Biliary dilatation induced by different opiate drugs: a case series of eight patients

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There is a described association between chronic methadone use and biliary dilatation but this is not widely appreciated and may lead to unnecessary, invasive and costly investigations. It was first described in 2000 in chronic hepatitis C patients who were current or former intravenous drug users on methadone substitution therapy. A 2009 study of 323 patients found that mean common bile duct (CBD) diameter was greater in methadone users compared to non-methadone users, and that methadone users were many times more likely to have biliary dilatation. In 2012, a retrospective cohort study of 618 patients found methadone users with initially normal calibre bile ducts were more likely to develop new biliary dilatation compared to non-methadone users. There does not seem to be a fixed obstructive aetiology behind the association.

Most patients studied in the literature had chronic hepatitis C, as they are often found to have incidental biliary dilatation on routine abdominal ultrasound. There are also a number of studies which have found an association between the recreational use of opium and increased bile duct diameter. This suggests a possible class effect of opiates but an association between biliary dilatation and other opiate drugs (e.g., morphine, oxycodone) has not been reported previously. There are also few data on liver function tests.

We studied eight patients with biliary dilatation who were taking methadone or another opiate drug. We report the effect on liver function tests in greater detail for the first time. We discuss appropriate investigation of newly diagnosed CBD dilatation.

Patients who were taking various opiates and found to have biliary dilatation on ultrasound were identified from gastroenterology outpatient clinics. Apart from taking opiates there was no reason for biliary dilatation. Relevant data were obtained by review of the medical records. Further investigations were performed in selected cases.

Patient data is summarised in Table 1. The mean CBD diameter was 14.4 mm. No patients had relevant symptoms. Six cases were associated with methadone, one with morphine and one with oxycodone. Six patients had both intrahepatic and extrahepatic biliary dilatation while the other two patients had only extrahepatic dilatation.

Five patients were investigated with either magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP), with no obstructive cause identified. The other three patients had ultrasound scans over several years, with unchanged findings. Seven of eight patients had follow-up imaging, with persistent biliary dilatation in all cases.

Seven of eight patients had normal bilirubin and seven of eight had normal alkaline phosphatase (ALP). The two values which were raised were only just above the upper limit of normal. This indicates that the ALP and bilirubin will likely be normal in the majority of these individuals. Other studies on methadone-associated biliary dilatation have not provided much information on liver function tests. Meyer found higher levels of AST (aspartate aminotransferase), ALP and bilirubin in patients on methadone compared to controls, but did not compare liver function tests between those with and without biliary dilatation.

Our study reports an association of biliary dilatation with morphine and oxycodone for the first time. Physiologically, it is most likely that the tonic effect of opiates on the sphincter of Oddi is responsible for bile duct dilatation in these cases. Studies of these patients utilising functional imaging,
such as secretin-MRCP and HIDA (hepato-biliary iminodiacetic acid) scintigraphy, would be useful to further define their physiologic abnormalities.

The effect of opiates is a diagnosis to consider in patients with asymptomatic bile duct dilatation on opiate treatment. This is important because there are now a large number of patients on long-term opiates for management of conditions causing chronic pain as well as those on opiate substitution therapy.

A strategy to investigate people on long-term opiates with asymptomatic bile duct dilatation is outlined. Causes for biliary dilatation, such as choledocholithiasis, malignancy, CBD stricture and choledochal cyst should be excluded. Given that most methadone users found to have biliary dilatation also have chronic hepatitis C, and many have cirrhosis, there is a significant risk of hepatocellular carcinoma. We recommend investigating patients with an ultrasound, plus either an ERCP, MRCP (with or without endoscopic ampullary visualisation) or endoscopic ultrasound (EUS).

In conclusion, a number of different opiate drugs appear to be associated with biliary dilatation when used long-term. This may involve both intrahepatic and extrahepatic dilatation. ALP and bilirubin are likely to be normal. Knowledge of this association may help clinicians alleviate patients’ anxiety and allow more focused investigation, potentially leading to cost savings.

### Competing interests:
Nil.

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