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Introduction

Substitution therapy has been employed, as part of a range of harm reduction activities, in many countries for several years. The process allows addicts regular access to pharmaceutical grade opioid drugs, under medical supervision, to replace street heroin. This has been shown to have a positive effect in reducing crime, lowering rates of infectious diseases – such as hepatitis and HIV – and improving the overall quality of life. Public and political pressures often play a large part in the availability of this form of treatment. In the past, this has restricted some substitution programmes and may do so in the future. However, it has become very clear that substitution therapy not only contributes to harm reduction but is also a valuable treatment for a problem increasingly perceived to be a medical condition.

A three-year pilot programme in Switzerland involving 1146 chronic addicts who received heroin from doctors at certified medical centres and prisons has recently been reported. This showed a substantial decrease in associated crime and an improvement in the addicts' health and quality of life. Recently, the Swiss public voted in a referendum to continue substitution therapy in their country (including the prescription of heroin to patients who had failed on methadone treatment). It would appear that attitudes towards drug misusers can sometimes be surprising.

In France, the attitude towards the treatment of heroin addiction has also recently changed. Originally, the treatment for opioid addiction was rapid detoxification, with or without concurrent treatment for withdrawal symptoms, until a sharp rise in heroin abuse, coupled with an increased HIV incidence, forced a change in policy in the early 1990s. Methadone was introduced as a substitution

agent in 1995 and, in the following year, buprenorphine, a relatively new substitution agent available in a sublingual tablet form, was launched for maintenance treatment of opioid-dependent patients (Subutex®)¹. Several clinical studies had shown that, when used in high doses (≥ 8 mg/day), buprenorphine was effective at reducing the intake of other illicit opioids. It was also effective in reducing opioid withdrawal symptoms. Since then, a number of investigations have been performed on the efficacy and safety of the drug for treating heroin addicts, and comparisons of buprenorphine with other agents have been made.

Although the majority of the published work on buprenorphine has emanated from the US, several studies have been undertaken in France where substitution treatment with Subutex® is licensed. A study of the efficacy of methadone and buprenorphine in Fribourg (Switzerland) has suggested that buprenorphine could be an ideal drug for initial induction in a substitution programme. This allows patients to be grouped according to the severity of their addiction, following which the most appropriate maintenance agent can be chosen. One major advantage of buprenorphine over methadone or heroin results from its μ -partial agonist profile. This means that it can suppress withdrawal symptoms in addicts, but also results in fewer withdrawal symptoms compared with methadone when addicts begin detoxification. This places buprenorphine as a very appropriate maintenance and detoxification agent with safety being a key attribute, particularly in

¹ Trademark registered to Reckitt & Colman; world wide distribution and marketing by Schering-Plough.

terms of respiratory depression. In France, buprenorphine can be prescribed for maintenance treatment by either specialist addiction clinics or General Practitioners (GPs). The GPs, together with pharmacists, are the primary providers of care and the interactions between the GPs, pharmacists and patients are of great interest. To date, comparisons between addicts treated by GPs and those treated at the addiction centres have shown no real differences between the outcomes with equally good efficacy, safety and retention. Other studies in this area have shown an improvement in the relationships between GPs, pharmacists and patients, with all groups expressing a preference for the treatment and relating few adverse effects. Early results from these ongoing assessments have shown the treatment programme with buprenorphine to be very successful.

In addition to its role in substitution and maintenance, trials of buprenorphine in rapid detoxification have also been undertaken. These have shown that the relatively mild withdrawal syndrome associated with buprenorphine reduces the need for additional medication in step-down detoxification programmes.

When treating pregnant addicts, the full agonist effects of methadone or slow-release morphine can cause a more severe neonatal abstinence syndrome than that observed with heroin. The ability to retain pregnant opioid users on maintenance programmes, while protecting the health of the unborn child, is a desirable therapeutic goal. Preliminary trials of buprenorphine in pregnancy have been very encouraging, with the neonates having normal birth-

weights and Apgar scores and, more significantly, little evidence of neonatal abstinence syndrome.

Concerns about diversion of maintenance drugs onto the illegal market, coupled with inadvertent overdose (especially by children of their parent's 'take-home' methadone) is one reason why maintenance therapy has been controversial, putting pressure on the availability of these agents outside of the clinical setting. A clinic-based programme, however, leads to the addict being forced to attend for treatment on a daily basis which fewer addicts are likely to comply with, along with the associated reduction in quality of life and difficulty in reintegrating into the community. To this end, the feasibility of less than daily dosing with buprenorphine has been explored. The long duration of action of the drug, coupled with its inherent safety in high doses, allows for dosing up to every third day without any detectable increase in morbidity or loss of efficacy.

The substitution agent, buprenorphine, appears to offer great potential in the treatment of opioid addiction. Research so far has shown it to be an effective treatment in all aspects of substitution therapy: induction, maintenance and detoxification. With the continuing changes in both political and public attitudes to the treatment of heroin addiction it is hoped that more patients will have the opportunity for take-home medication supplied by specific addiction clinics. In the light of this new evidence, the expansion of buprenorphine treatment for opioid addiction into more countries seems inevitable and is to be welcomed.