REVIEW

Methadone use and asymptomatic common bile duct dilation: Re-examining the link

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ABSTRACT

Opiates have long been implicated in causing common bile duct (CBD) dilation but few studies have been done to look at the association between synthetic opiates – methadone – and asymptomatic CBD dilation. The mechanism by which methadone could cause CBD dilation is poorly understood, but it has been postulated that increase in biliary pressures from contraction of the sphincter of Oddi is likely. In the below article, we review all the evidence pertaining towards methadone causing common bile duct dilation.

KEYWORDS

Common bile duct dilation, CBD, methadone, opioid, sphincter of Oddi

INTRODUCTION

Asymptomatic common bile duct (CBD) dilation is one of the frequently faced diagnostic dilemmas in this age of enhanced biliary imaging techniques. Although the aetiologies are quite extensive, clinicians primarily worry about looking at obstruction from malignancy or stones/sludge.[1] Despite the advancements with biliary imaging such as CT cholangiography, magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), and endoscopic ultrasound (EUS), regular transabdominal ultrasound is always the initial test of choice with a sensitivity of 99% for detecting CBD dilation; this can be done twice to confirm the CBD dilation.[2]

A finding of CBD dilation on imaging such as ultrasonography together with symptoms will alert a clinician to perform invasive biliary imaging based on the clinical situation. However, no guidelines have been in place for the management of asymptomatic CBD dilation.[1] According to the systematic review, an overall yield for a malignancy or a treatable condition from an invasive workup for patients with asymptomatic CBD dilation is low.[1] Although never quantified objectively, significant healthcare costs are attached to this workup. The purpose of this review is to examine the various studies that looked at the prevalence and the results of the workup for CBD dilation in patients on methadone.

METHODS

For the purpose of this review we searched PubMed (Medline), Embase and Cochrane until the end of October 2017. We searched combining the MESH terms "opiate", "methadone" and "common bile duct". This yielded 29 articles. These articles were individually reviewed by the authors and five articles were retained after considering the inclusion criteria as mentioned below. We also included the abstract published by our group in this review, making it a total of six studies. The inclusion criteria used for selection of these studies included those that have comparison of methadone as a primary or secondary group.

DISCUSSION

Opiate addiction is a rampant issue which is on the rise. In the United States, as of 2015, there have been at least 12.5 million people who misuse opiates, which is not surprising considering the fourfold increase of opiate prescriptions since 1999.[3] Methadone is one of the opiate substitutions used to treat patients with opiate addiction. According to the estimates from 2015, there are at least 1 million patients on methadone maintenance

therapy (MMT) for opiate addiction.[4] Also, there is a high prevalence of opiate addiction and hence methadone clinics in the inner-city population of major cities.[5] Methadone is a synthetic opiate which has a half-life of 14 hours and is not addictive.[6]

Opiates can cause biliary dilation and specifically CBD dilation, an attribute which is used in biliary scintigraphy to better visualise the biliary tract.[7] To date there have been some studies looking at common bile duct dilation with methadone use.[8-12] Although there is some disparity with the results, most of them support the fact that there could be some degree of CBD dilation in certain sets of patients on methadone. The mechanism by which methadone could cause CBD dilation is poorly understood, but it has been postulated that it could increase biliary pressures by constricting the sphincter of Oddi.[13] Despite the availability of these studies, none of them have a definitive conclusion on factors that could also affect the dilation. Recently, a retrospective single-centre observational study was done comparing the size of the common bile duct among methadone and non-methadone users in an inner city population of a major city. This is the largest study to date with 171 patients on MMT and 273 not on MMT.[14] This study included all patients who underwent abdominal ultrasound after excluding acute biliary pathology. It was found that the CBD diameter in patients on MMT is significantly greater than those not on MMT. It is also interesting to note from this study that the CBD size does not correlate with the dose of methadone, demographics or liver biochemical profile.[14]

An early prospective study on 334 hepatitis C infected patients out of which 36 were on methadone revealed that 3/36 (8.3%) patients on MMT had an asymptomatic dilated CBD, defined as size ≥ 9 mm as opposed to 1/298 (0.03%) in the non-MMT group. This only considered patients with hepatitis C and did not evaluate if there was a mean CBD size difference within the two groups.[8] Later, in 2003, a case series was published on six patients who were referred for ERCP due to CBD dilation revealing no endoscopic abnormalities. All these patients were found to be on methadone and the authors concluded that EUS might be a safer first option in such patients.[9]

A large retrospective cross-sectional study in 2009 included patients with either chronic hepatitis B or C, and compared 215 patients on MMT with 108 patients not on MMT. This study concluded that the patients on MMT have a significantly increased CBD diameter (5.87 mm) as compared with the control group (3.79 mm), $p < 0.001$. On multivariate logistic regression, 26.1% of patients on methadone have a CBD diameter of ≥ 8 mm when compared with 2.8% of patients who are not (OR of 17.5). However, interestingly, it is noted that the group of patients on MMT also have significantly higher aspartate transaminase, alkaline phosphatase and total bilirubin while the control group had more patients with cirrhosis.[10]

A study by Leopold et al., investigated a similar question in chronic hepatitis C patients who underwent hepatic ultrasonography as a part their pretreatment screening.[11] Patients were assessed for factors associated with CBD dilation, defined as a CBD diameter of ≥ 7 mm. Initially a univariate regression model was built and the variables whose p-value was less than 0.25 were included in a multivariate analysis. Increasing age by decades, being on MMT at the time of scan and the dose of methadone (categorised as no dose, low dose, intermediate dose and high dose) are found to be statistically significant for increased odds of having CBD dilation. There were no data on biochemical markers due to non-availability which was mentioned as a major limitation.[11]

A more recent retrospective study performed in Boston looked at all patients on MMT who underwent an abdominal CT or MRI after excluding the ones with acute biliary aetiologies.[12] In the same period, a total of 97 patients were included in the analysis and they were matched with controls imaged at the same date range. This study found that there is a statistically significant difference in the diameter of the CBD, intrahepatic bile duct and pancreatic duct between the two groups with patients on MMT being on the higher side.

CONCLUSION

In conclusion, it is not uncommon to find a dilated asymptomatic common bile duct in patients with chronic opioid use. Despite the search to find aetiology most of the cases rarely point to any structural aetiologies except opiate use. However, evidence is lacking on whether we can safely ignore these findings without performing any further investigations. Prospective control studies need to be performed before ascertaining for a fact that the dilation of the common bile duct in all chronic narcotic users is benign and warrants no further investigations.

DISCLOSURES

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