LONG-TERM OUTCOMES OF OPIOID USE IN HEPATIC IMPAIRMENT

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BACKGROUND

Safe prescribing of analgesia can be a challenge in hepatic impairment due to pharmacokinetic changes and sensitivity to adverse effects.[1,2]

In Australia, opioid use is associated with a mortality rate of 7.4 deaths per 100,000, and increasing hospitalisation due to opioid-related harm.[3]

Conversely, outcomes associated with long term opioid use in chronic liver disease have not been thoroughly explored despite increased susceptibility to adverse effects.

AIM

To examine hospitalisation and mortality associated with long-term opioid use in a cohort of hepatically impaired patients.

METHODS

- A retrospective audit of adult patients admitted to a tertiary hepatology centre was conducted using integrated electronic Medical Records.
- Patients were included if they were admitted under a Hepatologist between January and February 2016. Clinical outcomes were measured over a 12-month follow-up period.
- For cirrhotic patients, the Model for End-stage Liver Disease (MELD) and Child-Pugh scores were calculated.
- Oral morphine equivalence was determined using the ANZCA conversion App.
- Data are presented categorically (percent), or continuously as mean ± standard deviation or median [interquartile range] if non-parametric.
- The relationship between taking opioids and patients' clinical/demographic features, hospital admissions and mortality was determined using the Mann-Whitney-U or Kruskal-Wallis H test.
- A multivariable logistic regression model was developed to predict poor outcomes.
- All p-values were 2-sided and statistical significance was set at alpha=0.050.

REFERENCES

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DISCLOSURES

The authors have no conflicts of interest to declare.

RESULTS

85 eligible patients were identified. Mean age was 53.3±12.0 years, 65.9% were male. Primary disease aetiology was alcoholic liver disease in 22 (25.9%), hepatitis C in 35 (41.2%) and 'other' in 28 (32.9%). 61 patients with cirrhosis, 18.0% had Child-Pugh A, 45.9% had Child-Pugh B and 36.1% had Child-Pugh C; the median [IQR] MELD score was 23.0 [19.5–27.0].

At discharge from the initial encounter, 22 patients (25.9%) were prescribed at least one opioid (n=14 oxycodone, n=6 tramadol, n=6 'other'); median oMEDD was 30.0mg [22.3–52.5]. Opioid use could not be predicted by age, gender, current alcohol or smoking status, history of depression/anxiety.

HOSPITALISATION

62 patients re-presented. 18 (29.0%) were taking an opioid on discharge from the initial encounter. Patients prescribed an opioid had a higher number of admissions including:

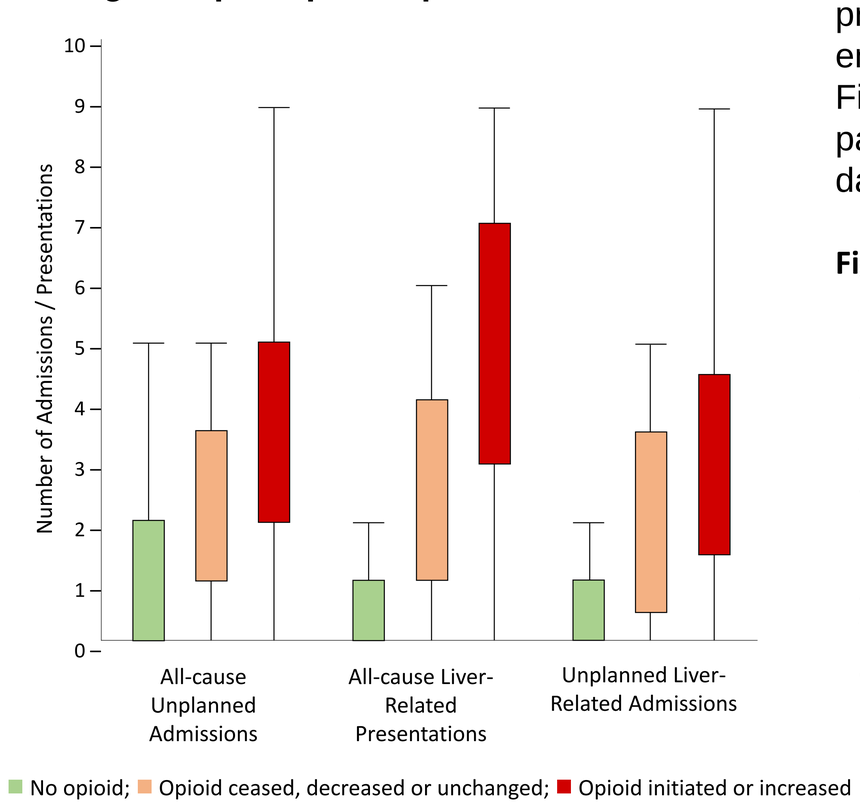
- All-cause *unplanned* admissions;
  - 1.5 [1.0-3.0] vs 0.0 [0.0-2.0], p=0.045.
- All-cause *liver-related* presentations;
  - 2.5 [0.0-4.0] vs 0.0 [0.0-1.5], p=0.041.
- *Unplanned liver-related* admissions;
  - 1.5 [0.0-3.0] vs 0.0 [0.0-1.0], p=0.001.

Among the 62 patients that re-presented:

- 7 had their opioid reduced or ceased;
- 5 did not change their overall oMEDD;
- 6 increased their opioid requirement, and;
- 10 were initiated on an opioid.

Those who were initiated on or had an increase in their oMEDD had a greater number of all-cause unplanned admissions (p<0.001), all-cause liver-related admissions (p=0.001) and unplanned liver-related admissions (p<0.001), as shown in Figure 1.

Figure 1. Number of admissions according to change in opioid prescription over time



MORTALITY

16 patients died during the 12-month follow-up period. In a multivariable logistic regression model, adjusted for hepatocellular carcinoma, serum albumin, and taking oMEDD ≥40mg, lower serum albumin (aOR 0.87, 95%CI 0.77-0.96) and taking oMEDD ≥40mg (aOR 5.48, 95%CI 1.07-28.04) were independently associated with mortality.

Table 1. Unadjusted and adjusted odds of all-cause mortality

Clinical / Demographic		Unadjusted Odds		Adjusted Odds		
		OR	95%CI	aOR*	95%CI	P
Age		1.04	0.99-1.10	1.07	0.99-1.15	0.084
Cirrhosis		1.90	0.49-7.36	0.42	0.08-2.33	0.324
	CTP^	1.31	0.98-1.74	1.40	0.91-1.08	0.131
	MELD^	1.04	0.94-1.15	1.05	0.92-1.18	0.487
HCC		4.59	1.39-15.14	3.11	0.77-12.55	0.111
Albumin		0.86	0.78-0.95	0.87	0.77-0.96	0.007
Opioid at DC		2.80	0.89-8.77	-	-	-
oMEDD ≥40		7.39	1.71-31.86	5.48	1.07-28.04	0.041

* Adjusted for the presence of hepatocellular carcinoma (HCC), serum albumin and taking oMEDD ≥40mg.
^ Analysis conducted in n=61 patients with cirrhosis.

Mean survival time was shorter among patients prescribed opioids at discharge from the initial encounter (307±97 vs. 339±80 days, p=0.061; Figure 2), and significantly shorter among patients taking oMEDD ≥40 (281±88 vs. 337±83 days, p=0.002).

Figure 2. Kaplan-Meier survival (all-cause mortality)

CONCLUSION & LIMITATIONS

People with liver disease taking opioids remain at higher risk of hospital admissions and death. However, causality cannot be implied without further evaluation of other risk factors. Individualised patient assessment and clinical judgment is advised when prescribing opioids in this population, as they may be at increased risk of adverse events. While the small sample size and selection bias may further limit generalisability, the Princess Alexandra Hospital is one of the largest hepatology centres in Australia and the only liver transplant centre in Queensland. Our findings are therefore likely reflective of patient management in south-east Queensland.