Pharmacological treatment of sex offenders

F. Thibaut (MD, PhD) a,e,b

a University Hospital Charles Nicolle, INSERM U 614, Faculty of Medicine, 1, rue de Germont, 76031 Rouen cedex, France
b Department of Psychiatry, CHU Charles-Nicolle, 1, rue de Germont, 76031 Rouen cedex, France

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Summary Sex offending is a major public health concern due to the potentially serious consequences for the victims (especially in case of rape or paedophilia). All care providers agree that imprisonment alone does not solve the question of repeat offences for these subjects and that a combined medical, psychological and social approach is needed for these offenders. A combination of psychotherapy (especially behavioral therapy) with pharmacological treatment is better than one or other therapy used alone. Two types of medication are used for these subjects: serotonergic antidepressants and antiandrogen treatments. Two antiandrogen treatments have obtained Health Agency approval in different European countries in this indication: cyproterone acetate and depot triptorelin (3-month formulation). Guidelines have been published in France by the National Health Authority and, at the international level, by the World Federation of Societies of Biological Psychiatry (www.wfsbp.org). In this paper, we will define the term paraphilia and report some epidemiological data, before summarizing the available literature about the efficacy of pharmacological treatment for paraphilias.

Introduction

Sex offending is a major concern for public health due to its serious consequences on the victims of rape or paedophilia. The prevalence of sex offending can be estimated on the basis of indirect elements such as the percentage of prisoners who are incarcerated for sex offences.

According to the French national prison service, sex offenders represented 14.3% of prisoners in 2010 versus 21.4% in 2006. In 2004, out of the 7956 prisoners charged with sex offences, only 2% were women and 73.5% of the offences were against minors. And yet male sex offenders who have committed sexual offences against children admit on average at least five prior sexual offences for which they were neither arrested nor charged (Elliott et al., 1995).

Several meta-analyses report reoffending rates and highlight the existence of risk factors (Craig et al., 2008; Hanson et al., 2003; Hanson and Morton-Bourgon, 2005). The rate of reoffending is reported to increase from 15% at 5 years to 27% after 20 years of follow-up in the absence of treatment. Paedophiles who are sexually attracted to boys present a higher risk of reoffending (35% at 15 years) compared to those who are exclusively interested in girls (16% at 15 years) or in cases of incest (13% at 5 years) (Harris and Hanson, 2004). A history of sex offences, alcohol or drugs also increases the risk.
A combination of psychotherapy (such as behavioural therapy) and pharmacological treatment is reported to be more effective than one or other of these treatments used alone (Hall and Hall, 2007). Two main types of medication are used to treat paraphilics: serotonergic antidepressants and antiandrogen treatments.

**Efficacy of Selective Serotonin Reuptake Inhibitors (SSRIs)**

SSRIs have shown that they are very useful in treating paraphilics despite the methodology limitations of published studies (Garcia and Thibaut, 2011; Thibaut et al., 2010).

They are mainly used to treat exhibitionists, compulsive masturbators, paedophiles (non-acting) and adolescents presenting paraphilias (Adi et al., 2002; Bradford, 2000; Bradford and Fedoroff, 2006; for review Garcia and Thibaut, 2011; Thibaut et al., 2010).

Amongst the most extensively studied SSRIs are fluoxetine and sertraline. The prescribed doses are progressively increased every four to six weeks according to the results obtained; the doses necessary for satisfactory clinical efficacy are close to the doses used to treat obsessive-compulsive disorders. Controlled studies still need to be conducted to confirm the indications of SSRIs for paraphilias and how they should be prescribed; these molecules are not authorised for this purpose.

**Available antiandrogen treatments**

**Cyproterone acetate (CPA)**

CPA is a synthetic steroid, similar to progesterone. CPA works by inhibiting the binding process of testosterone to receptors. It is authorized for use in more than 20 countries for "reduction of sexual urges in adult males presenting sexual deviations" (Androcur). It is marketed as tablets (50 and 100 mg) (50–200 mg/day) or as a slow-release injection (100 mg/ml) (200–400 mg per week or every other week).

**GnRH analogues (or agonists)**

GnRH analogues (or agonists) initially stimulate the release of LH and result in a temporary flare of serum testosterone levels. After this short period of initial stimulation (about a week), continued administration of GnRH analogues causes fast desensitisation of the GnRH receptors, resulting in a reduction of LH and testosterone within about two to four weeks. Two main GnRH analogues are used for such subjects;

1. Triptorelin (pamoate: 3 mg—1-month formulation, or 11.25 mg—3-month formulation); the 3-month dose has just obtained European authorisation to be used to induce "reversible reduction in testosterone levels down to castration serum levels in the aim of reducing sexual urges in adult males presenting sexual deviations" (triptorelin LA 11.25 mg, Salvacyl);
2. Leuprorelin exists as an intramuscular injection, either daily or as slow-release (3.75 or 7.5 mg—1-month formulation, or 11.25 mg for the 3-month formulation).

**Efficacy of cyproterone acetate**

About 700 men were included in the various studies (Bradford and Pawlak, 1993; Cooper, 1981; Cooper et al., 1992; for review of studies published by Thibaut et al., 2010).

Administration of CPA (50–300 mg/day by mouth or 275–300 mg by intramuscular injection every two weeks) over a period of between four and 12 weeks caused in 80–90% of cases, a significant drop in sexual thoughts and sexual activity reported by the subject, in addition to disappearance of the behaviour of sexual deviation. The efficacy of the treatment, equivalent to the control treatment, or better than the placebo, was continued for the duration of prescription which varied from one study to another with a maximum follow-up of 8 years (Laschet and Laschet, 1975). The effect of the CPA was entirely reversible one to two months after interruption of the treatment. At the end of the follow-up with treatment, the average rate of relapse was 6% compared to 85% before treatment, with a follow-up between two months and 4.5 years. Most of the repeat offences were committed by subjects who did not take the treatment. A significant number of subjects relapsed when the follow-up ended.

There is no good compliance marker for treatment with cyproterone acetate.

**Efficacy of GnRH analogues**

In nearly all studies, CPA (200 mg/day), or sometimes flutamide, were prescribed at the same time as GnRH analogues during the first weeks of treatment.

**Triptorelin**

In all, 72 paraphilic men were included in the various studies (Hansen and Lykke-Olesen, 1997; Rössler and Witztum, 1998; Thibaut et al., 1993, 1996, 1998). In parallel to a fast drop in serum testosterone, the deviant sexual behaviour disappeared with maximum effect after two or three months treatment, with the exception of one case where a threat of repeat sexual deviant behaviour was observed in spite of the treatment. One third (13) cases had previously been treated with CPA without success.

**Leuprorelin**

One hundred and one paraphilic males were treated with leuprorelin (Briken, 2002; Briken et al., 2001; Briken et al., 2004; Krueger and Kaplan, 2001; Schober et al., 2005; Schober et al., 2006). In parallel to a fast drop in serum testosterone, the deviant sexual behaviour and thoughts disappeared, with only one treated patient suffering a relapse and committing a sexual offence.

In an open retrospective study, Czerny et al., 2002 reported that efficacy of GnRH analogues was identical to CPA, with better tolerance to the GnRH analogues.
Duration of treatment

According to the experience of many authors and to international guidelines (Thibaut et al., 2010), it would appear that a minimum duration of 3 years treatment with antiandrogens is necessary in order to establish a relationship of trust with the patient and bring him to accept his paraphilia and the need to undergo hormone treatment. For some patients, a long-term antoandrogen treatment can be necessary.

Conclusion

It is essential to conduct a preliminary detailed assessment of the number and type of paraphilias, in addition to an estimation of the risk factors for repeat offences that might be present, and any response to previous treatment. Any psychiatric comorbidity that might require specific treatment must also be identified beforehand.

The guidelines proposed by the World Federation of Societies of Biological Psychiatry (WFSBP) suggest six levels of treatment according to the severity of the paraphilias (Thibaut et al., 2010). Psychotherapy (preferably cognitive behavioural therapy) is used in all cases although assessment studies on its efficacy remain necessary. In subjects affected by paraphilias with a high risk of relapse or reoffending, medication should be prescribed as a first line treatment, usually antiandrogen GnRH analogues given their efficacy for this indication, their acceptable tolerability providing proper clinical supervision and regular bone scans are provided, and most importantly, their good compliance results thanks to the existence of slow-release formulations by injection every three months.

In more moderate forms such as exhibitionism alone, or in paraphilias observed in adolescents, serotonergic antidepressants have shown themselves to offer satisfactory efficacy, but with only minor side-effects. Long term studies are still necessary in order to provide more information about the indications and long-term tolerance of these treatments.

Disclosure of interest

Expert for Debiopharm.

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