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ROUND THE CORNER

Pharmacological interventions for sex offenders: a poor evidence base to guide practice

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COMMENTARY ON… COCHRANE CORNER[†]

SUMMARY

Although a significant proportion of prisoners and patients in secure hospitals are sex offenders and victim surveys reveal a high level of hidden sexual victimisation, the authors of this Cochrane review found only very limited support for pharmacological intervention with sex offenders. Given the nature and extent of the problem of sexual offending and the promise shown by new drugs, there is a need for clinical scientists, lawyers and ethicists to rise to the challenge of ascertaining the effectiveness and safety of drugs which are being used to treat sex offenders, some involuntarily, without the evidence base to justify confidence as to their effectiveness and safety.

DECLARATION OF INTEREST

None

> 'Not only is it conceivable that a transient placebo effect may follow the use of any preparation, but also one is dealing with sexual offenders in many of whom the main motivation for accepting treatment is their wish to avoid further penalties and in whom the desire to lose the deviant sexual interest is difficult to assess' (Bancroft 1974)

Sexual offending is rarely out of the news. The prosecution of celebrities for historic child sexual abuse makes headlines, as do cases of alleged rape involving young people who have consumed too much alcohol. The effects of sexual offences on victims are less headline-grabbing, but sometimes receive sensitive coverage. Although sexual offending accounts for only a tiny proportion of all crimes committed in England and Wales (Eastman 2012), such figures grossly underestimate the size of a problem, much better quantified, but then only incompletely, by victim surveys; there is a high level of hidden sexual victimisation. Furthermore, sex offenders make up a significant proportion of the prison population and of patients in medium- and high-security hospitals (Taylor 1998; Duggan 2013). So, as Khan *et al*, the authors of this month's Cochrane Corner review, acknowledge, '(s)exual offending is a serious social problem, a public health issue, and a major challenge for social policy' (Khan 2015). The challenge to mental health professionals is two-fold: some perpetrators have mental disorders in the form of sexual preference disorders and paraphilias and many victims develop high levels of psychiatric morbidity.

Given the size of the problem and the extent to which, in some jurisdictions, the courts can order treatment for sexual offenders and treatment can be mandated following civil commitment, there is clearly a need to know which treatments work. This Cochrane review of the effectiveness of pharmacological interventions and a companion review of psychological interventions (Dennis 2012) assist, but this review does not assist very much.

The Cochrane review

The studies reviewed are of the effects of hormonal drugs that suppress libido and of drugs that affect libido through other means (Box 1). These are

BOX 1 Biological treatments of sexual offending

Hormonal drugs that suppress libido

- Progestogens, e.g. ethinyl oestradiol, medroxyprogesterone acetate (MPA)
- Anti-androgens, e.g. cyproterone acetate (CPA)
- Gonadotrophin-releasing hormone (GnRH) analogues, e.g. triptorelin, goserelin

Other medications that affect libido

- Antipsychotics, e.g. benperidol, chlorpromazine
- Selective serotonin re-uptake inhibitors (SSRIs)

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drugs that are administered with the objective of reducing, or completely eradicating, sexual desire and capacity, either temporarily for the purposes of attempting psychological therapy, or permanently. This contrasts with the objective of psychological therapy, which is to alter sexual behaviour without affecting libido, for example changing from non-consensual to consensual sexual activity.

Search method

The reviewers searched for studies up to July 2014 of prospective controlled trials of anti-libidinal medications taken for the purposes of preventing sexual offending where the comparator group received a placebo, no treatment or 'standard care', including psychological treatments. The studies' participants were adults convicted of, or cautioned for, sexual offences, offences with a sexual element or violent behaviour with a sexual element or adults who sought treatment voluntarily for sexual behaviours that would be classified as illegal. They excluded interventions for sexual offenders with intellectual disabilities, as this is the subject of a separate review (Ashman 2008), and they excluded studies concerning abnormal sexual behaviour or sexual disinhibition arising from dementia, as this is to be covered elsewhere. The reviewers excluded studies where there was no clear international consensus that the sexual behaviour was a crime, such as consenting same-sex acts between adults, consenting sado-masochism and transvestism. They included randomised controlled trials (RCTs) with or without masking (blinding) and excluded quasi-randomised trials such as those where allocation was undertaken by surname.

Search results: a small and dated haul

The investigators found only seven small trials, with a total of 123 participants for whom data were available, and the results of all of these were published before 1994. All studies but one were of the effects of testosterone-suppressing drugs, either progestogens or anti-androgens; a small study assessed antipsychotics (benperidol and chlorpromazine). This means that there have been no qualifying studies of the effects of the newer drugs currently in use, particularly selective serotonin reuptake inhibitors (SSRIs) or gonadotrophin-releasing hormone (GnRH) analogues, indeed apparently no RCTs of any pharmacological interventions for over two decades.

Sample sizes varied from 9 to 37. No study included a reference to any power calculation for change within this population. All participants were male. Offences ranged from exhibitionism to rape. The recorded age range was from 16 to 68 years, but the largest study included no data on age. Ethnicity was not reported in any study.

Meta-analysis was not possible for a number of reasons. These included heterogeneity of interventions, the differing length of treatment regimens, carry-over effects in cross-over studies, and placebo violation in that, in one study, the 'placebo phase was not a true placebo phase', differences in outcome measures or drop-out rates and inadequacy of data to calculate effect sizes. The reviewers therefore present their results in narrative form.

The limited evidence

Khan *et al* regarded the results for cyproterone acetate (CPA) as moderately encouraging, with reductions on targets such as physiological arousal, but there was no formal collection of recidivism data and follow-up was for only 13 months.

They found mixed results in studies involving medroxyprogesterone acetate (MPA). They state that there was no reported recidivism in two small studies (Hucker 1988; McConaghy 1988), but in one of these (Hucker 1988) no formal data were reported for sexual recidivism as measured by re-conviction, self-report or caution and its authors do no more than infer that 'no charges were made during the course of the trial'. Understandably, Khan *et al* describe the results of one trial of oral MPA (Langevin 1979) as discouraging, having regard to the high level of drop-out (even though treatment had been mandated by the court), and state that 20% of those who remained for combined drug and psychological treatment recidivated, but by 20% they mean 1 out of the 5 remaining participants.

Although three studies (Bancroft 1974; Cooper 1981; Bradford 1993) found that testosterone-reducing drugs reduced the frequency of self-reported sexual fantasies, in none of these was there a significant effect when objective assessment of sexual arousal was made by measurement of penile tumescence. However, where measured, hormonal levels, particularly testosterone, tended to correlate with measures of sexual activity.

Khan *et al* refer to the effect of drug therapy in reducing sexual recidivism as 'not compelling' and conclude that 'the evidence in support of any pharmacological intervention for those who sexually offend is very limited'. They recognise that this is frustrating for the many practising clinicians who are faced with providing treatment for sexual offenders in their everyday practice. They also recognise the difficulties for clinicians reporting to quasi-judicial bodies such as the Parole Board when there are such uncertainties

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about the evidence base for the treatments with which offenders have been treated and the success of which may influence decisions as to release or further incarceration.

Implications for further research

Although this review may therefore be of little assistance to those responsible for the treatment of sexual offenders, it may be of more assistance to researchers.

New drugs, new outcome measures

What may be regarded as the disappointing results of the research carried out hitherto should not deter further research in this field. Studies of treatment with GnRH analogues such as goserelin and triptorelin were not included in the review, but they are worthy of investigation because they appear to be more effective than CPA and MPA in the long-term reduction of testosterone to castration levels (McEvoy 2017) and because GnRH drugs are reported to be effective in men who are at high risk of sexual offending (Rösler 1998). Studies of SSRI drugs are needed not just because these drugs reduce libido, but because they may have a positive effect on some of the mental disorders prevalent in sexual offenders, for example depressive disorders, substance misuse and personality disorder (Fazal 2006). Briken & Kafka (2007) have reported that sexually impulsive men are more likely to have mood disorders and anxiety disorders as well as substance use disorders, attention-deficit hyperactivity disorder and neuropsychological conditions.

Such studies should therefore include measures of, for example, mood, substance misuse and impulsivity, in order to identify mechanisms by which sexual offending is reduced. Although there have been trials of SSRIs in sexual offenders, there have been no RCTs and the studies have been small.

Homogeneity v. heterogeneity

People convicted of sexual offending are a heterogeneous population. Some of the most obvious distinctions are between paedophiles, exhibitionists and rapists. These, and probably other subgroups, have different aetiologies, different presenting characteristics and different rates of reoffending over different time periods (Prentky 1997; Firestone 2000). Separating the subgroups for studies of the effects of pharmacological interventions is likely to lead to more meaningful results and, in particular, to results that can be applied by those working with different subgroups.

Sample size and length of follow-up

Having regard to the relative infrequency of sexual reoffending, reported in one study to be 13% over 4–5 years' follow-up (Hanson 1998), and the very long persistence of recidivism, especially for paedophilia (Prentky 1997), there has to be a substantial difference between the two trial conditions for an effect to be demonstrated and follow-up needs to extend over many years – at least 5 years – in order to ensure the correct classification as to reoffending. So, sample sizes must be large enough and follow-up long enough. Sufficiently long follow-up is also necessary to assess the side-effects of chronic drug administration for what may be life-long disorders.

Outcome measures

Careful attention must be paid to outcome measures.

Self-reports of sexual arousal, frequency of masturbation and spontaneous erections, sexual preferences and actual sexual offending must be treated with caution in populations with higher than usual propensities for deception and where the participants know that decisions about hospital leave, parole, discharge and release from compulsory treatment may be influenced by such reports. This is illustrated in three of the studies. In the study by Bancroft *et al* (1974), where both ethinyl oestradiol and CPA were found to decrease sexual activity as measured by the number of times that masturbation or 'any overt sexual acts' were reported to lead to orgasm, phallometric data (erectile responses to fantasy, slides and films) did not demonstrate a statistically significant effect for ethinyl oestradiol and only a mild effect for CPA. In the study of antipsychotics (Tennent 1974), chlorpromazine was superior to benperidol in reducing self-reported 'sexual activity', but when arousal to erotic stimuli was measured, no significant differences between the drugs, or placebo, could be detected. Measurement of physiological capacity for sexual arousal should always be included because participants probably know when they have been treated with the active drug and respond by reporting what they regard as improvement.

Reoffending may occur but not be reported or detected.

Outcome measures also need to take into account the findings of research into dynamic risk factors in sexual offending. Thus, diaries or scales of intrusive deviant fantasies should be used to measure sexually anomalous urges or sexual obsessions; psychometric instruments should be used to measure anxiety and anger or aggression

because anxiety and anger may be influenced by drugs that suppress testosterone.

Dropping out of treatment

An important outcome is dropping out of treatment. This is important when considering the potential adverse effects of the drugs being studied, although not many participants were identified as dropping out as a result of actual or possible drug side-effects. In the study by Langevin *et al* (1979), although only two participants reported any side-effects (weight gain and nausea), all five participants in the medication-only (MPA) group discontinued treatment soon after the study commenced, and 12 out of the 17 being treated with a combination of MPA and assertiveness training dropped out before the full course was completed, whereas only 3 of the 12 being treated with assertiveness alone dropped out. In one study (Bradford 1993) two participants dropped out following what was described as an excellent response to CPA. In another study (Hucker 1988) four participants who appeared to have had 'higher frequency of fantasies about children' dropped out.

The need for robust methodology

It should go without saying, but it has to be said because 'each [study] contained several methodological flaws' (Khan 2015), that robust methodology is required. This means careful attention to sequence generation (randomisation), allocation concealment, masking of participants and personnel, incomplete outcome data, selective reporting and other potential sources of bias such as the phenomenon of unwillingness to participate. In cross-over studies the carry-over of effects of the active drug into the placebo phase and rebound increases in testosterone levels on cross-over from active drug to placebo present methodological challenges.

The ethical paradox

Briken *et al* (2017) spent 6 years planning a double-blind RCT of triptorelin in sexual offenders with severe paraphilic disorders who were detained in a German forensic psychiatric hospital, but the Federal Institute for Drugs and Medical Devices rejected the proposal, referring to the German Drug Law, and the Hamburg Medical Association considered that the study would be unethical as the participants were detained patients. The study team observed that this illustrates 'how legal regulations that should protect vulnerable groups in medical research, in a specific case can lead to the fact that a therapy form relevant to the corresponding patient group cannot be scientifically investigated' (Briken 2017).

Paradoxically, a third of sex offenders detained in German forensic psychiatric institutions are being treated with drugs (Turner 2013). Thus, on the one hand Germany allows the treatment of sex offenders with drugs of uncertain effectiveness and little understood profiles of adverse effects, including two officially approved agents, but on the other hand it will not allow the research necessary to assess the effectiveness and the safety of these drugs; the purpose of an RCT is to determine whether the intervention is effective and that it does no harm.

Conclusions

As Khan *et al* themselves observe when noting the absence of good-quality trial evidence to support the use of some promising new drugs, such as SSRIs and GnRH analogues, 'This neglect of an important area of clinical practice requires urgent attention' and, in the meantime, the 'absence of good quality evidence places the practitioner in an unenviable position' and perpetuates 'uncertainty […] with detrimental effects for both perpetrator and victim' (Khan 2015). Clinical scientists, lawyers and ethicists need urgently to unite to face this challenge.

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