
Well, What Can You Do?: "He is a dying man..."

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Abstract

Narcotic abuse is a significant problem in this country. Thanks to government initiatives, a growing number of drug abusers are entering rehabilitation where some are put on methadone maintenance therapy. When these patients seek medical, they may complain of pain and other symptoms that require the use of other opioids. Difficulties may then arise because of the complicated history of some of these patients. This paper describes one such case and aims to present a strong argument for all doctors to learn more about methadone and the patients on it.

THE CASE

B was initially admitted to hospital with an infective exacerbation of chronic obstructive pulmonary disease (COPD). He still smoked and had previously misused opioids. At the time of admission, he was on methadone maintenance therapy.

B's chest radiograph had shown a "suspicious mass" on admission. Further investigations eventually lead to a diagnosis of extensive non-small cell lung cancer. His prognosis was deemed poor. Our only option was to palliate.

B was homeless. Now that he was known to have a terminal condition and would require long-term oxygen therapy, alternate living arrangements were needed. All these took time. B therefore stayed in hospital longer.

Two weeks after his admission, B was observed talking to another patient on the ward about buying benzodiazepines from another inpatient. He was given a verbal warning. No further concerns were noted after that.

Over the next few weeks, B began to complain of breathlessness and chest pain. Dexamethasone had been started soon after cancer was diagnosed. Nebulised bronchodilator and oxygen therapy had continued. Oral morphine sulphate was thus prescribed. His dose requirements however escalated rapidly. Prescribing increasingly larger "prn" and regular slow release doses of morphine that should have supported his calculated daily requirements did not affect this.

This was a difficult situation. On one hand, we could see that

B was clearly distressed each time he asked for more morphine. We knew that his disease was "a real one" and that his condition was terminal. On the other, we were aware that drug dependency had continued to be a problem for him. B never exhibited any signs of overdosing and did appear to be more comfortable each time after he received morphine. He never truly "settled" however.

It was difficult to differentiate between the two possibilities. It was also felt that it would be unkind to try to do so now during his last days – "he is a dying man..." was the general feeling among staff. So, the situation continued.

The social worker eventually found B an apartment. After a package of care was implemented, he was discharged from hospital. Follow up arrangements were also made with the community MacMillan team and methadone clinic.

B was found near collapse the following day due to severe breathlessness at home. He was therefore readmitted. His breathlessness and pain continued to be difficult to control despite a trial of different opioids and other anxiolytics. He was eventually sent to the local hospice.

COULD WE HAVE DONE THINGS "BETTER"?

As always, the retrospectroscope (and a literature review) provides one with 20/20 vision. Therefore, the answer is "yes". It is necessary to revisit the main questions of this case to explain how and why:

What was actually going on - addiction, dependence, tolerance or "real" pain and breathlessness?

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Keeping in mind B also had other "real" physical diseases, what was the likelihood that his somatic complaints were that severe?

If the answer to question 2 is yes, then what (else) should we have done?

WHAT WAS B'S PROBLEM?

As Table 1 demonstrates, physical dependence, tolerance and addiction are separate phenomena but may also co-exist (1). Difficulties arose in this case because B's comorbidities contributed to his symptoms. Pain, breathlessness and anxiety are common complaints of patients with advanced cancer (Table 2) (2). His COPD and smoking would not have helped either.

Figure 1

Table 1: Clarification of terms (,,)

Abuse/addiction: <i>A primary, chronic, neurobiological condition with genetic, psychosocial and environmental factors influencing its development and manifestations. Characterised by psychological abuse and/or dependence with one or more of the following: craving, impaired control, compulsive use, overuse and continued use despite harm.</i>
Misuse; Aberrant, problematic, compulsive or impulsive use of substances: <i>The intentional use of a medication characterised by overuse or use to achieve a desired psychic effect.</i>
Pseudoaddiction <i>An iatrogenic syndrome created by the undertreatment of pain. Problematic behaviours resolve when pain is effectively treated.</i>
Tolerance <i>A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.</i>
Dependence <i>A drug class specific withdrawal syndrome produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or an antagonist.</i>

Figure 2

Table 2: Prevalence of symptoms in cancer patient populations ()

Symptom	Prevalence (per cent)
Pain	50 – 70
Weight loss	45 – 70
General weakness/fatigue	40 – 50
Anorexia	40 – 75
Insomnia	30 – 60
Constipation	25 – 50
Depression	20 – 30
Dyspnoea	20 – 50
Anxiety	10

COULD HIS PAIN AND BREATHLESSNESS REALLY HAVE BEEN THAT SEVERE?

Pain and dyspnoea, either separately or in combination, is known to contribute the most to symptom burden in seriously ill hospitalised patients (3). These would thus be legitimate complaints, especially for a patient with B's comorbidities.

Could B not have obtained adequate analgesia from methadone? It would appear not. Patients on methadone often develop tolerance or resistance to its narcotic, analgesic and tranquilising properties. They therefore feel at least as much pain as any other patient (4).

Others have suggested that these patients may be even more intolerant to pain, compared to certain other drug-free former addicts. This is believed to be a result of a hyperalgesic state induced by chronic opioid administration (5).

B's symptoms were therefore "real" and that severe. He was also still physically dependent on opioids. Before he became sicker, he might have continued to misuse drugs had the opportunity have presented itself. However, as his disease progressed, things probably did change. Pseudoaddiction, worsened by general anxiety, then became the problem.

WHAT COULD WE HAVE DONE BETTER?

WHAT OTHER TREATMENT COULD WE HAVE OFFERED HIM?

Unfortunately not, if the pain is severe enough to require an opioid. The easiest would be to continue the methadone and supplement it with intermittent doses of short-acting

narcotics. Opiate-dependent individuals metabolise narcotic analgesics faster and therefore require increased doses at more frequent intervals (6). (This would explain why B needed more and more morphine at shorter intervals over time.)

If the methadone cannot be continued orally, it can still be administered intramuscularly or subcutaneously. "30 mg is still 30 mg" in any other formulation (6). However, other formulations of methadone are harder to obtain in the general hospital because of Department of Health (8) advice for methadone to only be prescribed as 1mg/1ml mixtures only.

Another way would be to increase the dose of methadone (if oral administration of the drug were still possible). At least three doses would still be required per day and tolerance would still occur after a time (6). However, apart from being an unfamiliar drug to many doctors, methadone can be difficult to titrate and has interactions with other medications (Table 3).

So, another option would be to stop the methadone and add a shorter acting opioid. This might however, hasten the development of drug tolerance and increase the risk of withdrawal (6).

Current consensus suggests a multimodal approach to pain control. The patient's usual methadone dose should be continued with the addition of short-acting opioid, local anaesthesia and other opioid-sparing measures. The latter would include anti-inflammatories, adjuvant analgesia such as ketamine, and paracetamol (9) as well as non-pharmacological techniques.

WHAT ABOUT HIS BREATHLESSNESS?

There are several other treatment options in the palliative setting (Table 4). Nonetheless, opioids remain at the top of the list as well.

WHAT (ELSE) COULD WE HAVE DONE FOR B?

- We could have been more open about our concerns and discussed them directly with B sooner
- Other adjuncts could have been added
- We could have asked for help sooner from other "experts"

Figure 3

Table 3: Methadone (, ,)

<p>What is it? Synthetic opioid Antagonises N-methyl-D-aspartate (NMDA) receptor Inhibits serotonin/noradrenaline reuptake</p> <p>How does it work for treatment of addiction and withdrawal? Heroin and other opioids release an excess of dopamine Methadone occupies the same opioid receptor Thus euphoric rush high and lows as well as cravings are reduced However potential for physical dependency still present</p> <p>Slow onset and long duration of action Relatively low need for dose escalation because of tolerance High inter-patient variability</p> <p>Drug interactions Anti-retroviral agents Cytochrome P450 inducers Avoid Opioid antagonists Mixed agonist/antagonists Partial agonists May cause withdrawal</p> <p>Major hazards Respiratory depression QT interval prolongation, torsades de pointes Systemic hypotension Potential problems related to pregnancy, breastfeeding <i>*fatalities usually related to combined illicit substances</i></p>

Figure 4

Table 4: Treatment of intractable breathlessness in palliative care (, ,)

<p>Non-pharmacological measures:</p> <p><u>Good evidence</u> Using a fan Breeze from open window Exercise Education and information Positioning Pacing Supporting family/other relationships Promoting well-being Rituals for crises End-of-life planning Positive psychology</p> <p><u>Some evidence</u> Music Relaxation therapy Acupuncture</p> <p><u>Less evidence</u> Oxygen</p> <p>Pharmacological measures:</p> <p><u>Good evidence</u> Opioids Corticosteroids Bronchodilators Diuretics</p> <p><u>Some evidence</u> Phenothiazines</p> <p><u>Less evidence</u> Benzodiazepines</p>
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WHY IS THIS CASE IMPORTANT?

This case serves as a reminder that our current training and resources remain inadequate in this area. Thus far this year, 177052 opioid "misusers" have entered treatment in England (15). This figure is expected to rise in the future.

Patients on methadone maintenance therapy often have other health conditions that bring them to seek medical attention. This population may present in any area of healthcare. Some of their complaints then might be related to misuse of substances while others might not.

Quite often however, pain is a related complaint. Acute pain might be due to traumatic injury, infection or cancer.

Chronic pain is also a major problem here. Zero to 40% of chronic pain sufferers may have substance use disorders (4). The reverse also applies. Rosenbaum et al in 2003 (16) found that 24% - 37% of patients on methadone maintenance have chronic pain.

Drug rehabilitation is not routinely included in our medical curriculum. Thus we still struggle in complicated cases, especially since methadone clinics are not directly connected to hospital services. Similar concerns could arise for patients on newer medications such as buprenorphine and lofexidine (17).

Finally, we also need to be more familiar with methadone because palliative care doctors may be using it in the future. Methadone is, after all, fairly cheap and easily manufactured (18). This is already happening across the Atlantic although physicians in the UK remain slower on the uptake (19).

IN SUMMARY

- Patients on methadone maintenance therapy may present in any area of medicine
- When they do, they are at risk of poor symptom relief because of misconceptions on either side
- We need to learn more about methadone and patients on drug rehabilitation therapy

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