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The Unique Role of Diamorphine in British Medical Practice: A Survey of General Practitioners and Hospital Doctors

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Key Words
Diamorphine (heroin) · Treatment of medical conditions · British system

Abstract
Aims: Diamorphine (heroin) is one of the longest established medications with a 130-year history. In British medicine diamorphine is sometimes used as a maintenance treatment for opiate addiction but is also routinely used in clinical practice to treat a number of general medical conditions. These uses are very different but are often confused by observers of the British system. The routine clinical use of diamorphine in medicine is unique to the UK, but this is not well known outside the UK. The present study investigates the use of diamorphine to treat medical conditions by general practitioners and by hospital doctors. ***Method:*** In a survey of 141 medical practitioners who had prescribed diamorphine for the treatment of a medical condition, data were collected on conditions prescribed for, numbers of patients, dosage, routes of administration, duration of treatment, worries about prescribing diamorphine and observed adverse effects. ***Findings:*** Many doctors had prescribed diamorphine to a large number of patients. The four main conditions for which diamorphine had been prescribed in the previous year were myocardial infarction, palliative care, pulmonary oedema, and post-operative pain. More than half of the sample (57%) reported no reservations about prescribing diamorphine. Of the doctors (n = 60, 43%) who expressed worries, this was most often about possible problems of respiratory depression or respiratory arrest. Respiratory arrest/failure was also the most frequent observed adverse effect. Relatively few doctors reported worries about addiction. ***Conclusions:*** Although diamorphine was widely used and most doctors regarded it as a useful medication, there remains insufficient research information about current clinical practice. At a time when diamorphine may be coming under increased scrutiny, more detailed information is required of its uses and applications.

Introduction

Diamorphine (heroin) is one of the oldest medicines currently still being used in medicine. In recent years it has been the subject of renewed interest in a number of countries [1–3]. Commentators on the use of diamorphine often make reference to the British experiences with prescribing diamorphine. This interest in the 'British sys-

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tem' [4] has most often focused upon the prescribing of diamorphine in opiate addicts. This practice has waxed and waned over the years, and is currently used very infrequently [5]. However, there is another, quite different feature of the British medical experience with diamorphine. This involves the prescribing of diamorphine for general medical conditions. Within the UK, the medical uses of diamorphine are so completely taken for granted that the practice has been the subject of very little research attention and has tended to remain 'invisible'. Outside the UK, the medical uses of diamorphine are regarded as controversial [6], and current British practice is not well known and is sometimes misunderstood.

These two uses of diamorphine (for the treatment of opiate addiction and within general medicine) are completely distinct, though they are often confused by observers of British practice, and this leads to continuing misunderstandings about diamorphine prescribing in the UK. For example, a recent overview of opiate substitution treatment in Europe stated that 'heroin is prescribed by general practitioners and currently there are believed to be about 500 individuals in this kind of substitution treatment in the UK today' [7, p. 478]. This statement is misleading and illustrates the confusion between the uses of diamorphine for the treatment of addiction and for the treatment of medical conditions.

Within the UK, the uses of diamorphine in general medicine are, in many respects, so 'ordinary' that it is seldom realised what a unique phenomenon this is. Diamorphine is unavailable for medical use in most other countries. In many countries it is specifically prohibited. In the USA, for example, its use was completely banned from medical practice through the Narcotic Control Act of 1956 [8]. A recent but unsuccessful attempt was made to reintroduce it into US medicine in the Compassionate Pain Relief Act [9] which was defeated in 1985. Attempts have also been made to prohibit the medical use of diamorphine in the UK. During the 1950s, both Houses of Parliament debated the merits of a complete ban on the prescribing of diamorphine in the UK: in the end, no prohibition was introduced.

Morphine is the main active ingredient of opium, and was isolated in 1803. Diamorphine (heroin) is a semisynthetic derivative of morphine which has similar pharmacological properties but greater potency. Diamorphine was first synthesised at St Mary's Hospital, London, by Charles Alder Wright in 1874 [10]. However, diamorphine was not used as a medicine until after 1898 when it was marketed by the Bayer pharmaceutical company. One of the earliest reports was that in *JAMA* (1906) which recommended its use for the treatment of bronchitis, pneumonia, whooping cough, laryngitis, and hay fever [11]. Other early reports described a wide range of systemic and local indications, in adults as well as children. Among the conditions for which it was used were: angina pectoris, heart failure, aortic aneurysm, dysphagia, cancerous stomach, influenza, multiple sclerosis, gynaecological diseases, inducing labour, and narcosis: it was also prescribed for fever, high blood pressure, and diabetes, and used to treat dementia, depression, and psychosis [12].

The UK situation with regard to the use of diamorphine to treat opiate addiction is quite different. In 1926, the Rolleston Committee stated that diamorphine could be prescribed in Britain to opiate addicts under certain conditions. However, except for a short period after the establishment of the clinic system (1968–1974), diamorphine prescribing to opiate-addicted patients has not been widely used in the UK. By 1992, less than 1% of British opiate addicts receiving maintenance treatment were receiving prescribed heroin compared to about 98% who were receiving prescribed methadone. In UK Department of Health guidelines (1999) [13] this issue was addressed in a single brief paragraph which stated that as a treatment for opiate addiction, 'there is very little clinical indication for prescribed (heroin)' [23, p. 57]. The drug may be prescribed *for this purpose* in the UK only by physicians who have a special Government licence. There are currently about 164 doctors who hold such a licence, and all are specialists in addiction treatment [14].

The increased interest in recent years in prescribing diamorphine as a treatment for opiate addiction has been reflected in the large-scale clinical trials that have been carried out in Switzerland and the Netherlands. The Swiss trial [2] showed reductions in the use of illicit heroin and cocaine, as well as reduced criminal activity among opiate addicts receiving prescribed heroin. In the Dutch trial [15], patients treated with methadone + heroin did better than those treated with methadone alone on most measures of outcome. One interesting feature of the Swiss trial was that there was less demand for this treatment than had been anticipated. In some programmes, not all available places were filled. This may have been due to the requirement for diamorphine to be taken only under medical supervision in a clinic setting.

The present study is concerned with the ways in which diamorphine is used in general medicine in routine clinical practice in Britain to treat general medical conditions. Despite its widespread use for such purposes in British medicine, there is little documented information about

Table 1. Prescribing practices for diamorphine

	Prescribing %	To 10+ patients, %	Typical dose (%)[a]	Typical route (%)	Typical duration of prescribing (%)
Myocardial infarction	64	29	2–5 mg (73)[b]	i.v. (94)	Single dose (73)
Palliative pain	55	16	2–5 mg (33)	s.c. infusion (67)	More than 4 weeks if required (88)
Pulmonary oedema	40	13	2–5 mg (85)	i.v. (96)	Single dose (93)
Post-operative pain	25	11	2–5 mg (73)	i.m. (74)	1 day to 1 week (71)
Cough/lung cancer	1	0	–	–	–
Other	19	6	2–5 mg (43)	s.c. (40), i.v. (33)	Very variable

[a] Typical is defined as the modal (most frequently used) dose, route of administration, and duration of prescribing.
[b] Percentages shown for doses and routes of administration are for prescribing doctors only.

the manner in which the drug is used in day-to-day practice, and the beliefs and worries of medical practitioners about its use under normal clinical conditions. The uses of diamorphine in British medical practice deserve to be more widely known and are likely to be of particular interest to those concerned with the treatment of addiction. This paper reports the uses of diamorphine to treat medical conditions (not opioid addiction) by general practitioners (GPs) and by hospital doctors.

In particular, the study investigates the types of medical conditions, for which the drug is prescribed, the frequency with which it is used, and doses and duration of diamorphine prescribing. The study also investigates worries reported by medical practitioners about the uses of diamorphine, and observed adverse effects associated with the administration of diamorphine.

Methods

Study Population

The study sample comprised 141 medical practitioners who had prescribed diamorphine for the treatment of a medical condition (excluding the treatment of a drug addiction problem) at any time during their medical career. The study sample was recruited at two separate sites. The first was King's College Hospital, London. This is the largest general hospital in south London. It is a major teaching hospital with all major medical and surgical specialities available, and afforded the opportunity to recruit physicians into the study with a wide and varied background and who have experience of working in a number of specialities. The second site was a post-graduate vocational study training programme for primary care physicians in the south of England.

Of the doctors in our sample, 39 (28%) worked as GPs in primary care settings. The remaining 102 (72%) worked in hospitals; 40 (28%) in surgical specialties (including general surgery, vascular surgery, neurosurgery, cardiothoracic surgery, urology, orthopaedics, maxillofacial, and obstetrics and gynaecology), 51 (36%) in medical specialties (including general medicine, cardiology, nephrology, gastroenterology, and paediatrics), and 11 (8%) working as anaesthetists. The sample was not randomly selected. Of the 143 doctors who were approached, only 2 refused to participate (for reasons of lack of time).

Data were collected by means of a self-completion questionnaire constructed for the purposes of this study. The questionnaire collected data on the conditions for which diamorphine was prescribed, numbers of patients, dosage, routes of administration, and duration of treatment. Questions were asked about worries about prescribing diamorphine and observed adverse effects. Ethical approval for this study was granted by the South London and Maudsley Trust.

Results

The doctors in our sample had been in medical practice for between 2 and 38 years (average 10.9 years). The GPs had been in practice for longer than the hospital doctors (21.9 vs. 6.6 years, $t = 13.54$, $p < 0.001$). Among the hospital doctors, 69% were working as Senior House Officers, and 31% were working as Specialist Registrars. As part of their training rotation, 2 of these doctors were working in a hospice.

During their careers, 37% of the doctors (n = 52) had prescribed diamorphine to more than 100 patients; 23% (n = 32) had prescribed to between 51 and 100 patients; 22% (n = 31) had prescribed to 21–50 patients; 8% (n = 11) to 11–20 patients; 9% (n = 13) to between 2 and 10 patients, and 1% (n = 2) had prescribed diamorphine to only 1 patient.

The four main conditions for which diamorphine had been prescribed in the previous year were myocardial infarction, palliative care, pulmonary oedema, and post-operative pain (table 1). The condition for which diamor-

phine was most often prescribed was myocardial infarction (64% of doctors prescribed for this). Myocardial infarction was also the condition for which the greatest number of patients received the drug, with 29% of the doctors reporting having prescribed diamorphine to more than 10 such patients in the previous year. Diamorphine was used for the treatment of other conditions by 19% of the doctors. Other conditions for which diamorphine was used in more than a single case included painful sickle cell crisis (9 cases), sedation in intensive care (2 cases), and treatment of acute pain (2 cases).

Prescribed doses of diamorphine were generally between 2 and 5 mg. The drug tended to be administered by intravenous injection for myocardial infarction and pulmonary oedema, by intramuscular injection for post-operative pain, or by subcutaneous infusion pump for palliative care. Duration of prescribing varied according to the condition being treated. For myocardial infarction and pulmonary oedema, single doses were given. Diamorphine was typically prescribed for between 1 day and 1 week for the treatment of post-operative pain. Longer term prescribing was reported for the treatment of palliative care (table 1).

Most doctors had not prescribed high doses of diamorphine. For more than half (59%) of the doctors in our sample, the highest dose of diamorphine given was $\leq$10 mg or less: 76% had not prescribed more than 20 mg. Some reported having used diamorphine in much higher doses; 16% (n = 21) had given more than 50 mg, and 10% (n = 14) had prescribed doses of more than 100 mg. The conditions for which they had prescribed the highest dose of diamorphine included myocardial infarction (31%), palliative care (27%), post-operative pain control (10%), sickle cell crisis (8%), and pulmonary oedema (7%).

GPs reported having prescribed higher doses of diamorphine than the hospital doctors. Among hospital doctors, only 13% had ever prescribed diamorphine at a dose greater than 20 mg. Among the GPs, 57% reported that they had prescribed 20 mg or more ($\chi^2 = 27.35$, $p < 0.001$). The conditions for which GPs and hospital doctors reported prescribing diamorphine tended to differ. More than half of the GPs (61%) reported having given the highest dose of diamorphine for palliative pain relief in the previous year compared to only 16% of the hospital doctors ($\chi^2 = 24.08$, $p < 0.001$). Diamorphine was used in the highest dose by 22% of GPs in the treatment of myocardial infarction and by 36% of the hospital doctors ($\chi^2 = 7.36$, $p = 0.06$).

More than half of the sample (57%) reported no worries or reservations about prescribing diamorphine. Of the 60 doctors (43%) who expressed worries, 75% (n = 45) were worried about possible problems of respiratory depression/failure or respiratory arrest, and 17% (n = 10) about addiction/dependence. Issues concerning keeping the drug safely or legal controls were not an important worry (2%, n = 1), nor was lack of experience with use of the drug (2%, n = 1).

Worries about the prescribing of diamorphine were more often voiced by hospital doctors than by GPs. More than half of the doctors working in hospital settings (52%) reported at least one worry about the prescribing of diamorphine compared to 18% of the GPs ($\chi^2 = 16.01$, $p < 0.01$). No GPs reported worries about potential addiction problems.

More than half of the sample (51%) reported having observed adverse effects in their own clinical practice. Adverse effects reported by at least 2% of the sample included: respiratory depression/failure (observed by 28% of the sample), nausea and/or vomiting (12%), constipation (11%), itching (7%), respiratory arrest (6%), hypotension (6%), addiction (5%), sedation (4%), drowsiness (4%), and confusion (2%).

There was a statistically significant difference between medical specialties terms of having observed adverse effects. Hospital doctors were more likely to observe adverse effects than GPs ($\chi^2 = 43.38$, $p < 0.001$). Adverse effects were reported by 66% of those working in general medicine, by 63% of those working in surgery, and by 100% of the anaesthetists, but by only 8% of the GPs.

Since respiratory depression/failure was most often reported as an observed adverse effect, a further analysis was conducted to compared differences between doctors working in different medical specialties. GPs were least likely to report having observed respiratory depression after prescribing diamorphine ($\chi^2 = 22.55$, $p < 0.001$). Only 5% of GPs reported having observed this adverse effect compared to 35% of the doctors working in general medicine, and 28% of those working in surgical specialties. All of the anaesthetists reported having observed respiratory depression as an adverse effect.

To determine the extent to which observed adverse effects were related to concerns about prescribing diamorphine, a logistic regression procedure with backward elimination of covariates was used (with concern as the dependent variable) and 10 observed adverse effects as covariates (respiratory depression/failure, respiratory arrest, addiction, confusion, constipation, drowsiness, hypotension, itching, sedation, and nausea/vomiting). Three covariates were retained in the final, statistically significant model ($\chi^2_{[3]} = 14.92$, $p < 0.01$). The observed adverse

effect which was most strongly, and statistically significantly related to concerns about prescribing diamorphine was respiratory depression ($Wald_{[1]} = 7.27$, $p < 0.01$). The effects of the other two covariates, although retained in the final model were not statistically significant as individual variables (respiratory arrest, $Wald_{[1]} = 2.77$, $p = 0.096$, and addiction, $Wald_{[1]} = 3.32$, $p = 0.068$).

Discussion

Diamorphine was reported to have been used for the treatment of a range of medical conditions, but it was most often used for the relief of pain [16, 17]. The specific conditions for which it was most often used included those requiring palliative care, for myocardial infarction, and post-operative pain. Diamorphine was also quite frequently prescribed to patients. Many doctors had prescribed diamorphine to more than 50 patients during their career, and more than one-third had prescribed the drug to more than 100 patients.

The nature of diamorphine prescribing tended, understandably, to differ when used in different circumstances and for the treatment of different conditions. When used to relieve pain associated with myocardial infarction or in the treatment of pulmonary oedema, diamorphine was typically administered in a single intravenous dose of 2–5 mg. This practice is not regarded as, in any way, exceptional. With regard to the treatment of acute myocardial infarction, for example, the *Oxford Textbook of Medicine* recommends that 'The most immediate practical procedure ... is to relieve the patient's pain with an adequate dose of intravenous morphine or diamorphine' [18, p. 2336]. In palliative care, diamorphine is typically administered by subcutaneous infusion, in repeated doses, and over varying periods of time. Most doctors reported their willingness to prescribe diamorphine for periods of more than a month.

Diamorphine is widely used in the treatment of the terminally ill, and diamorphine has been described as having important advantages over morphine when injections are required and especially when high doses are required. When used in palliative care by the parenteral route, diamorphine is preferred to morphine, because it is more soluble and can be given in a smaller volume [19, 20]. It also causes less nausea and hypotension than morphine. Indications for diamorphine prescribing are acute (myocardial infarction) and chronic pain (palliative care, post-operative pain) and acute pulmonary oedema. Choice of diamorphine is primarily determined by severity of pain [21, 22], and not by brevity of prognosis [20]. Parkes [23] found 'severe and mostly continuous pain' among 28% of patients in the terminal phase of cancer. More recently, several authors have expressed concern that palliative care patients often have poorly controlled pain [24, 25]. Subcutaneous delivery of diamorphine, usually in combination with another drug (such as midazolam, levomepromazine or haloperidol) is a common practice within specialist palliative care units throughout the UK.

Diamorphine has been used with patients having total hip replacements [26, 27], and for the treatment of phantom pain after lower limb amputation [28]. In a double-blind study of primigravidae, epidural diamorphine has been found to effective for pain relief in labour [29]. Diamorphine has been used after Caesarean section for analgesia [30], and has been found to be safe in a double-blind study of patients undergoing Caesarean section with pain scores and other adverse effects reduced in a dose-dependent manner by intrathecal diamorphine [31]. It is an indication of the relaxed attitude of British physicians to diamorphine that it is also used with newborn infants and with children. Diamorphine has been used intravenously and subcutaneously as an analgesic with children in accident and emergency units [32], and to treat acute post-operative pain after abdominal surgery [33]. Intravenous infusion of diamorphine has been found to reduce the stress response in ventilated newborn infants [34].

Diamorphine is also used by physicians in primary care. In our survey, the GPs and hospital doctors differed in their attitudes towards, and experiences of prescribing diamorphine. GPs were more likely to have prescribed higher doses of the drug and they were also more likely than the hospital doctors to have prescribed diamorphine for palliative care. Others have also found that GPs tend to express fewer concerns than surgeons and neurologists about potential problems of long-term opiate prescribing [6].

The doctors in our sample did not report unusual levels of concern about the adverse effects or side-effects of diamorphine. Others have also suggested that the use of opiates for the relief of pain may have beneficial effects with fewer problems than have often been assumed [35]. Just over half of our sample reported having observed at least one adverse effect of diamorphine. The most frequent observed adverse effect was respiratory depression. Some adverse effects were relatively minor, such as drowsiness or itching. As with worries about the drug, hospital doctors were more likely than the GPs to report having observed adverse effects. There were further differences between specialities in the likelihood of having observed

adverse effects, with all of the anaesthetists reporting adverse effects, compared to about two-thirds of the hospital doctors working in medical or surgical specialties, but only 1 in 12 of the GPs.

GPs were less likely than other doctors to report having observed respiratory depression after prescribing diamorphine. This is important since having observed respiratory depression was the single factor which was most strongly related to worries about the use of diamorphine. Clearly hospital doctors have greater opportunity to observe the occurrence of adverse drug effects in the hospital setting. All of the anaesthetists reported having observed respiratory depression as an adverse effect of diamorphine. It is possible that the GPs were less likely to report having observed respiratory depression because the clinical circumstances in which they were working did not allow for detailed and prolonged clinical observation, or because they were not present to observe it.

One in 20 of the doctors reported having observed problems of addiction in one or more of the patients to whom they had given diamorphine. Much of the heightened emotion that surrounds the medical uses of diamorphine is probably linked to the view of the drug as the archetypical illegal drug of addiction and as 'one of the most feared... drugs in the world' [36]. It has been suggested that many doctors have an exaggerated fear of inducing addiction in their patients and are reluctant to prescribe effective doses of opiates [20].

It is interesting, therefore, that the majority of the doctors in our sample expressed no special worries or concerns about the medical uses of diamorphine. Among those doctors who reported worries, these focussed upon recognised risks. The most frequently expressed concern identified the risk of respiratory depression or respiratory failure. Relatively few of the doctors (7%) reported worries about the risks of addiction. This is understandable since diamorphine was prescribed only in single doses for many conditions, or was prescribed to patients requiring palliative care and for whom the prescribing was likely to be both time-limited and the risks of physical dependence of secondary importance to the need to relieve intractable pain. Interesting, none of the GPs, who were more likely to use the drug for palliative care, expressed concerns about the risks of addiction. GPs were also less likely than the hospital doctors to express any worries about the use of diamorphine.

In discussing these results, it is necessary to note certain limitations of the study. The sample was not chosen to be representative of doctors in the UK either in terms of age, sex, seniority or speciality, though there is no reason to believe that the sample was specifically biased or necessarily unrepresentative of British doctors. Also, no data were gathered about attitudes and experiences of doctors who did not use diamorphine in their practice. For both of these reasons, caution should be exercised in generalising for the present findings. However, diamorphine is often used by medical practitioners in the UK for a variety of conditions and it should also be noted that the study was not intended to provide evidence regarding the appropriateness or effectiveness of diamorphine treatments. The study does however provide information about the ways in which doctors working within British medicine use diamorphine in their routine clinical practice.

In conclusion, we note that diamorphine has a long (over 100 years) history of use in British medicine. It is widely used and has established itself as a useful medication within routine clinical practice. Indeed, despite its extraordinary reputation outside medicine, it has established itself as an 'ordinary' medication within the pharmacopoeia, with indications and contraindications, which are not greatly different from those of other medications. At different times during its history, diamorphine has attracted special attention, usually because of its associations with drug addiction.

Various attempts have been made over the last century to ban its use in the UK, and it seems probable that further changes may be introduced regarding the control of diamorphine in GP and hospital practice. The NHS National Prescribing Centre [37] has been reviewing the legal and regulatory frameworks concerning the prescribing of control drugs by medical practitioners in England and their report and recommendations should be available in the near future. The Shipman Inquiry recommends tighter rules on controlled drugs [38]. At a time when increasing weight is given to evidence-based decision-making in medicine, the use of diamorphine is medicine remains a topic which is often characterised by unsubstantiated opinion and muddled thinking. The relative scarcity of well-controlled trials of the effectiveness of diamorphine for the treatment of the medical conditions described in this study constitutes an obstacle to our proper understanding of this important issue. The future of diamorphine within medicine is likely to depend upon the accumulation of improved evidence about its applications and effectiveness.

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