

Opioids and Driving – A Review

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Opioid use is prevalent and well established in patients with chronic, as well as cancer pain. It is the most efficacious medication for controlling severe pain and is effective for a broad spectrum of pain conditions. It is increasingly used for long term treatment of non-malignant pain in many countries. A recent study showed that it was used in 20% of patients with neuropathic pain in the United Kingdom.¹ A study surveying the use of opioid in a Danish population also showed an increase of users from 17% to 20% of patients with cancer pain.²

The ability to drive is an important marker in measurement of quality of life. It is an important feature of modern living and features prominently in an independent lifestyle. It is, however, a great responsibility and it involves the safety of passengers, fellow drivers and pedestrians. This is especially so since driving a car is a complex task requiring mental alertness and a variety of cognitive functions, such as perception, attention, learning, memory and decision making.³ There is increasing public concern about driving with prescribed opioids and with its increased usage, the numbers will increase.

There are currently no clear guidelines regarding the use of long-term opioids and driving in the law. Driving under the influence of alcohol (defined as a blood concentration of more than 0.05%) is prohibited in many countries. In Australia, the Austroads 2003 Assessing Fitness to Drive⁴ states that patients who are on analgesics, including codeine and other opioids, should be cautioned about driving if using these medications due to their sedative side effects. Patients on methadone may drive if under periodic review and stable. They should be cautioned about the effects of dosage changes. Austroads 2000 publication "Drugs and Driving in Australia"⁵ mentioned that legislation dealing with drugs and driving should be based on the observable impairment of the driver. How this can be assessed is not clearly defined. The relationship between the concentration of a drug in the body fluids of a driver and the risk of that driver crashing are not well understood. No equivalent to the blood alcohol level exists for other substances. However, it is known that combinations of two or more drugs, or with alcohol, usually have greater effects than a single substance. It also states that the driver's impairment from medications is best addressed by good quality advice from doctors, pharmacists and other health professionals. This advice needs to be consistent and provided in the context of the overall health, medication use and other substance use of each individual. It is essential that the advice provided will allow the individual to assess their own fitness to drive and make an informed decision as to whether driving is advisable while at the same time ensuring they comply with the regimen of medication needed for their continued good health. In view of this, failure to do so may have medico-legal consequences for the practitioner in the event of a crash involving the patient, particularly in the case of commercial vehicle drivers.

The overall health of the driver is an important consideration in the assessment of fitness to drive. It is then logical to assume that a driver, who is in pain, could potentially have impaired ability to drive. This is especially so when several studies have demonstrated the impairment on psychomotor and cognitive performance in relation to matched controls that are not in pain.⁶ But can this be translated to the ability to drive? This has not been studied until recently, when a study tried to examine the possible effects of patient with chronic non-malignant pain on highway driving performance.⁷ The participants performed a standardized on-the-road driving test during normal traffic on a primary highway, using the Standard Deviation of Lateral Position (SDLP) as the primary parameter. The results demonstrate that a subset of chronic non-malignant pain

patients has SDLPs that were higher than the matched healthy controls, indicating worse highway driving performance, which was significantly different. They also rated their subjective driving quality to be normal, although their ratings were significantly lower than those of the healthy controls. Driving related skills such as tracking, divided attention, and memory were examined in the laboratory with no significant effects found. This study had a small sample size and certainly more studies of the relationship between chronic pain and driving ability are needed.

This leads to the argument that if pain is well-controlled, patients should be allowed to drive. However, the pain management of 20% of patients with chronic or cancer pains involve the prescription of opioids. Opioids are centrally-acting drugs that produce analgesia and also a considerable spectrum of unwanted side effects, which may interfere with driving. Central effects include sedation, dizziness or mental clouding. When opioid naïve patients are given single doses of opioids, the reaction time, muscle coordination, attention and short-term memory are impaired, which could affect driving and other skilled activities.⁸ Hence, opioid naïve patients should avoid driving if exposed acutely to a single dose opioid. The issue becomes less clear-cut when it involves chronic or cancer pain patients on long term opioids.

In 2003, the first structured evidence-based review by Fishbain et al⁹ was published. 48 relevant published reports were included and analysed under 5 subject areas. It found that there was moderate, generally consistent evidence for no impairment of psychomotor abilities of opioid maintained patients. There was inconclusive evidence on multiple studies for no impairment on cognitive function of opioid-maintained patients. There was strong consistent evidence on multiple studies for no impairment of psychomotor abilities immediately after being given doses of opioids. There was strong, consistent evidence for no greater incidence in motor-vehicle violations/motor vehicle accidents versus comparable controls of opioid-maintained patients. There was also consistent evidence for no impairment as measured in driving simulators off/on road driving of opioid maintained patients. Based on those results, they concluded that opioids did not appear to impair driving-related skills in opioid dependent/tolerant patients. However, evidence was consistent in only four out of the five research areas, but inconclusive in one. Thus, it was proposed that additional control studies were required.

Is there a difference between patients with cancer and chronic non-malignant cancer patients on stable doses of opioids? This has not been compared directly in a study though studies have been done to evaluate them separately. Jamison et al¹⁰ found that non-cancer patients on stable oral opioids did not show evidence of impaired performance using psychometric testing. Sabatowski et al¹¹ found that stable doses of transdermal fentanyl in non-cancer patients are not associated with significant impairments in psychomotor and cognitive performance. This was compared with healthy volunteers. Schindler et al¹² found that addicts receiving stable doses of methadone performed adequately when compared to normal controls. Byas-Smith et al¹³ compared the psychomotor performance and driving ability of patients with chronic pain managed with stable regimens of opioid analgesics with that of normal healthy volunteers. It involved evaluation for errors while driving their own automobile and for speed and accuracy on trials through an obstacle course. Patients also completed the Test of Variables of Attention and the Digit Symbol Substitution Test. It showed that there were no observed differences among groups. Fishbain et al¹⁴ also found no epidemiological evidence suggesting that people on opioids were at increased risk of being in fatal or non-fatal car accidents.

The above findings probably cannot be applied directly onto cancer patients. Cognitive impairment in cancer patients is not uncommon and can be ascribed to various disease related, as well as treatment-induced causes.¹⁵ The available research focused on driving in cancer patients on opioids is more restricted. Vainio et al¹⁶ found that there were no differences in surrogate tests for driving in cancer patients on stable opioids with pain-free cancer patients not on opioids. Nonverbal basic intelligence, attention, concentration, fluency of motor-reactions, peripheral vision tests, reaction times, thermal discrimination and body sway with open eyes did not differ significantly. Only the balancing ability with closed eyes was worse in the morphine group. Banning et al¹⁷, however, found that reaction times in cancer patients on opioids compared to cancer patients on non-opioid pain medications, were significantly impaired. Clemons et al¹⁸ compared healthy volunteers, cancer patients taking stable opioids and cancer patients not taking opioids. The tests include assessments of alertness, cognition, memory and reaction time. The cancer groups performed worse than the healthy volunteers but were similar to

each other. It illustrated that the disease itself has the greatest impact on alertness. Hence, the evidence to support driving in cancer patients taking opioids is not conclusive. There are many factors involved and further clinical research, though necessary, presents multiple difficulties in interpretation and applicability.¹⁹

A further examination in the literature was done to evaluate if any particular long-acting opioid is safer. Once again the amount of information regarding this is limited. Most studies were conducted on patients taking methadone as reflected in the review article by Fishbain et al.⁹ Sabatowski¹¹ examined the driving ability under long-term treatment with transdermal fentanyl and concluded that stable doses of transdermal fentanyl for the treatment of chronic non-cancer pain are not associated with significant impairments in psychomotor and cognitive performance. Soyka et al.²⁰ found that there was less impairment in some of the subtests of the psychomotor battery in buprenorphine-maintained than in methadone-maintained patients. It may indicate a less severe effect on cognitive-motor performance of a mixed agonist/antagonist opioid compared with a full agonist. However, there were no clear significant differences in most of the items parameters tested. It could be confounded by the small sample size (n=46) and the fact that cannabis or other substances were found in both groups of patients.

When is it safe to drive after commencement of opioid therapy? A prospective clinical and experimental study on six patients before and 7-14 days after stable morphine medication by Lorenz et al.²¹ showed no negative influence on mood, reaction time or vigilance and cognitive decline due to sedation. Further studies need to be done on the other opioids which have different pharmacokinetic and pharmacodynamic effects. This may also have an impact on advice given to patients regarding the length of time, after dosage changes in a background of stable opioid doses, after which it will be 'safe' to drive again.

The situation becomes more complex when concomitant medications are taken. The use of psychoactive drugs is prevalent amongst patients with chronic pain. This includes antidepressants, anticonvulsants and benzodiazepines. The habit of taking additional medications not specified to the pain specialist is also a common phenomenon. It has been recommended that psychoactive drugs under investigation for behavioural toxicity should be compared to alcohol.^{22, 23} This reflects the potential effect on the cognitive and psychomotor functions especially when taken with opioids. Hence, most studies would not recommend driving in patients with concomitant usage of other psychoactive drugs, even if the patient is taking stable doses of opioids.

The majority of published studies demonstrated no significant psychomotor and cognitive impairment of patients under stable long-term opioid therapy for non-malignant pain. Hence there is sufficient evidence that opioid treatment per-se does not preclude patients from driving a motor vehicle. In fact, untreated pain has been shown to affect driving. The underlying disease process, including some patients with cancer, may itself affect the ability to drive. There are some recommendations and 'rules' that are suggested in some publications.^{9, 24} This includes:

1. It is a personal decision which needs to be reviewed constantly and they should not drive if they feel sedated.
2. Stable doses of opioids and no concomitant use of other psychoactive drugs.
3. The physician, and only one prescriber, should have continuous control of the therapy. The patients should not make changes to their medication regimens unilaterally.
4. Written documentation of the advice.

Despite the above information, the physician should not be able to recommend if a patient can drive. The research information available could be quoted and opioid side effects mentioned. The specific question of whether a patient can drive can only be determined in a driving simulator and/or on-road driving tests.

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