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Efficacy of lidocaine* in the treatment of pruritus in patients with cholestatic liver diseases

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*In Australia, this drug is called **lignocaine**.

Background: Pruritus can be an unrelenting source of distress for patients with advanced cholestatic liver disease. Bile acid resins are poorly tolerated and opioid antagonists risk withdrawal problems. Other interventions lack clear efficacy or have intolerable side effects. Cholestasis-induced itching may be produced by the neurotransmission and neuromodulation of opioid and serotonergic receptors. It follows that lidocaine, a sodium channel blocker, may provide valuable relief.

Methods: Eighteen patients with cholestatic liver disease and treatment-resistant pruritus were randomised (2:1) to a single 100mg infusion of lidocaine (n=12) versus placebo (n=6). This double-blind study took place between 1999 and 2002 in Buenos Aires. All patients had generalised persistent pruritus during the preceding 3 months and were receiving ursodeoxycholic acid. Electrocardiographic monitoring was conducted during intravenous infusion of 100 mg lidocaine (5cc saline) or placebo (5cc saline) over 5 minutes. Participants were carefully monitored for adverse reactions. Vital signs were recorded at baseline and throughout the first hour post-infusion. Pruritus and fatigue were recorded on a 100 mm visual analogue scale (VAS; 0=no pruritus and 100=unbearable intensity) at baseline and every 12 hours for 7 days.

Results: In the lidocaine group, mean age was 45 and 20% male; in the placebo group, mean age was 48 and 50% male. Aetiologies included primary biliary cirrhosis (n=13), primary sclerosing cholangitis (n=4), and drug-induced chronic cholestasis (n=1). Mean serum alkaline phosphatase was 704 ± 34 U/L (normal 31-100 U/L).

Lidocaine significantly reduced pruritus severity when compared with placebo, (day 2 mean pruritus VAS 39 ± 23 vs. 71 ± 8 , $p < 0.05$). In the lidocaine group, three patients noted immediate relief within the hour, and four additional patients reported at least temporary relief by day 1. Lidocaine also significantly reduced fatigue severity which was most evident on days 4 and 5 (day 4 mean fatigue VAS approximated from graph 48 ± 12 vs. 78 ± 18 , $p < 0.05$). This may be a result of a reduction of pruritus and the consequence of improved sleep. There were no severe adverse events or changes in liver function with lidocaine.

Commentary: Growing evidence suggests that the central nervous system plays a significant role in maintenance of pruritus. Lidocaine is thought to inhibit abnormal activity in peripheral nerve endings. This study raises the possibility that active sodium channels within the superficial layers of skin and mucus membrane may contribute to the pathogenesis of pruritus in cholestatic liver disease.

Lidocaine is a novel, physiologically-sound approach to the treatment of cholestatic pruritus. In this small randomised controlled trial, a single dose of

lidocaine provided tangible relief of pruritis and fatigue with minimal toxicity. These data are early and definitive randomised trials are needed. Until then, palliative care clinicians may want to consider using lidocaine, under controlled settings, as an experimental treatment for refractory pruritis.

Reviewer

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Dr. Amy Abernethy is Assistant Professor of Medicine and Assistant Professor of Nursing at Duke University School of Medicine in North Carolina, USA, and an adjunct Associate Lecturer at Flinders University. She directs the Palliative Care Clinical Research Initiative, based at Duke University. Dr. Abernethy obtained her medical degree and post-graduate training in Internal Medicine, Haematology, and Medical Oncology at Duke University, and subsequent training in Palliative Medicine and Cancer Pain Management at Flinders University. Dr. Abernethy's research focuses on conducting high quality clinical trials that generate evidence-based solutions for common problems in that affect the quality of life of people with life-limiting illness, such as pain, breathlessness, and health service delivery models. Ongoing clinical research studies are evaluating innovative whole person interventions in cancer care, new education models for patients with cancer pain, interventions to reduce refractory breathlessness, and methods of rapidly assessing and responding to patient distress in the oncology clinic setting.