Sexual Arousal Disorders	Orgasmic Disorders	Sexual Pain Disorders	Sexual Dysfunction due to a General Medical Condition	Substance Induced Sexual Dysfunction	Sexual Dysfunction not Otherwise Specified
– hypoactive sexual desire disorder – sexual aversion disorder	– female sexual arousal disorder – male erectile disorder	– female orgasmic disorder – male orgasmic disorder – premature ejaculation	– dyspareunia – vaginismus			

comastia) in their definition of sexual dysfunction which is not in keeping with international classifications (ICD-10, DSM-IV-TR), and which may therefore have affected the data on prevalence rates.

Also, the definition of sexual dysfunction (► **Table 1**) used by some investigators [13,14,16,18] included only “decreased libido” and “impotence/sexual dysfunction”, without considering other areas of sexual dysfunction. Despite this, psychiatrists frequently do not address issues relating to the sexual health of their patients [9,19–23] and they are uncomfortable [24] or reluctant to discuss this subject [3,22] with the result that the prevalence of sexual dysfunction is underestimated [14,23,25–28]. Sexual side effects however, increase the risk of inadequate compliance or discontinuation of drug therapy: in fact, they are one of the most important factors associated with poor compliance with treatment [29–37].

The burden of sexual dysfunction is not only relevant to drug compliance: sexual functioning impacts significantly on quality of life. Sexual dysfunction secondary to the use of antipsychotics can adversely affect quality of life and therefore is an important outcome measure of treatment.

The data on antipsychotic-induced sexual dysfunction tend to show high and variable prevalence rates. Baggaley [30] identified that between 30% and 80% of female schizophrenic patients and between 45% and 80% of male schizophrenic patients reported impaired sexual functioning. Other studies have documented much higher rates: for example those of Macdonald et al. [38] (82% of men and 96% of women) and Fan et al. [39] (between 65% and 94% for both sexes, depending on the different scales used). Other studies have reported lower rates: approximately 58% of men and 33% of women in the study by Ghadirian et al. [40], 59.3% of men and 49.1% of women in the study by Fujii et al. [41] while only 10% (for both sexes) in the research by Knegtering et al. [42].

The variation in prevalence rates is related to several factors, but is mainly due to the different methodological approaches adopted by different studies: studies that relied only on spontaneous reporting of side effects, report low rates of sexual dysfunction, while studies using structured interviews or questionnaires show higher rates of sexual dysfunction [3,11,12]. It should be noted that some researchers [13–18] included iatrogenic endocrine disorders (amenorrhea, galactorea and gynecomastia) in their definition of sexual dysfunction which is not in keeping with international classifications (ICD-10, DSM-IV-TR), and which may therefore have affected the data on prevalence rates. Also, the definition of sexual dysfunction used by some investigators [13,14,16,18] only included “decreased libido” and “impotence/sexual dysfunction”, without considering other areas of sexual dysfunction.

Table 2 Probable mechanisms of action of antipsychotic-induced sexual dysfunction (from Baggaley [30]; Compton [20]; Haddad and Wicak [44]; Knegtering et al. 2003 [3,45]).

Drug effect	Physiological effect	Sexual function effect
dopamine receptor antagonism	inhibition of motivation and reward	decreased desire
dopamine D2 receptor antagonism (tuberoinfundibular pathway)	hyperprolactinemia	decreased desire, impaired arousal, impaired orgasm
histamine receptor antagonism	sedation	impaired arousal
cholinergic receptor antagonism	reduced peripheral vasodilation	erectile dysfunction
α-adrenergic α receptor antagonism	reduced peripheral vasodilation	priapism, decreased erection/lubrication, abnormal ejaculation

Mechanism of action of antipsychotics on sexual function

Antipsychotic drugs exert numerous different actions on cell receptors in the central nervous system (CNS). They can also cause endocrine disturbances by increasing prolactin.

Different hypotheses have been suggested for the mechanism of action of antipsychotics on sexual function (► **Table 2**), including [3,20,23,30,43–47]: (i) dopaminergic antagonist action, (ii) increased prolactin (secondary to dopaminergic antagonist action), (iii) blockage of alpha-adrenergic receptor (anti-adrenergic action), (iv) blockage of acetylcholine receptors (anticholinergic action), (v) serotonin antagonist action, (vi) histamine antagonist action.

Binding to dopaminergic, cholinergic, histaminergic and α-adrenergic receptors may directly affect sexual function by inhibiting motivation and reward, increasing sedation and reducing peripheral vasodilation [3,25,30,44,45].

Sthal [48] suggests that the neurotransmitters involved in the 3 stages (desire, arousal and orgasm) of the human sexual response cycle have different mechanisms of action. For example, in stage 1 (desire), dopamine (DA) exerts a positive influence, while serotonin (5HT) has negative effects. In stage 2, several neurotransmitters facilitate sexual arousal, including norepinephrine (NE), acetylcholine (Ach), and dopamine (DA). As with desire, serotonin has a negative effect. Stage 3 (orgasm), is inhibited by serotonin and facilitated by norepinephrine; dopamine may have weak positive influences.

However, the exact nature of involvement of the various neurotransmitters in antipsychotic induced sexual dysfunction remains unclear.

Differences in receptor-affinity profiles of antipsychotics may help explain the differences in their sexual side-effect profiles [49]. For example, antipsychotics with α-adrenergic antagonis-

tic properties are associated with priapism [50]. Although antipsychotics can induce relatively isolated effects on the neurotransmitters involved in the response cycle, the mechanism of action leading to sexual dysfunction is more complex. Sexual side effects often occur in combination, and pharmacological effects on one component may have an indirect effect on another area of sexual functioning. Furthermore, the etiology of sexual dysfunction may in many cases be multifactorial [2].

Hyperprolactinemia is caused by blockage of dopamine D2 receptors in the hypothalamic infundibular system [51–55]. Dopamine (DA) has an antagonistic effect on the production of prolactin (one of the hormones most implicated in sexual response). Hence, the use of antipsychotics can lead to a decrease in dopamine and a consequent rise in prolactin, which can inhibit sexual function.

Sexual dysfunction is most prevalent in patients with hyperprolactinemia; a correlation between antipsychotic-induced hyperprolactinemia and sexual dysfunction rates has also been documented [2,3,5,20,26,30,44,51,56–61]. This correlation, however, is neither confirmed [15,62–67] nor clear [68,69] in other studies. There have also been reported cases of sexual dysfunction with normal prolactin levels [70,71]: in these cases, the sexual dysfunction was probably associated with other physical (e.g., diabetes) or psychological (e.g., quality of partner relationship) factors.

It is unclear whether sexual dysfunction correlates to a direct effect and/or an indirect effect of hyperprolactinemia. Increased prolactin levels, inhibit the hypothalamic release of GnRH (gonadotropin releasing hormone), a hormone that releases gonadotropins, follicle stimulating hormone (FSH) and luteinizing hormone (FSH) from the anterior pituitary gland. The end result of an increase in prolactin, may therefore consist of a reduction in levels of gonadal hormones (e.g., decreased levels of estrogen in women and testosterone in men) [9,44,72]. During long-term treatment with typical antipsychotics, it is reported that women have significantly more elevated prolactin levels than men [73]. Increased prolactin levels are also more common among women [3,74]. Smith et al. [75], for example, found that after 2 years on antipsychotics medication, 75% of women and 34% of men had high levels of prolactin.

An increase in prolactin is very common among psychotic patients treated with a first generation antipsychotic, but also with risperidone and amisulpride [3,23,59,76,77].

Based on these observations, some authors make the distinction between antipsychotics that elevate prolactin levels (so-called "prolactin-raising") and those that have minimal and/or transient effects on prolactin levels ("prolactin-sparing") (● **Table 3**) [59,72,78,79].

It is worth highlighting that hyperprolactinemia is not always accompanied by clinical symptoms (such as amenorrhea, or gynecomastia) [73].

In addition to direct pharmacological effects (such as, for example, the antagonistic action on dopamine receptors) and endocrine dysfunction, other pharmacological side effects including sedation (mainly related to antihistaminergic action), extrapyramidal effects and weight gain, can indirectly reduce sexual desire [85].

It is difficult to evaluate the effects of antipsychotic drugs on sexual function in patients with schizophrenia because they are often superimposed on sexual impairment caused by the disease itself [25]. In a comparison group study comparing schizophrenic patients on antipsychotic medication with schizophrenic

Table 3 Prolactin and antipsychotics (from Baggaley [30], Maguire [54]; Montejo [59]; Montgomery et al. [84]).

	Prolactin-raising	prolactin-sparing
amisulpride	●	
aripiprazole		⊙
asenapine	?	?
clozapine		⊙
haloperidol	●	
iloperidone	?	?
lurasidone	?	?
olanzapine		⊙
paliperidone	●	
quetiapine		⊙
risperidone	●	
ziprasidone		⊙
other typical antipsychotics	●	

? = limited data available, although some evidence to indicate minimal effect on prolactin levels for asenapine [80,81], iloperidone [82], and lurasidone [83]

patients taking no medication and healthy individuals with no schizophrenia, there was a high rate of sexual dysfunction in both patient groups [86].

Antipsychotics and sexual dysfunction

Antipsychotic-induced side effects on sexual function are usually inhibitory in nature and may affect all phases of the sexual response cycle.

These effects include decreased sexual desire ("libido"), difficulties with erection, achieving orgasm and sexual satisfaction, as well as ejaculation disorders (delayed or inhibited ejaculation, retrograde ejaculation, spontaneous ejaculation in the absence of sexual stimulation, decreased ejaculatory volume) [20,72,85,87,88].

Data from the early literature generally showed that (i) all antipsychotics are associated with decreased sexual desire [89]. (ii) Most antipsychotics are associated with erectile dysfunction. Those most frequently cited in the literature include: chlorpromazine, pimozide, thioridazine, thiotixene and sulpiride [90]. (iii) Thioridazine was probably one of the first antipsychotic drugs identified as having the ability to cause delayed ejaculation [90]. (iv) There are many case reports on antipsychotic-induced anorgasmia: among these, the most frequently cited antipsychotic is thioridazine [89], followed by trifluoperazine [91]. (v) Priapism is a possible side effect of all antipsychotic drugs [92], particularly for phenothiazines (chlorpromazine, fluphenazine and thioridazine), although more recently isolated cases have been reported with aripiprazole [93], clozapine, flupenthixol [89], olanzapine, quetiapine [94,95], risperidone [25] and ziprasidone [95–97].

To date, most of the studies conducted have been observational comparison studies of various typical and atypical antipsychotic drugs. The number of randomized controlled trials that specifically focus on antipsychotic induced sexual dysfunction is small [4].

The interpretation of data relating to the assessment of sexual functioning is complex because of the different assessment tools and study methods adopted in the various studies, making it difficult to compare findings. The conclusions reached by the various researchers as summarized below, are not definitive and they are difficult to interpret and need to be confirmed by further studies [98–100].

In this review we have provided a summary of the main conclusions reached by studies in the current literature, as well as summarizing the most salient information on individual drugs.

Serretti et al. [11], in a recent meta-analysis (which included data on studies investigating sexual dysfunction related to treatment with antipsychotics) showed that quetiapine, ziprasidone, perphenazine and aripiprazole were associated with relatively low rates of sexual dysfunction (16–27%), whereas olanzapine, risperidone, haloperidol, clozapine and thioridazine were associated with higher rates of sexual dysfunction (40–60%).

In the randomized double-blind study by Kelly et al. [101] (with a sample size of only 27 patients) the side effects of fluphenazine, quetiapine and risperidone were compared. Patients experienced high rates of sexual dysfunction with each of these drugs (78% with fluphenazine, 50% with quetiapine, and 42% with risperidone). Symptom improvement, mainly with regards to arousal/erection, was observed during the trial only in those patients treated with quetiapine. The authors concluded that quetiapine has a better side effect profile than the other two drugs. In a randomized open label comparison study by Knegtering et al. [102] (comparing the atypical antipsychotics, risperidone and olanzapine), 46 patients initially taking a typical antipsychotic, were switched to risperidone or olanzapine. Olanzapine was found to cause less sexual dysfunction.

In a study on 199 patients using combined data from an open and combined study, Knegtering et al. [3] concluded that typical antipsychotics and risperidone (considered to be prolactin-raising) are associated with higher rates of sexual dysfunction (decreased libido, problems with orgasm) compared to prolactin-sparing antipsychotics (clozapine, olanzapine, quetiapine and sertindole).

In an observational study by Bobes et al. [103] conducted in Spain on 636 patients, lower rates of sexual dysfunction were found with quetiapine (18%) compared to olanzapine (35%), haloperidol (38%) and risperidone (43%).

In another observational study by Uçok et al. [104] conducted on 827 stable patients, it was reported that over 50% of patients experienced sexual dysfunction. Patients receiving poly-pharmacy experienced more severe side effects than those taking a single second-generation antipsychotic.

In the study by Nakonezny et al. [105] (conducted on a sample of 22 men) a switch from risperidone to quetiapine was not associated with any improvement in sexual function, assessed using a 5 item questionnaire.

Byerly et al. [106] using adjusted average ASEX (Arizona Sexual Experience Scale) rating scale scores, reported less severe sexual dysfunction with quetiapine compared to olanzapine and risperidone: however, these differences, were not clinically significant. Nagaraj et al. [107] also found no statistically significant differences in sexual dysfunction induced by risperidone, olanzapine and quetiapine: in this study, sexual function was measured using the SFQ (Sexual Functioning Questionnaire), which revealed a reduction in overall sexual functioning in 96% of cases for risperidone, 90% for olanzapine and 88% for quetiapine.

Another study by Byerly et al. [108] did not show any statistically significant difference in sexual functioning (as assessed by ASEX) after switching from risperidone to quetiapine.

Dossenbach et al. [31] conducted an observational study on 3838 patients. Sexual problems were common among all patients taking antipsychotic drugs, although there were no sta-

tistically significant differences in prevalence: haloperidol (71%), risperidone (68%), quetiapine (60%), olanzapine (56%).

In an observational study by Strouse et al. [109], conducted over only 12 weeks, comparing risperidone, olanzapine and clozapine, a worsening of sexual performance was reported in men only for each of these 3 drugs.

A study by Bitter et al. [110] showed a mild improvement in sexual function with olanzapine (compared to risperidone), which however was limited to libido.

In a study by Mahmoud et al. [111], it was reported that sexual functioning (as measured by the SR-DISF: Derogatis Interview for Sexual Function) of 42 schizophrenics improved after a switch from typical to atypical antipsychotics (amisulpride, olanzapine, quetiapine and risperidone) in spite of the fact that two of the atypical antipsychotic drugs prescribed (amisulpride and risperidone) are noted for their capacity to induce sexual dysfunction.

Montejo et al. [112] conducted an observational cross-sectional study on a sample of 243 patients with a diagnosis of psychotic disorder and found (using the PRSexDQ-SalSex) that 46% of patients experienced sexual dysfunction, among whom those treated with risperidone and typical antipsychotics had a significantly increased risk of sexual dysfunction. In the **Table 4** we have summarized the effect of individual antipsychotic drugs on sexual dysfunction (SD).

Treatment of sexual dysfunction induced by antipsychotics

Some recommended treatment approaches for the management of sexual dysfunction induced by antipsychotic drugs include the following: (i) A thorough clinical evaluation, to exclude comorbid conditions (physical and psychiatric) or sexual dysfunction secondary to alcohol or illicit drug use or other prescribed medication. The assessment should include measurement of serum prolactin in patients presenting with side effects suggestive of hyperprolactinemia [2, 74]. (ii) Modification of risk factors (where possible, avoid use of other drugs associated with sexual dysfunction, smoking cessation, abstinence from alcohol and illicit drugs, maintaining normal blood sugar levels in diabetic patients, treatment of hypertension and hypercholesterolemia). (iii) In the early phase of treatment, if possible, consider waiting for a spontaneous improvement in side effects [63]. (iv) Reduction in dose of antipsychotic drug responsible for side effects. (v) Switch to another antipsychotic drug with a more tolerable side effect profile (ideally to a "prolactin-sparing" antipsychotic) [59]. (vi) Addition of symptom targeted therapy – using dopaminergic drugs (amantadine, bromocriptine, cabergoline) or drugs with specific effects on sexual functioning (such as phosphodiesterase inhibitors or yohimbine) [1, 2, 5, 23, 72, 140, 141]. In a study by Inder et al., selegiline was not found to alleviate symptoms of antipsychotic-induced sexual dysfunction [142]. Sildenafil may be a useful option in the treatment of antipsychotic-induced sexual dysfunction in men [141]. In general, the evidence supporting the addition of symptomatic therapies is weak [1, 2, 143].

Conclusions

▼ All antipsychotics drugs can cause sexual dysfunction, although it is extremely difficult to accurately determine the true prevalence. This review confirms that antipsychotic-induced sexual

Table 4 Sexual dysfunction (SD) and antipsychotics.

amisulpride	High rates of SD similar to paliperidone, risperidone, quetiapine, clozapine and typical antipsychotics. Amisulpride tends to elevate prolactin levels [113–115].
aripiprazole	Lower SD for aripiprazole as compared with other antipsychotics. Aripiprazole seems to reduce rates of SD in patients previously treated with other antipsychotics [116–118]. Switch from other antipsychotics or add aripiprazole seems to normalize prolactin levels [55, 78, 119–121].
clozapine	High rates of SD but significantly lower as compared with olanzapine, risperidone, and typical antipsychotics [12, 23, 25, 63, 122–125].
haloperidol	High rates of SD, more than 70%. No significant difference in SD compared to risperidone. Haloperidol tends to elevate prolactin levels [14, 31, 63, 103].
olanzapine	Contrasting evidence exists. High SD rates (>50%) similar to haloperidol or other typical antipsychotics reported in some studies [126], but other studies report significantly lower rates [102]. Some studies suggest that olanzapine may be associated with a lower incidence of SD than risperidone, amisulpride, clozapine and quetiapine. [3, 13, 16, 106, 110, 127]. Switching from typical antipsychotics or risperidone to olanzapine may improve sexual functioning in men and women [128]. Olanzapine causes a transient increase in prolactin, which returns to normal after a few weeks in most but not all patients [22, 25].
quetiapine	Prevalence of sexual dysfunction induced by quetiapine varies between 50% and 60%, and is therefore similar or lower to that of risperidone [101, 129] and similar to that of olanzapine [31]. Severity of sexual dysfunction seems to be lower compared to patients taking risperidone, haloperidol or olanzapine [101, 106, 108, 130, 131, 133]. A case of increased libido is reported [132]. Quetiapine is not associated with increased prolactin [25].
risperidone and paliperidone.	Risperidone: high rates (60–70%) of SD similar to those for haloperidol, other typical antipsychotics and clozapine [14, 58, 64, 134]. Significantly higher levels of SD compared to quetiapine and olanzapine [14]. Commonly reported SD included decreased libido, erectile dysfunction, ejaculatory problems, impaired orgasm, menstrual irregularities and decreased vaginal lubrication [3, 14, 22, 101, 103, 135]. Risperidone tends to elevate prolactin levels: some authors have proposed that it is a dose-dependent effect [3, 64, 79, 136], although this is disputed by Konarzewska et al. [65]. These authors also reported markedly higher prolactin levels in patients treated with risperidone compared to those treated with olanzapine. In contrast, in the study by Eberhard et al. [15], the authors argue that high levels of prolactin induced by risperidone, tend to decline over a period of years and that prolactin levels did not correlate significantly with sexual dysfunction. Paliperidone: causes elevated prolactin levels similar to risperidone [137].
ziprasidone	No significant differences in rates of sexual side effects between ziprasidone and olanzapine [126]. Switching from typical and atypical antipsychotics to ziprasidone was related to a significant reduction of SD [138, 139].

dysfunction is common among patients taking antipsychotic medication.

The conclusions reached by the different researchers are not definitive and are difficult to interpret mainly because of the significant differences in methods used for assessing sexual function: further studies are needed on the underlying causes and types of sexual dysfunction, and on the factors linking antipsychotic use and sexual dysfunction, in particular with regard to the specific mechanisms of action including alterations in prolactin levels and binding to dopaminergic, histaminergic, cholinergic, serotonergic and α -adrenergic receptors.

Some evidence suggests that second-generation antipsychotics (with some exceptions, for example, risperidone) seem to have a better sexual side effect profile compared to traditional first generation antipsychotics.

The impact of antipsychotic-induced sexual dysfunction negatively affects quality of life; it has potential implications for patient adherence to medication and the success of antipsychotic treatment. Antipsychotic-induced sexual dysfunction adversely affects compliance, and is one of the factors that must be taken into account when selecting treatment. Further well designed randomized control trials, investigating the effectiveness of different strategies of managing antipsychotic-induced sexual dysfunction are needed [144–146].

Conflict of Interest

▼
The authors declare no conflicts of interest.

References

- Berner MM, Hagen M, Kriston L et al. Management of sexual dysfunction due to antipsychotics drug therapy. *Cochrane Database of Systematic Reviews* 2007; 1–24 doi:10.1002/14651858.CD003546.pub2
- Compton MT, Miller AH. Antipsychotic-induced hyperprolactinemia and sexual dysfunction. *Psychopharmacol Bull* 2002; 36: 143–164

- Knegtering H, Van den Moolen AEGM, Castelein S et al. What are the effects of antipsychotics on sexual dysfunction and endocrine functioning? *Psychoneuroendocrinology* 2003; 28: 109–123
- Labbate LA. Psychotropics and sexual dysfunction: the evidence and treatments. *Adv Psychosom Med* 2008; 29: 107–130
- Gitlin M. Sexual dysfunction with psychotropic drugs. *Expert Opin Pharmacother* 2003; 4: 2259–2269
- Tardieu S, Micallef J, Bonierbale M et al. Sexual behaviour in schizophrenic patients: the impact of antipsychotics. *Encephale* 2006; 32: 697–704
- Akhtar S, Thompson JA Jr. Schizophrenia and sexuality: a review and a report of twelve unusual cases, part I. *J Clin Psychiatry* 1980; 41: 134–142
- Akhtar S, Thompson JA Jr. Schizophrenia and sexuality: a review and a report of twelve unusual cases, part II. *J Clin Psychiatry* 1980; 41: 166–174
- Peuskens J, Sienaert P, De Hert M. Sexual dysfunction: the unspoken side effect of antipsychotics. *Eur Psychiatry* 1998; 13: 23s–30s
- Dervaux A, El Omari F. Sexual dysfunction in schizophrenic patients, the role of antipsychotics. *Presse Med* 2005; 34: 529–532
- Serretti A, Chiesa A. A meta-analysis of sexual dysfunction in psychiatric patients taking antipsychotics. *Int Clin Psychopharmacol* 2011; 26: 130–140
- Serretti A, Chiesa A. Sexual side effects of pharmacological treatment of psychiatric diseases. *Clin Pharmacol Ther* 2011; 89: 142–147
- Brugnoli R, Novick D, Belger M et al. Effectiveness of antipsychotic treatment for schizophrenia: Italian results of the pan-European Schizophrenia Outpatient Health Outcomes (SOHO) study after 12 months. *Giornale Italiano di Psicopatologia* 2006; 12: 283–292
- Dossenbach M, Erol A, el Mahfoud Kessaci M et al. Effectiveness of antipsychotic treatments for schizophrenia: interim 6-month analysis from a prospective observational study (IC-SOHO) comparing olanzapine, quetiapine, risperidone, and haloperidol. *IC-SOHO Study Group. J Clin Psychiatry* 2004; 65: 312–321
- Eberhard J, Lindström E, Holstad M et al. Prolactin level during 5 years of risperidone treatment in patients with psychotic disorders. *Acta Psychiatr Scand* 2007; 115: 268–276
- Haro JM, Salvador-Carulla L. The SOHO (Schizophrenia Outpatient Health Outcome) study. Implications for the treatment of schizophrenia. *CNS Drugs* 2006; 20: 293–301
- Mullen B, Brar JS, Vagnucci AH et al. Frequency of sexual dysfunction in patients with schizophrenia on haloperidol, clozapine, or risperidone. *Schizophr Res* 2001; 48: 155–158

- 18 Treuer T, Anders M, Bitter I et al. Effectiveness and tolerability of schizophrenia treatment in central and eastern Europe: results after 1 year from a prospective, observational study (IC-SOHO). *Int J Psychiatr Clin Pract* 2006; 10: 78–90
- 19 Assalian P, Fraser R, Tempier R et al. Sexuality and quality of life of patients with schizophrenia. *Int J Psychiatr Clin Pract* 2000; 4: 29–33
- 20 Compton MT, Miller AH. Sexual side effects associated with conventional and atypical antipsychotics. *Psychopharmacol Bull* 2001; 35: 89–108
- 21 Higgins A, Barker P, Begley CM. Neuroleptic medication and sexuality: the forgotten aspect of education and care. *J Psychiatr Ment Health Nurs* 2005; 12: 439–446
- 22 Kelly DL, Conley RR. Sexuality and schizophrenia: a review. *Schizophr Bull* 2004; 30: 767–779
- 23 Murthy S, Wylie K. Sexual problems in patients on antipsychotic medication. *Sex Relation Ther* 2007; 22: 97–107
- 24 Lukoff D, Gioia-Hasick D, Sullivan G et al. Sex education and rehabilitation with schizophrenic male outpatients. *Schizophr Bull* 1986; 12: 669–677
- 25 Cutler AJ. Sexual dysfunction and antipsychotics treatment. *Psychoneuroendocrinology* 2003; 28: 69–82
- 26 Dossenbach M, Hodge A, Anders M et al. Prevalence of sexual dysfunction in patients with schizophrenia: international variation and underestimation. *Int J Neuropsychopharmacol* 2005; 8: 195–201
- 27 Fortier P, Mottard JP, Trudel G et al. Study of sexuality-related characteristics in young adults with schizophrenia treated with novel neuroleptics and in a comparison group of young adults. *Schizophr Bull* 2003; 29: 559–572
- 28 Nnaji RN, Friedman T. Sexual dysfunction and schizophrenia: psychiatrist attitudes and training needs. *Psychiatric Bull* 2008; 32: 208–210
- 29 Apantaku-Olajide T, Gibbons P, Higgins A. Drug-induced sexual dysfunction and mental health patients' attitude to psychotropic medications. *Sex Relation Ther* 2011; 26: 145–155
- 30 Baggaley M. Sexual dysfunction in schizophrenia: focus on recent evidence. *Hum Psychopharmacol* 2008; 23: 201–209
- 31 Dossenbach M, Dyachkova Y, Pirildar S et al. Effects of atypical and typical antipsychotic treatments on sexual function in patients with schizophrenia: 12-month results from the Intercontinental Schizophrenia Outpatients Health Outcomes (IC-SOHO) study. *Eur Psychiatry* 2006; 21: 251–258
- 32 Hamer S, Haddad PM. Adverse effects of antipsychotics as outcome measures. *Br J Psychiatry* 2007; 191: s64–s70
- 33 Kelly DL, Conley RR. Evaluating sexual function in patients with treatment-resistant schizophrenia. *Schizophr Res* 2003; 63: 195–196
- 34 Khawaja MY. Sexual dysfunction in male patients taking antipsychotics. *J Ayub Med Coll Abbottabad* 2005; 17: 73–75
- 35 Lambert M, Conus P, Eide P et al. Impact of present and past antipsychotic side effects on attitude toward typical antipsychotic treatment and adherence. *Eur Psychiatry* 2004; 19: 415–422
- 36 Rosenberg KP, Bleiberg KL, Koscis J et al. A survey of sexual side effects among severely mentally ill patients taking psychotropic medications: impact on compliance. *J Sex Marital Ther* 2003; 29: 289–296
- 37 Smith SM, O'Keane V, Murray R. Sexual dysfunction in patients taking conventional antipsychotic medication. *Br J Psychiatry* 2002; 181: 49–55
- 38 Macdonald S, Halliday J, MacEwan T et al. Nithsdale schizophrenia surveys 24: sexual dysfunction. Case-control study. *Br J Psychiatry* 2003; 182: 50–56
- 39 Fan X, Henderson DC, Chiang E et al. Sexual functioning, psychopathology and quality of life in patients with schizophrenia. *Schizophr Res* 2007; 94: 119–127
- 40 Ghadirian AM, Chouinard G, Annable L. Sexual dysfunction and plasma prolactin levels in neuroleptic-treated schizophrenic outpatients. *J Nerv Ment Dis* 1982; 170: 453–467
- 41 Fujii A, Yasui-Furukori N, Sugawara N et al. Sexual dysfunction in Japanese patients with schizophrenia treated with antipsychotics. *Prog Neuropsychopharmacol Biol Psychiatry* 2010; 34: 288–293
- 42 Knegtering H, Blijd C, Boks MPM. Sexual dysfunction and prolactin levels in patients using classical antipsychotics, risperidone or olanzapine. *Schizophr Res* 1999; 36: 355–356
- 43 Haddad PM, Sharma SG. Adverse effects of atypical antipsychotics: differential risk and clinical implications. *CNS Drugs* 2007; 21: 911–936
- 44 Haddad PM, Wieck A. Antipsychotic-induced hyperprolactinaemia. Mechanisms, clinical features and management. *Drugs* 2004; 64: 2291–2314
- 45 Knegtering H. Antipsychotic treatment and sexual functioning, the role of prolactin. University of Groningen; The Netherlands: 2003 Available on line at <http://irs.ub.rug.nl/ppn/254939104>
- 46 Knegtering H, Bruggeman R. What are the effects of antipsychotics on sexual functioning? *Prim Psychiatry* 2007; 14: 51–56
- 47 Westheide J, Cohen S, Bender S et al. Sexual dysfunction in psychiatric inpatients: the role of antipsychotic medication. *Pharmacopsychiatry* 2007; 40: 140–145
- 48 Stahl SM. Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Applications. (third edition). New York: Cambridge University Press; 2008
- 49 Nasrallah HA. Atypical antipsychotic-induced metabolic side effects: insights from receptor-binding profiles. *Mol Psychiatry* 2008; 13: 27–35
- 50 Andersson F, Schmedt N, Weinmann S et al. Priapism associated with antipsychotics: role of alpha1 adrenoceptor affinity. *J Clin Psychopharmacol* 2010; 30: 68–71
- 51 Bhuvaneshwar CG, Baldessarini RJ, Harsh VL et al. Adverse endocrine and metabolic effects of psychotropic drugs. *CNS Drugs* 2009; 23: 1003–1021
- 52 Goodnick PJ, Rodriguez L, Santana O. Antipsychotics: impact on prolactin levels. *Exp Opin Pharm* 2002; 3: 1381–1391
- 53 Madhusoodanan S, Parida S, Jimenez C. Hyperprolactinemia associated with psychotropics. A review. *Hum Psychopharmacol Clin Exp* 2010; 25: 281–297
- 54 Maguire GA. Prolactin elevation with antipsychotic medications: mechanisms of action and clinical consequences. *J Clin Psychiatry* 2002; 63: 56–62
- 55 Potkin SG, Saha AR, Kujawa MJ et al. Aripiprazole, an antipsychotic with a novel mechanism of action, and risperidone vs placebo in patients with schizophrenia and schizoaffective disorder. *Arch Gen Psychiatry* 2003; 60: 681–690
- 56 Conley RR, Kelly DL. Second-generation antipsychotics for schizophrenia: a review of clinical pharmacology and medication-associated side effects. *Isr J Psychiatry Relat Sci* 2005; 42: 51–60
- 57 Hummer M, Huber J. Hyperprolactinaemia and antipsychotic therapy in schizophrenia. *Curr Med Res Opin* 2004; 20: 189–197
- 58 Liu-Seifert H, Kinon BJ, Tennant CJ et al. Sexual dysfunction in patients with schizophrenia treated with conventional antipsychotics or risperidone. *Neuropsychiatr Dis Treat* 2009; 5: 47–54
- 59 Montejo AL. Prolactin awareness: an essential consideration for physical health in schizophrenia. *Eur Neuropsychopharmacol* 2008; 18: S 108–S 114
- 60 Rettenbacher MA, Hofer A, Ebenbichler C et al. Prolactin levels and sexual adverse effects in patients with schizophrenia during antipsychotic treatment. *J Clin Psychopharmacol* 2010; 30: 711–715
- 61 Smith SM. The impact of hyperprolactinaemia on sexual function in patients with psychosis. *J Psychopharmacol* 2008; 22: 63–69
- 62 Howes OD, Wheeler MJ, Pilowsky LS et al. Sexual function and gonadal hormones in patients taking antipsychotic treatment for schizophrenia or schizoaffective disorder. *J Clin Psychiatry* 2007; 68: 361–367
- 63 Hummer M, Kemmler G, Kurz M et al. Sexual disturbances during clozapine and haloperidol treatment for schizophrenia. *Am J Psychiatry* 1999; 156: 631–633
- 64 Kleinberg DL, Davis JM, de Coster R et al. Prolactin levels and adverse events in patients treated with risperidone. *J Clin Psychopharmacol* 1999; 19: 57–61
- 65 Konarzewska B, Wolczyński S, Szulc A et al. Effect of risperidone and olanzapine on reproductive hormones, psychopathology and sexual functioning in male patients with schizophrenia. *Psychoneuroendocrinology* 2009; 34: 129–139
- 66 Johnsen E, Kroken R, Loberg EM et al. Sexual dysfunction and hyperprolactinemia in male psychotic inpatients: a cross-sectional study. *Adv Urol* 2011 article ID 686924
- 67 Yasui-Furukori N, Fujii A, Sugawara N et al. No association between hormonal abnormality and sexual dysfunction in Japanese schizophrenia patients treated with antipsychotics. *Hum Psychopharmacol* 2012; 27: 82–89
- 68 Knegtering H, Van den Bosch R, Castelein S et al. Are sexual side effects of prolactin-raising antipsychotics reducible to serum prolactin? *Psychoneuroendocrinology* 2008; 33: 711–717
- 69 Westheide J, Cvetanovska G, Albrecht C et al. Prolactin, subjective well-being and sexual dysfunction: an open label observational study comparing quetiapine with risperidone. *J Sex Med* 2008; 5: 2816–2826
- 70 Istikoglou C, Vlissides D, Michelidakis K et al. Quality of life: sexual dysfunction in young people with schizophrenia treated with ziprasidone. *Eur Neuropsychopharm* 2009; 19: S511

- 71 Van Bruggen M, Van Amelsvoort T, Wouters L *et al.* Sexual dysfunction and hormonal changes in first episode psychosis patients on olanzapine or risperidone. *Psychoneuroendocrinology* 2009; 34: 989–995
- 72 Dickson RA, Glazer WM. Neuroleptic-induced hyperprolactinemia. *Schizophr Res* 1999; 35: S75–S86
- 73 Wieck A, Haddad M. Antipsychotic-induced hyperprolactinaemia in women: pathophysiology, severity and consequences. Selective literature review. *Br J Psychiatry* 2003; 182: 199–204
- 74 Marder SR, Essock SM, Miller AL *et al.* Physical health monitoring of patients with schizophrenia. *Am J Psychiatry* 2004; 161: 1334–1349
- 75 Smith S, Wheeler MJ, Murray R *et al.* The effects of antipsychotic-induced hyperprolactinaemia on the hypothalamic-pituitary-gonadal axis. *J Clin Psychopharmacol* 2002; 22: 109–114
- 76 American Psychiatric Association. *Practise guidelines for the treatment of patients with schizophrenia*. Second edition. April 2004. Available on line at http://www.psychiatryonline.com/pracGuide/pracGuideTopic_6.aspx
- 77 Conley RR, Mahmoud R. A randomized double-blind study of risperidone and olanzapine in the treatment of schizophrenia or schizoaffective disorder. *Am J Psychiatry* 2001; 158: 765–774
- 78 Chrzanowski WK, Marcus RN, Torbeyns A *et al.* Effectiveness of long-term aripiprazole therapy in patients with acutely relapsing or chronic, stable schizophrenia: a 52-week, open-label comparison with olanzapine. *Psychopharmacology* 2006; 189: 259–266
- 79 Volavka J, Czobor P, Cooper TB *et al.* Prolactin levels in schizophrenia and schizoaffective disorder patients treated with clozapine, olanzapine, risperidone, or haloperidol. *J Clin Psychiatry* 2004; 65: 57–61
- 80 Potkin SG. Asenapine: a critical overview. *J Clin Psychiatry* 2011; 72: 14–18
- 81 Weber J, McCormack PL. Asenapine. *CNS Drugs* 2009; 23: 781–792
- 82 Citrome L. Iloperidone: a critical overview. *J Clin Psychiatry* 2011; 72: 19–23
- 83 Kane L. Lurasidone: a critical overview. *J Clin Psychiatry* 2011; 72: 24–28
- 84 Montgomery J, Winterbottom E, Jessani M *et al.* Prevalence of hyperprolactinemia in schizophrenia: association with typical and atypical antipsychotic treatment. *J Clin Psychiatry* 2004; 65: 1492–1498
- 85 Baldwin D, Mayers A. Sexual side-effects of antidepressant and antipsychotic drug. *Adv Psychiatric Treatment* 2003; 9: 202–210
- 86 Aizenberg D, Zemishlany Z, Dorfman-Etrog P *et al.* Sexual dysfunction in male schizophrenic patients. *J Clin Psychiatry* 1995; 56: 137–141
- 87 Boora K, Chiappone K, Dubovsky S *et al.* Ziprasidone-induced spontaneous orgasm. *J Psychopharmacol* 2010; 24: 947–948
- 88 Freeman SA. Iloperidone-induced retrograde ejaculation. *Int Clin Psychopharmacol* 2013, [Epub ahead of print] doi:10.1097/YIC.0b013e32835e9112
- 89 Orazzo C, Bortolotti F, Monteleone P. Gli psicofarmaci e la funzionalità sessuale nella pratica clinica. Available on line at <http://www.psychiatryonline.it/ital/riviste/quaderni/orazzo.htm> (latest access on 18 february 2013)
- 90 Kotin J, Wilbert DE, Verburg D *et al.* Thioridazine and sexual dysfunction. *Am J Psychiatry* 1976; 133: 82–85
- 91 Degen K. Sexual dysfunction in women using major tranquilizers. *Psychosomatics* 1982; 23: 959–961
- 92 Compton MT, Miller AH. Priapism associated with conventional and atypical antipsychotic medications: a review. *J Clin Psychiatry* 2001; 62: 362–366
- 93 Mago R, Anolik R, Johnson RA *et al.* Recurrent priapism associated with use of aripiprazole. *J Clin Psychiatry* 2006; 67: 1471–1472
- 94 Penaskovic KM, Haq F, Raza S. Priapism during treatment with Olanzapine, Quetiapine, and Risperidone in a patient with schizophrenia: a case report. *Prim Care Companion J Clin Psychiatry* 2010; 12: PCC.09100939 doi:10.4088/PCC.09100939yel
- 95 Torun F, Yilmaz E, Gumus E. Priapism due to a single dose of quetiapine. *Turk Psikiyatri Derg* 2011; 22: 195–199
- 96 Kaufman KR, Stern L, Mohebbati A *et al.* Ziprasidone-induced priapism requiring surgical treatment. *Eur Psychiatry* 2006; 21: 48–50
- 97 Reeves RR, Kimble R. Prolonged erections associated with ziprasidone treatment: a case report. *J Clin Psychiatry* 2003; 64: 97–98
- 98 Malik P. Sexual dysfunction in schizophrenia. *Curr Opin Psychiatry* 2007; 20: 138–142
- 99 Malik P. Sexual dysfunction in schizophrenia. *Focus* 2008; 6: 234–238
- 100 Rico-Villademoros F, Calandre EP. Antipsychotic-induced sexual dysfunction and the strength of the evidence. *J Clin Psychiatry* 2005; 66: 1074–1075
- 101 Kelly DL, Conley RR. A randomized double-blind 12-week study of quetiapine, risperidone or fluphenazine on sexual functioning in people with schizophrenia. *Psychoneuroendocrinology* 2006; 31: 340–346
- 102 Knegtering H, Boks M, Blijd C *et al.* A randomized open-label comparison of the impact of olanzapine versus risperidone on sexual functioning. *J Sex Marital Ther* 2006; 32: 315–326
- 103 Bobes J, Garcia-Portilla MP, Rojas J *et al.* Frequency of sexual dysfunction and other reproductive side-effects in patients with schizophrenia treated with risperidone, olanzapine, quetiapine, or haloperidol: the results of the EIRE Study. *J Sex Marital Ther* 2003; 29: 125–147
- 104 Uçok A, Incensu C, Aker T *et al.* Sexual dysfunction in patients with schizophrenia on antipsychotic medication. *Eur Psychiatry* 2007; 22: 328–333
- 105 Nakonezny PA, Byerly MJ, Rush AJ. The relationship between serum prolactin level and sexual functioning among male outpatients with schizophrenia or schizoaffective disorder: a randomized double-blind trial of risperidone vs. quetiapine. *J Sex Marital Ther* 2007; 33: 203–216
- 106 Byerly MJ, Nakonezny PA, Bettcher BM *et al.* Sexual dysfunction associated with second-generation antipsychotics in outpatients with schizophrenia or schizoaffective disorder: an empirical evaluation of olanzapine, risperidone, and quetiapine. *Schizophr Res* 2006; 86: 244–250
- 107 Nagaraj AK, Pai NB, Rao S. A comparative study of sexual dysfunction involving risperidone, quetiapine, and olanzapine. *Indian J Psychiatry* 2009; 51: 265–271
- 108 Byerly MJ, Nakonezny PA, Rush AJ. Sexual functioning associated with quetiapine switch vs. risperidone continuation in outpatients with schizophrenia or schizoaffective disorder: A randomized double-blind pilot trial. *Psychiatry Res* 2008; 159: 115–120
- 109 Strous RD, Kupchik M, Roitman S *et al.* Comparison between risperidone, olanzapine, and clozapine in the management of chronic schizophrenia: a naturalistic prospective 12-week observational study. *Hum Psychopharmacol* 2006; 21: 235–243
- 110 Bitter I, Basson BR, Dossenbach MR. Antipsychotic treatment and sexual functioning in first-time neuroleptic-treated schizophrenic patients. *Int Clin Psychopharmacol* 2005; 20: 19–21
- 111 Mahmoud A, Hayhurst KP, Drake RJ *et al.* Second generation antipsychotics improve sexual dysfunction in schizophrenia: a randomised controlled trial. *Schizophrenia Research and Treatment* 2011, Article ID 596898 doi:10.1155/2011/596898
- 112 Montejo AL, Majadas S, Rico-Villademoros F *et al.* Frequency of sexual dysfunction in patients with a psychotic disorder receiving antipsychotics. *J Sex Med* 2010; 7: 3404–3413
- 113 Cookson J, Hodgson R, Wildgust HJ. Prolactin, hyperprolactinaemia and antipsychotic treatment: a review and lessons for treatment of early psychosis. *J Psychopharmacol* 2012; 26: 42–51
- 114 Paparrigopoulos T, Liappas J, Tzavellas E. Amisulpride-induced hyperprolactinemia is reversible following discontinuation. *Prog Neuropsychopharmacol Biol Psychiatry* 2007; 31: 92–96
- 115 Raj R, Sidhu BS. Hyperprolactinaemia with amisulpride. *Indian J Psychiatry* 2008; 5: 54–56
- 116 Kerwin R, Millet B, Herman E *et al.* A multicentre, randomized, naturalistic, open-label study between aripiprazole and standard of care in the management of community-treated schizophrenic patients. *Schizophrenia Trial of Aripiprazole: (STAR) study*. *Eur Psychiatry* 2007; 22: 433–443
- 117 Montejo AL, Campos MC, Fombellida C *et al.* Prospective, multicenter, open-label, observational study of sexual function in patients beginning aripiprazole treatment. *Eur Psychiatry* 2008; 23: S133–S134
- 118 Mir A, Shivakumar K, Williamson RJ *et al.* Change in sexual dysfunction with aripiprazole: a switching or add-on study. *J Psychopharmacol* 2008; 22: 244–253
- 119 Casey DE, Carson WH, Saha AR *et al.* Switching patients to aripiprazole from other antipsychotic agents: a multicenter randomized study. *Psychopharmacol* 2003; 166: 391–399
- 120 Lee BH, Kim YK, Park SH. Using aripiprazole to resolve antipsychotic-induced symptomatic hyperprolactinemia: a pilot study. *Prog Neuropsychopharmacol Biol Psychiatry* 2006; 30: 714–717
- 121 Marder SR, McQuade RD, Stock E *et al.* Aripiprazole in the treatment of schizophrenia: safety and tolerability in short-term, placebo-controlled trials. *Schizophr Res* 2003; 61: 123–136
- 122 Aizenberg D, Modai I, Landa A *et al.* Comparison of sexual dysfunction in male schizophrenic patients maintained on treatment with classical antipsychotics versus clozapine. *J Clin Psychiatry* 2001; 62: 541–544

- 123 Deschenes S, Courtois F, Lafond J. Potential side effects of clozapine on the sexual function of schizophrenic man. *J Sex Educ Ther* 2001; 26: 334–339
- 124 Breier AF, Malhotra AK, Su T-P *et al.* Clozapine and risperidone in chronic schizophrenia: effects on symptoms, Parkinsonian side effects, and neuroendocrine response. *Am J Psychiatry* 1999; 156: 294–298
- 125 Yusufi B, Mukherjee S, Flanagan R *et al.* Prevalence and nature of side effects during clozapine maintenance treatment and the relationship with clozapine dose and plasma concentration. *Int Clin Psychopharmacol* 2007; 22: 238–243
- 126 Grootens KP, Van Veelen NM, Peuskens J *et al.* Ziprasidone versus olanzapine in recent-onset schizophrenia and schizoaffective disorder: results of an 8-week double-blind randomized controlled trial. *Schizophr Bull* 2011; 37: 352–361
- 127 Costa AM, de Lima MS, Faria M *et al.* A naturalistic, 9-month follow-up, comparing olanzapine and conventional antipsychotics on sexual function and hormonal profile for males with schizophrenia. *J Psychopharmacol* 2007; 21: 165–170
- 128 Kinon BJ, Ahl J, Liu-Seifert H *et al.* Improvement in hyperprolactinemia and reproductive comorbidities in patients with schizophrenia switched from conventional antipsychotics or risperidone to olanzapine. *Psychoneuroendocrinology* 2006; 31: 577–588
- 129 Knegtering R, Castelein S, Bous H *et al.* A randomized open-label study of the impact of quetiapine versus risperidone on sexual functioning. *J Clin Psychopharmacol* 2004; 24: 56–61
- 130 Atmaca M, Kuloglu M, Tezcan E. A new atypical antipsychotic: quetiapine-induced sexual dysfunctions. *Int J Imp Res* 2005; 17: 201–203
- 131 Byerly MJ, Lescouffair E, Weber MT *et al.* An open-label trial of quetiapine for antipsychotic-induced sexual dysfunction. *J Sex Marital Ther* 2004; 30: 325–332
- 132 Menon A, Williams RH, Watson S. Increased libido associated with quetiapine. *J Psychopharmacol* 2006; 20: 125–127
- 133 Montejo González AL, Rico-Villademoros F, Tafalla M *et al.* A 6-month prospective observational study on the effects of quetiapine on sexual functioning. *J Clin Psychopharmacol* 2005; 25: 533–538
- 134 Wirshing DA, Pierre JM, Marder SR *et al.* Sexual side effects of novel antipsychotic medications. *Schizophr Res* 2002; 56: 25–30
- 135 Peuskens J. Risperidone in the treatment of patients with chronic schizophrenia: a multinational, multicentre, double-blind, parallel-group study versus haloperidol. *Br J Psychiatry* 1995; 166: 712–726
- 136 David SR, Taylor CC, Kinon BJ *et al.* The effects of olanzapine, risperidone, and haloperidol on plasma prolactin levels in patients with schizophrenia. *Clin Ther* 2000; 22: 1085–1096
- 137 Berwaerts J, Cleton A, Rossenu S *et al.* A comparison of serum prolactin concentrations after administration of paliperidone extended-release and risperidone tablets in patients with schizophrenia. *J Psychopharmacol* 2010; 24: 1011–1018
- 138 Montejo AL, Rico-Villademoros F. Changes in sexual function for outpatients with schizophrenia or other psychotic disorders treated with ziprasidone in clinical practice settings: a 3-month prospective, observational study. *J Clin Psychopharmacol* 2008; 28: 568–570
- 139 Rossi A, Vita A, Tiradritti P *et al.* Assessment of clinical and metabolic status, and subjective well-being, in schizophrenic patients switched from typical and atypical antipsychotics to ziprasidone. *Int Clin Psychopharmacol* 2008; 23: 216–222
- 140 Duncan AL, Taylor D. Treatment of psychotropic-induced hyperprolactinaemia. *Psychiatric Bull* 1995; 19: 755–757
- 141 Gopalakrishnan R, Jacob KS, Kuruvilla A *et al.* Sildenafil in the treatment of antipsychotic-induced erectile dysfunction: a randomized, double-blind, placebo-controlled, flexible-dose, two-way crossover trial. *Am J Psychiatry* 2006; 163: 494–499
- 142 Kodesh A, Weizman A, Aizenberg D *et al.* Selegiline in the treatment of sexual dysfunction in schizophrenic patients maintained on neuroleptics: a pilot study. *Clin Neuropharmacol* 2003; 26: 193–195
- 143 Costa AM, Lima MS, Mari Jde J. A systematic review on clinical management of antipsychotic-induced sexual dysfunction in schizophrenia. *Sao Paulo Med J* 2006; 124: 291–297
- 144 Inder WJ, Castle D. Antipsychotic-induced hyperprolactinaemia. *Aust N Z J Psychiatry* 2011; 45: 830–837
- 145 Nunes LV, Moreira HC, Razzouk D *et al.* Strategies for the treatment of antipsychotic-induced sexual dysfunction and/or hyperprolactinemia among patients of the schizophrenia spectrum: a review. *J Sex Marital Ther* 2012; 38: 281–301
- 146 Schmidt HM, Hagen M, Kriston L *et al.* Management of sexual dysfunction due to antipsychotic drug therapy. *Cochrane Database Syst Rev* 2012, doi:10.1002/14651858.CD003546.pub3