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Brief Article

A Retrospective Evaluation of Inpatient Transfer from High-Dose Methadone to Buprenorphine Substitution Therapy

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ABSTRACT

The product license of buprenorphine/naloxone for opioid substitution therapy indicates reducing methadone concentrations to 30 mg or less per day for a minimum of 1 week before transferring patients to buprenorphine and no sooner than 24 hours after the last methadone dose, because of the risk of precipitated withdrawal and a corresponding high risk of relapse to opioid use. There are few studies describing high-dose methadone transfers. This retrospective case review assessed the feasibility of transferring patients on methadone doses above 30 mg/day to buprenorphine or buprenorphine/naloxone in the inpatient setting. Six of seven patients on 60–120 mg/day of methadone successfully completed the transfer, and four cases tested negative for opiates at long-term follow-up (6–15 months). This suggests that methadone transfer to buprenorphine can be performed rapidly without the need to taper methadone doses in patients indicated for a therapeutic switch. This small study is hypothesis-generating; larger, well-designed trials are needed to define a protocol that can be used routinely to improve and widen transfers to buprenorphine when indicated.

1. Introduction

Methadone is the most commonly prescribed opioid substitution treatment (OST) for opioid dependency. The UK National Treatment Agency in 2009 — 2010 reported that 153,632 persons were receiving substitute prescriptions in the UK, the vast majority of which were for methadone (McKeganey, Russell, & Cockayne, 2013). Since methadone's introduction as an OST more than 50 years ago, other treatment options have become available, including buprenorphine as monotherapy and as a combination product with the pure opioid antagonist, naloxone (buprenorphine/naloxone), to discourage misuse. Naltrexone is also available for relapse prevention (Volkow, Frieden, Hyde, & Cha, 2014).

In the United Kingdom, the National Institute for Health and Clinical Excellence (NICE) guidance notes that OST choice should be made on a case-by-case basis, taking into account a risk–benefit analysis that includes the person's history of opioid dependence, commitment to a particular long-term management strategy and consideration of the person's lifestyle and family situation, performed by the responsible clinician in consultation with the patient (National Institute for Health and Care Excellence, 2007). For some patients, buprenorphine is more suitable than methadone for maintenance OST for a number of reasons. Due to its pharmacological profile, buprenorphine reduces the risk of respiratory depression in overdose; has less cardiac effects, in particular QT interval prolongation; can successfully block other opioids from central opioid receptor sites and its slower dissociation from the receptor lends itself to less frequent dosing than methadone if clinically appropriate (Center for Substance Abuse Treatment, 2004). Buprenorphine leads to a reduction in physical dependence and a less severe opiate withdrawal syndrome (Center for Substance Abuse Treatment, 2004). The latter is important for patients wishing to detoxify and cease OST, especially in those patients that have previously found it difficult to reduce and cease methadone. The mental clarity reported by some patients on buprenorphine can be an advantage (Fischer et al., 1999) and it may have other social advantages such as reduced stigma when compared to methadone (Conroy & Hill, 2014). The combination of these factors may facilitate the path to recovery. For others, the motivation to switch to an alternative OST relates to the side effects experienced on methadone, which in some cases are intolerable (Lintzeris et al., 2006).

The product license indicates that the dose of methadone should be reduced to 30 mg or less per day for a minimum of 1 week before transferring patients to buprenorphine and no sooner than 24 hours after the last methadone dose, because of the risk of precipitated withdrawal and a corresponding high risk of relapse to opioid use. Guidelines note that patients on a dose of methadone greater than 30 mg are less likely to tolerate transfer to buprenorphine (Center for Substance Abuse Treatment, 2004; Department of Health (England) & the devolved administrations, 2007). They advise that such a transfer should be undertaken only after consultation with a specialist or experienced prescriber and should be based on clinical judgment and mindful of the patient's subjective and objective findings (Center for Substance Abuse Treatment, 2004).

In terms of identifying patients suitable to switch from higher doses of methadone to buprenorphine, there was insufficient evidence to formulate recommendations (Center for Substance Abuse Treatment, 2004). More recently, successful transition of patients on higher doses of methadone has been reported, with protocols for inpatient and

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outpatient transfer published (Conroy & Hill, 2013; Glasper, Reed, de Wet, Gossop, & Bearn, 2005; Wallace, 2011) and a randomized assessment of split dosing of buprenorphine/naloxone to minimize precipitated withdrawal from methadone 100 mg reported (Rosado, Walsh, Bigelow, & Strain, 2007). Recent Australian National Guidelines for Medication-Assisted Treatment of Opioid Dependence group patients into high risk and low risk for transfer from methadone to buprenorphine and specify methadone doses of more than 60 mg per day as a high-risk factor for poor outcome (Gowing, Ali, Dunlop, Farrell, & Lintzeris, 2014).

In order to determine the feasibility of inpatient transfer from high-dose methadone in patients indicated for a therapeutic switch, a single-centre retrospective case review was conducted with the goal of establishing if patients in the past had been successfully transferred from high-dose methadone and discharged on buprenorphine.

2. Material and methods

2.1. Setting and participants

The Community Addiction Unit (CAU), Cardiff Royal Infirmary, provides maintenance prescribing programs and both community and inpatient drug and alcohol detoxifications as well as managing other medical and mental health issues to adults living within Cardiff and the Eastern Vale of Glamorgan. There are General Practitioner (GP) Shared Care schemes in place for OST, in which patients remain under the care of their GP (including health assessments and prescriptions) but also receive support from the specialist addiction service and are dispensed OST by Community Pharmacists. Patients who wish to transfer from methadone to buprenorphine are assessed and those deemed at high risk of failure, such as polysubstance users, those with a significant psychiatric history, and those on a methadone dose >30 mg, are admitted to our dedicated detoxification unit.

The author performed a retrospective case review of those inpatients under the care of CAU who were admitted between January 2007 and May 2014 who underwent a transfer from methadone to buprenorphine. Patients were included in this case review if they met the following criteria: (1) had been on methadone treatment for at least 6 months; (2) had consented to a transfer from a methadone dose of >30 mg/day to buprenorphine that was approved by the treatment team; (3) the transfer was performed in the inpatient setting.

2.2. Data collection

The medical records of all individuals who met the inclusion criteria were reviewed and the following information when available was recorded in a standardized data abstraction form: gender, date of birth, how long the individual had been in treatment with CAU, duration of methadone and dose history, details of opiate dependency, details on intravenous drug use (IVDU), treatment received pre-transfer, details of other substance misuse, and previous psychiatric history. In addition, the rationale for transferring the individual from methadone to buprenorphine/naloxone was determined, and any further information collected from the patient's medical history recorded as free text. Available results from the urine drug screen (UDS) collected at each clinic visit, which includes cocaine, amphetamine, tetrahydrocannabinol, benzodiazepine, opiates, buprenorphine, and methadone, were recorded.

2.3. Procedures

Patients were asked to consume their last dose of methadone on the day prior to their scheduled admission and liaise with their keyworker, with the intention that they were experiencing some opiate withdrawal on admission to the unit. Patients were assessed by the medical staff, a UDS was performed and they were placed on the 11-item Clinical Opiate Withdrawal Scale (COWS) to measure their withdrawal over time (Wesson & Ling, 2003). Patients were monitored for withdrawal severity and vital signs every 2 hours. Mono-buprenorphine was used at CAU until 2012, when it was replaced by buprenorphine/naloxone. An initial dose of 4 mg buprenorphine was administered when mild/moderate withdrawal was apparent (COWS >10). Additional dosing of buprenorphine was administered as required to reduce withdrawal symptoms, up to a maximum of 24 mg (buprenorphine/naloxone) or 32 mg (buprenorphine) over a 24-hour period. During the transfer, symptomatic medications including lofexidine, ibuprofen, diazepam, butyl scopolamine and temazepam were used as required to overcome withdrawal discomfort.

Typically, the dose of buprenorphine titrated within the first 24 hours is the dose that patients are discharged on. Patients remain on the ward for a variable period, typically 2 or 3 days, but longer in more complex cases. In the period after discharge, patients are screened for drug use/misuse and doses of buprenorphine are recorded. This is performed either by the patient's primary care practice as part of the Shared Care Scheme or the community keyworker at CAU.

2.4. Data analysis

The main outcome was successful transfer from methadone to buprenorphine or buprenorphine/naloxone, defined as receiving a stable dose of OST upon ward discharge. Although not the primary intention of conducting this review, an assessment of treatment retention was made based on the available data. In addition, the relationship between methadone dose and the timing of mild/moderate withdrawal defined as COWS > 10 was assessed using a scatter plot and simple linear regression. Descriptive statistics included percentages, ranges, means and medians.

3. Results

During the review period, seven patients (six male and one female) who presented to the CAU and were admitted for transfer from methadone to buprenorphine fulfilled the criteria for review. The demographics of the patients are shown in Table 1. The mean age at the time of transfer was 35.6 years (range 31 to 42 years). Patients had been receiving methadone for a mean of 50 months (range 13 to 120 months). Before switching to buprenorphine, patients were on methadone doses ranging from 50 to 120 mg per day. COWS scoring >10 commenced between 42 and 76 hours after the last dose of methadone. Patients were admitted to the ward for 1–18 days (median 5 days) (Table 1). Five patients had a past history of IVDU of heroin, including groin use (Table 2). Three patients were opiate positive prior to admission. Patients were transferred to buprenorphine (Subutex®) ($n = 2$) or buprenorphine/naloxone (Suboxone®) ($n = 5$). They were discharged on doses ranging from 4 to 20 mg (Table 3).

Six of seven patients were successful in completing the transfer from methadone to buprenorphine. One patient was unsuccessful (C7). He consumed his last dose of methadone 2 days before admission. He experienced withdrawal the morning after admission and received 4 mg of buprenorphine/naloxone. He became anxious and indicated that he was experiencing severe withdrawal and did not wish to continue with the transfer and discharged himself from the ward. He admitted consuming heroin on the morning of admission. He was recommenced on methadone (25 mg) the next day.

UDS results performed on day of admission (except C2 on day −13 and C3 on day −6) are shown in Table 2. Information was unavailable for C4 due to the patient being managed in primary care (under a shared care scheme). Three patients had a notable psychiatric history (Table 2). C3 had chronic low mood and episodes of deliberate self-harm and had been admitted to a psychiatric ward in 2000. C4 suffered from anxiety, low mood and symptoms of obsessive–compulsive disorder and had also had a crisis house admission in June/July 2011 after expressing thoughts of committing suicide (Table 1).

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