Liver Injury Is Common Among Chronic Abusers of Ketamine

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Abuse of ketamine leads to liver injury. We investigated the histopathologic and radiologic features of ketamine abusers with significant liver injury in a cross-sectional survey of 297 consecutive chronic abusers of ketamine with urinary tract dysfunction. Liver biopsy and magnetic resonance cholangiopancreatography were performed in patients with liver injury (concentrations of bilirubin, alkaline phosphatase, and/or alanine aminotransferase >2-fold the upper limit of normal). The prevalence of liver injury was 9.8% (all cases cholestatic). Bile duct injury was observed in all 7 patients assessed by liver biopsy. Two patients had bridging fibrosis despite their young age. Three of 6 patients who underwent magnetic resonance cholangiopancreatography examination were found to have prominent or dilated common bile ducts without obstructions or extrinsic compressions. Ketamine abuse therefore appears to lead to common bile duct dilatation, microscopic bile duct injury, and even significant liver fibrosis.

Keywords: Drug Abuse; Liver Damage; Hepatobiliary Disease; Clinical Report.

Recreational usage of ketamine among young adults is a rising health problem in Southeast Asian regions including Hong Kong and Singapore.[1,2] Several case reports and series reported liver fibrosis, bile duct injury,[2–5] and sclerosing cholangitis–like hepatobiliary disease[6] in chronic ketamine abusers. Here we report a large cohort of chronic ketamine abusers who had comprehensive clinical assessments at the time of referral.

Methods

Study Population

This was a cross-sectional study of consecutive chronic ketamine abusers presenting with ketamine-associated urinary tract dysfunction to the Youth Urological Treatment Centre, Prince of Wales Hospital, Hong Kong from December 2011 to March 2013. All patients were current ketamine abusers or ex-chronic abusers who were symptomatic for urinary tract dysfunction at the time of assessment. All the subjects were evaluated by using a standard protocol at baseline.

Evaluation

At the first visit, a full medical history and blood tests were obtained. Patients were defined to suffer from liver injury manifested when they had raised parameters above 2 times the upper limit of normal in the liver biochemistry panel.[7] The type of liver injury was classified according to the pattern of serum enzymes.[8,9] All the cases were evaluated by the Roussel Uclaf Causality Assessment Method.[10] Patients found to have abnormal liver biochemistry would have further assessment including blood tests for hepatitis B surface antigen, antibody to hepatitis C virus, and autoimmune markers and trans-abdominal ultrasonography. Liver histology was assessed by pathologists specialized in liver diseases (P.C.L.C., A.W.H.C.).[11] Magnetic resonance cholangiopancreatography (MRCP) was performed with a standard protocol, with acquisition aligned to the common bile duct (CBD) in the head of the pancreas.[12]

Results

Patients

Two hundred ninety-seven subjects with baseline assessments were included for analysis. The mean age was 25 ± 4 years, and 157 patients (53%) were female; all subjects abused ketamine by nasal insufflation. One hundred ninety (64%) were current abusers, and the remaining 107 patients were ex-abusers. Among the 149 patients (50%) who consumed alcohol; cocaine (41%), crystal methamphetamine, (9%) and Ecstasy (7%) were

Abbreviations used in this paper: CBD, common bile duct; MRCP, magnetic resonance cholangiopancreatography.

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other substances commonly abused in these subjects (Supplementary Table 1). Common liver diseases (eg, viral hepatitis, alcoholic and autoimmune liver diseases) were excluded.

Female gender (adjusted odds ratio, 3.0; 95% confidence interval, 1.2–7.3; $P = .02$) was an independent risk factor of liver injury in multivariable analysis. Duration and amount of ketamine abuse were not associated with liver injury. On the other hand, female gender, serum C-reactive protein level, and current abuser were the independent risk factors of abnormal liver biochemistry (Supplementary Table 2).

Histopathologic Features and Liver Stiffness Measurement

Percutaneous liver biopsy was performed for 7 patients who had significantly abnormal enzymes. All 7 patients had varying degrees of active biliary injury histologically. Active biliary injury was featured by biliary epithelial disarray, lymphocytic cholangitis, and ductular reaction resembling sclerosing cholangitis (Figure 1*A*–*C*). Portal tracts were infiltrated by mononuclear inflammatory cells and occasional eosinophils (Figure 1*B* and *C*). Chronicity features in terms of chronic cholate stasis (Figure 1*D*) and fibrosis were observed in 3 patients. Among these 3 patients, 1 had portal fibrosis, and other 2 had periportal and bridging fibrosis (Figure 1*E* and *F*). Bilirubinostasis, large duct obstruction, florid duct lesion, portal granuloma, ductopenia, or periductal fibrosis were absent. Mild lobular necroinflammatory activity was found in only 1 patient, who had modest elevation of alanine aminotransferase (191 IU/mL). None of 7 patients had any significant steatosis.

Radiologic Abnormalities

One patient was found to have a 1.6-cm hypoechoic lesion at segment IVa of liver. Her subsequent contrast-enhanced computed tomography scan demonstrated 2 arterial enhancing lesions measured 13 mm at segment IV and 7 mm at segment VIII, respectively. As the lesions became isodense with rest of liver parenchyma in portovenous phase and delayed phase; the enhancement pattern was characteristic of hepatic adenoma or focal nodular hyperplasia (Figure 2*A* and *B*).

Three of 6 patients had abnormal MRCP findings. One patient had fusiform dilatation of the CBD up to 12 mm in the mid portion, with no filling defect or compression identified (Figure 2*C*). One patient was found to have prominent CBD up to 7.5 mm with gradual distal tapering, and yet no filling defect or extrinsic compression was identified (Figure 2*D*). Another patient was noted to have dilated proximal CBD to 11 mm, again with gradual smooth distal tapering toward its entrance into duodenum without any filling defect or extrinsic compression identified (Figure 2*E*).

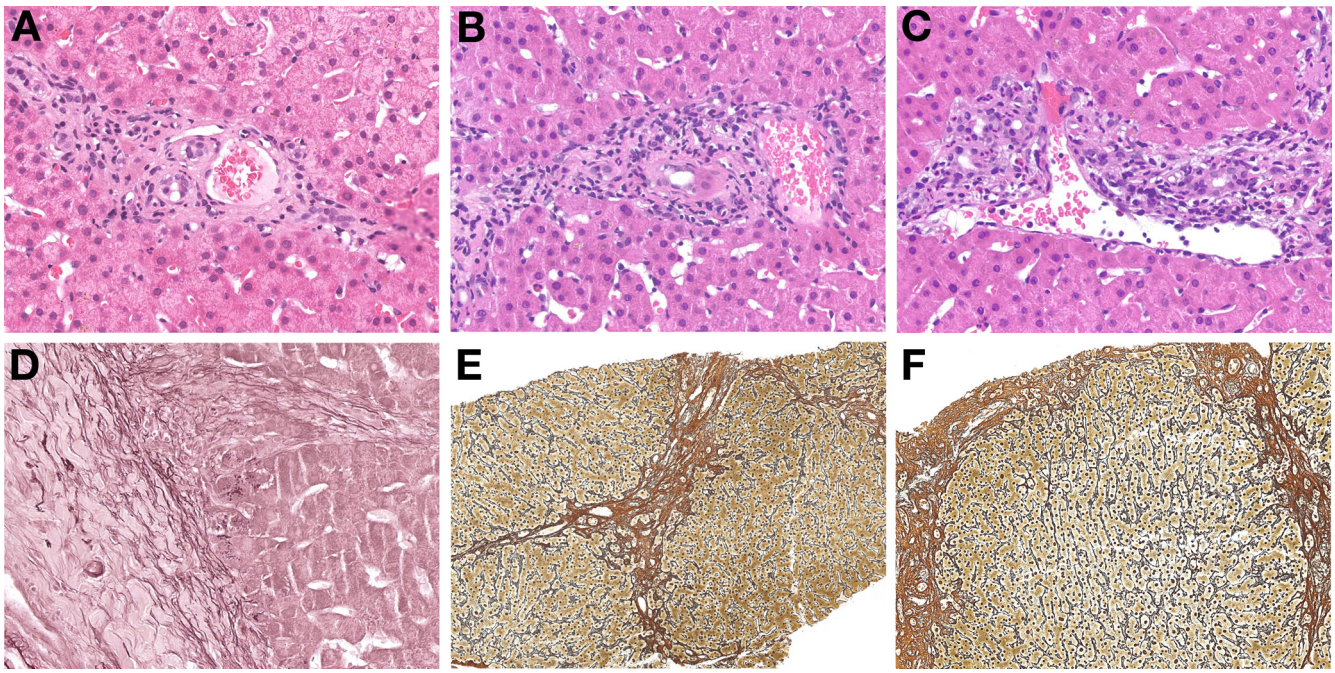

Figure 1. Histopathologic features of ketamine abusers. (*A*) Mild active bile duct injury was featured by degenerating biliary epithelial cells with pyknotic nuclei and cytoplasmic vacuolation. (*B*) An interlobular bile duct showed epithelial disarray and focal intraepithelial lymphocytic infiltrate. (*C*) An injured interlobular bile duct was accompanied by portal inflammatory infiltrate and ductular reaction. Scattered eosinophils were present. (*D*) Chronic cholate stasis was evident by deposition of copper-associated protein in the periportal hepatocytes (Orcein stain). (*E*) Portal and periportal fibrosis was present (Gordon-Sweets reticulin stain). (*F*) Bridging fibrosis was accompanied by an incomplete hepatocellular nodule (Gordon-Sweets reticulin stain).