



Prevalence of ADHD in prisoners and effectiveness of treatment with atomoxetine

Background

Childhood ADHD is associated with significant morbidity and health service burden and may additionally be associated with undesirable and costly adult outcomes including educational and employment failure, difficulties in interpersonal relationships, poor self-esteem, impulsivity and irritability, drug and alcohol misuse, antisocial behaviour and crime (Hechtman, 1999). Approximately 50% of children with ADHD develop antisocial behaviour that may manifest in childhood as conduct disorder and persist into adulthood as an antisocial personality disorder (ASPD) (Pratt *et al.* 2002; Stan *et al.* 2004). Studies using screening questionnaires have also estimated that up to 50% of adult prisoners have had childhood ADHD, with approximately 10-25% remaining symptomatic (Rasmussen *et al.* 2001; Retz *et al.* 2004; Rösler *et al.* 2004). Symptomatic ADHD has also been associated with an increased frequency of aggressive incidents amongst male prisoners (Young *et al.* 2009).

Yet the prevalence of ADHD and its management within the prison setting has been little investigated (Appelbaum, 2008). To date there has only been a single randomised controlled trial (RCT) of treatment for ADHD in a prison setting. This relatively small Swedish study found that treatment with stimulant medication (methylphenidate) significantly improved symptom severity and functioning amongst male prisoners with ADHD. However, the impact of co-morbidities such as ASPD on treatment response remains unknown. This is important because the UK National Institute for Health & Clinical Excellence (NICE) has recommended stimulant medications as clinically and cost-effective treatments for adults with ADHD (NICE, 2009). This guideline also highlights the importance of the identification and treatment of individuals with ADHD in forensic settings as this may increase the effectiveness of other forensic rehabilitation activities and treatments provided. Furthermore, whilst this guideline recommends the first-line use of stimulant medications such as methylphenidate, it acknowledges that in certain settings such as prison, where there is increased potential for diversion and misuse, the second-line non-stimulant drug atomoxetine should be considered for first-line use.

Aims

The proposed study aims to address two specific gaps in the literature: (i) the accurate determination of the prevalence of ADHD in prisoners using validated diagnostic interviews complemented by collateral information gathering and (ii) the effectiveness of pharmacological intervention with atomoxetine in adult prisoners with an established diagnosis of ADHD.

Design

The research design is an initial 1 year feasibility/pilot study followed by a randomised, double-blind placebo-controlled trial of 40-100mg of atomoxetine/day for 6 months in prisoners with ADHD in custody at a local prison to take place over 1-2 years.

Phase I – Screening

Consecutive adult prisoners between the ages of 18 and 65 received into custody at HMP Lewes over the recruitment period¹ will be screened using the CAARS-Self:SV as part of the general reception health screening programme. Prisoners received directly into the healthcare centre due to acute mental illness will be excluded. Based on reception statistics for the prison, approximately 1,250 prisoners are expected to be received during this period. It is anticipated that at least 10% of those screened (125) will meet the screening threshold for symptomatic ADHD and be eligible to enter Phase II for diagnostic assessment.

Phase II – Eligibility Assessment

Prisoners scoring ≥ 20 on the CAARS will be enrolled to this phase following informed consent. No studies have yet used diagnostic interviews and collateral history to confirm ADHD diagnosis in prisoners. However, the diagnostic sensitivity of the CAARS is estimated to be approximately 80% (Erhardt *et al.* 1999). Hence it is anticipated that approximately 100 prisoners of those screened over the 6 month recruitment period of the feasibility study will meet diagnostic criteria for ADHD. The number of eligible patients consenting to enter Phase III will be used to estimate the recruitment rate for the follow-on RCT.

Phase III – Intervention

This will be a double-blind acute treatment phase. Randomisation will be managed by the Mental Health and Neurology Clinical Trials Unit at King's College London, using an internet accessed system to ensure independence of participant assignment. Participants will be randomised on an individual level using stratified block allocation (of varying block length) and stratified on personality disorder, established using the Structured Clinical Interview for DSM-IV Axis II Disorder (SCID-II).

¹ 6 months for feasibility study, duration to be confirmed for follow-on study

In the pilot study, all patients consenting to participate in the trial will be randomised over the 6 month recruitment period, expected to be a maximum of 100.

Patients will be randomised at Evaluation 2 (week 0) to receive to receive 40-100mg atomoxetine, as tolerated, or placebo, for 26 weeks. Subsequent evaluations will take place at weeks 2, 4, 6, 10, 14, 22, and 26 – Evaluations (E)3-9. After 2 weeks (E3), the dose will be increased to 80mg/day, unless precluded due to tolerability problems and/or adverse events. After 6 weeks (E5), the dose can be increased to 100mg/day depending on continued symptoms and/or tolerability issues.

Phase IV – Follow up

The primary outcome measure (total ADHD symptoms score on the CAARS-Inv:SV) and secondary measures (incidents of self-harm/suicide attempts and aggression/violence) will be assessed at evaluation points over a 6 month follow-up period after randomisation at 2, 4, 6, 10, 14, 22 and 26 weeks (E3-9): The CAARS have been validated for use in forensic settings with the publication of the CAARS For Use in Correctional Settings Supplement (Conners *et al.* 2004).

Statistical Analysis

Data from the initial feasibility/pilot study will be analysed separately as external pilot study using descriptive statistics. Efficacy analyses for the follow on RCT will be conducted on an intention to treat basis. The primary outcome will be analysed through repeated measures mixed model analysis of post baseline values of the CAARS. Treatment differences and change over time will be analysed for the continuous CAARS score. CAARS collected at 7 post baseline time points (2, 4, 6, 10, 14, 22 and 26 weeks) will be analysed within a longitudinal generalised linear model frame adjusting for baseline score, stratification factors and any clinically relevant covariates with contrasts for placebo vs. atomoxetine. This analysis approach will examine the differences between treatment arms and the time course. If responses are correlated, a generalised estimating equation model will be implemented to allow specification of a suitable covariance structure. The same statistical methods will also be applied to other important secondary outcome measures.

Research Team

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