LATE GRAFT IRON ACCUMULATION IN PATIENTS TRANSPLANTED FOR ALCOHOL-RELATED CIRRHOSIS IS ASSOCIATED WITH EXPLANT IRON OVERLOAD

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Introduction Iron accumulation can occur in individuals who drink alcohol to excess, and iron overload has been reported in up to 50% of alcohol-related cirrhosis (Mueller and Rausch, 2014). Hepcidin is a key peptide regulator for iron homeostasis; alcohol is thought to act within hepatocytes and suppress hepcidin production with consequent increased iron absorption from the intestine (Harrison-Findik et al., 2009). Having anecdotally noted that patients transplanted for alcohol-related cirrhosis accumulate iron post-transplant, we analysed this with respect to liver iron loading pre-transplant to gain some insight into potential mechanisms.

Methods Retrospective analysis of 223 patients transplanted for alcohol-related cirrhosis since January 2010 identified 47 patients with no iron in their time zero biopsy (immediately post-transplant) who had a liver biopsy at least 12 months post-transplantation. This cohort of 47 patients was then further analysed considering explant iron accumulation and grade, late graft iron accumulation (>1 year post-transplant) and evidence of recidivism.

Results Of the cohort of 47 patients, 20/47 (43%) had a degree of iron (mean grade 2) in their explant livers. Regarding late graft biopsies, 7/47 patients (15%) had evidence of iron loading (mean grade 1) in their graft at least a year post-transplantation. Of these 7 patients, 6/7 (86%) also had iron accumulation in their explant livers. 3/7 of the patients with late graft iron demonstrated recidivism post-transplant with only one patient with no evidence of explant iron accumulation developing recurrence (severe steatohepatitis) on late graft biopsy. Of note, HFE mutations were not present in any of the 7 donors.

Although numbers are small, these results are statistically significant with a Chi-squared test rejecting the null hypothesis that explant iron and late graft iron accumulation are independent of each other (p = 0.012), indicating that there is an association between the two groups.

Conclusion Iron accumulation in end-stage alcohol-related liver disease is common, and is comparative in our cohort (43%) with published figures (up to 50%). Based on our results, late graft iron accumulation is statistically associated with explant iron loading. This association does not seem to be related to recidivism or disease recurrence, and is not due to donor HFE mutations; in our experience liver donors with HFE mutations have iron at baseline.

These results may imply extra-hepatic and/or non-alcohol related stimuli post-transplantation which may or may not affect hepcidin expression causing iron overload. Future study of serum hepcidin concentrations in this context is merited.

INTRODUCTION AND AIM Minimum unit price (MUP) of 50 pence per unit of alcohol was introduced in Scotland on the 1st of May 2018. This was one of several measures which hoped to reduce alcohol harm and alcohol-related liver disease (ArLD) in particular. Standard discharge coding for ArLD is not sufficiently accurate to determine differences between variable clinical presentations. We aimed to assess the effect of MUP on the presentation of patients with ArLD to Glasgow Royal Infirmary (GRI).

Methods The medical records of all patients discharged from the Gastroenterology/Liver wards at GRI in the fourth quarter (Q4) of the years 2015–2019 were reviewed (pre-MUP 2015–17; post-MUP 2018–19). All patients with ArLD were identified and admission data were collected retrospectively detailing clinical features of liver disease, blood test results and recent drinking history. Over this time there has been no change to the placement of ArLD patients in GRI. The National Institute of Alcohol Abuse and Alcoholism definition for alcoholic hepatitis (AH) was used. MELD scores were determined for all patients. Active drinking was defined as alcohol use within 8 weeks of admission. The 90-day mortality and readmission rates were assessed.

Results In total 1875 inpatient episodes were reviewed (1164 pre-MUP; 711 post-MUP) of which 377 were with ArLD (241 pre-MUP; 136 post-MUP). Overall, the mean number of ArLD in-patient episodes fell (80.3 pre-MUP; 68 post-MUP) with a similar fall in the individual patients in each quarter (70.7 pre-MUP; 53.5 post-MUP). The proportion of active drinkers was lower post-MUP (64.7%) compared with pre-MUP (70.5%). There were no differences in the proportion of patients presenting with ascites (45.2% cf. 47.8%), encephalopathy (21.2% cf. 24.3%) or AH (18.3% cf. 19.1%) pre- and post-MUP. However, there was a reduction in presentations with acute upper GI bleeding (AUGIB): 15.8% cf. 7.4%; p=0.02; odds ratio 0.42. The overall severity of liver disease remained unchanged (mean MELD 16 for both time periods). The 90-day mortality (12.4% cf. 13.2%) and readmission (48.5% cf. 54.4%) rates were not significantly different pre- and post-MUP.

Conclusion Since the introduction of MUP there has been a reduction in the absolute numbers of ArLD in-patient episodes and number of individual patients involved at GRI. However the pattern of clinical presentation was largely unaffected other than a reduction in the proportion of patients presenting with AUGIB. The overall ArLD severity, readmission rates and 90-day mortality were similar pre- and post-MUP.