RESEARCH

Safety and efficacy of long-term nasobiliary drainage to treat intractable pruritus in cholestatic liver disease

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ABSTRACT

Introduction Cholestasis related pruritus, secondary to intrahepatic and/or extrahepatic biliary obstruction is a common manifestation in chronic liver disease. Pruritus is difficult to treat, and results are often suboptimal. A stepwise medical approach is usually employed, followed by a trial molecular adsorbents recirculation system in medication resistant cases. Pruritus resulting in reduced quality of life is a variant syndrome eligible for liver transplantation in the setting of preserved synthetic function.

Aim This case series describes the use of long-term (LT) nasobiliary drainage (NBD) in three patients with intractable pruritus. This case series tests the hypothesis that LT-NBD could be successfully used to alleviate cholestasis related pruritus, and prevent or delay the need for liver transplantation.

Method LT-NBD was carried out in three female patients (mean age 43 years) with intractable pruritus secondary to primary biliary cirrhosis (PBC) (n=2), and benign recurrent intrahepatic cholestasis (n=1). NBD was carried out through the endoscopic placement of a 6 French Cook Medical nasobiliary catheter into the common bile duct.

Results Symptomatic relief of pruritus was described by all three cases within 24 h of NBD placement. LT-NBD was stopped in the patient with benign recurrent intrahepatic cholestasis after 8 weeks due to complete resolution of pruritus. In one patient with PBC, LT-NBD was undertaken over 12 months, with complete resolution of pruritus. In the second patient with PBC, LT-NBD was carried out over 14 months, with complete resolution of pruritus.

Discussion This case series supports the efficacy of LT-NBD in the treatment of intractable pruritus. We propose that NBD offers an accessible modality for the treatment of intractable pruritus in liver disease, potentially avoiding the need for liver transplantation.

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INTRODUCTION

Cholestasis related pruritus secondary to intrahepatic and or extrahepatic biliary disruption is a common clinical manifestation in liver disease. The pathogenesis is poorly understood, hypotheses include bile acid and bile salt accumulation in the systemic circulation,[1] other theories suggest that pruritus associated with cholestasis is centrally mediated by increased opioidergic tone, and a third theory involves the role of elevated histamine levels. Pruritus in chronic liver disease is difficult to manage and results are often suboptimal. A well-recognised stepwise medical approach to treatment is often employed, involving bile acid resins, opioid antagonists, ursodeoxycholic acid, gabapentin, selective serotonin reuptake inhibitors and sedating antihistamines. In medication resistant cases, molecular adsorbents recirculation system (MARS) can be trialled, however this modality is not freely available.[2]

Cholestasis related pruritus, resulting in reduced quality of life is a variant syndrome eligible for liver transplantation in the setting of preserved liver synthetic function. The UK currently employs a 'Centre Liver Allocation Scheme' with organ allocation based primarily on risk of death without transplant, and secondarily on ability for transplantation to improve quality of life. When a 'National Liver Allocation Scheme' model is adopted, organ allocation will be purely based on the UK model for end-stage liver disease score, rendering transplant for

improved quality of life virtually impossible. Currently at the tertiary referral liver transplant unit where this procedure was trialled, patients listed for orthotopic liver transplant secondary to reduction in quality of life make up 6% of the total number of patients listed.

Temporary nasobiliary drainage (NBD), (mean length of drainage 19 days) has previously been described in the treatment of intractable pruritus secondary to benign recurrent intrahepatic cholestasis (BRIC) and primary biliary cirrhosis (PBC), further supporting the theory that bile salts are potent pruritogens.[3–6] This case series describes the use of long-term (LT)-NBD in three patients with intractable pruritus, testing the hypothesis that removal of bile salts from the body via a nasobiliary catheter quickly and dramatically alleviates pruritus secondary to cholestasis thus preventing, or at least delaying the need for liver transplantation. For the purpose of this case series we defined LT as any drain *in situ* for longer than 4 weeks.

CASE SERIES

LT-NBD was carried out in three female patients (mean age 43 years) for intractable pruritus secondary to biopsy proven PBC (n=2) and BRIC (n=1). All three patients had intractable pruritus despite stepwise medical therapy and MARS. All had preserved synthetic liver function at the time of drain placement (Child-Pugh A), and were active on the liver transplant waiting list. The indications for listing for transplant were reduction in quality of life secondary to intractable pruritus in both patients with PBC. The indications for the patient with BRIC were nutritional failure and reduction in quality of life secondary to pruritus. Laboratory parameters prior to drain insertion were as follows: patient 1 with PBC—alanine transaminase (ALT) 65 μ/L, alkaline phosphatase (ALP) 1406 μ/L, bilirubin 22 μmol/L, albumin 42 g/L, patient 2 with PBC—ALT 94 μ/L, ALP 1917 μ/L, bilirubin 28 μmol/L, albumin 44 g/L, patient 1 with BRIC—ALT 46 μ/L, ALP 1968 μ/L, bilirubin 376 μmol/L, albumin 39 g/L. Reference ranges: *ALT 0–55 μ/L, ALP 25–130 μ/L, bilirubin 0–22 μmol/L, albumin 35–50 g/L*. NBD was carried out through the endoscopic placement of a 6 French 250 cm Cook Medical nasobiliary catheter into the common bile duct. A sphincterotomy was performed in patient 2 with PBC to facilitate deep cannulation of the duct. The position of the nasobiliary catheter was confirmed under screening. Prior to drain insertion all three cases completed an itch severity questionnaire. All three cases described their pruritus as involving more than three areas of the body, lasting all day, unbearable in severity, disturbing sleep and resulting in an inability to work, complete errands and derive pleasure from leisure activities. Within 24 h of NBD placement all three cases were completely free of pruritus. In two cases, drain insertion was complicated by postprocedure abdominal pain and rise in serum amylase, but neither case fulfilled Cotton criteria for postendoscopic retrograde cholangiopancreatography pancreatitis.[7] The only other complication documented, in relation to NBD was that of luminal occlusion and cessation of flow of bile. In the first instance, this complication was overcome by flushing the catheter with normal saline and commencing UDCA, however on tube reocclusion, a repeat endoscopic retrograde cholangiopancreatography and catheter change was carried out. LT-NBD was stopped in the patient with BRIC after 8 weeks due to complete resolution of pruritus. Prior to drain removal, liver function tests revealed ALT 46 μ/L, ALP 509 μ/L, bilirubin 12 μmol/L. In one patient with PBC, LT-NBD was undertaken over 12 months, with complete resolution of pruritus (tube replacement after 10 months due to blockage of the catheter lumen). In the second patient with PBC, LT-NBD was carried out over 14 months, with complete resolution of pruritus (tube replaced three times). In both cases where the nasobiliary catheter became blocked there was rapid return of the patient's pruritus. Since drain removal, the patient with BRIC has had no further episodes of cholestasis and has been removed from the transplant waiting list. In both PBC cases, the end point was orthotopic liver transplantation due to deteriorating synthetic function.

DISCUSSION

This is the first case series supporting the efficacy of LT-NBD for symptomatic relief of intractable pruritus. In this case series, LT-NBD was successfully used for up to 14 months, delaying the need for liver

Significance of this study

What is already known on this subject?

Medication resistant pruritus is a common manifestation in liver disease resulting in a reduction in a patient's quality of life. Temporary nasobiliary drainage has previously been associated with transient improvement in symptoms.

What this study adds?

This case series demonstrates that LT-NBD is an accessible treatment modality leading to rapid symptom relief in three cases of intractable pruritus with no significant side effects or complications encountered.

How it might impact on clinical practice in the foreseeable future?

The use of LT-NBD in cases of intractable pruritus could potentially avoid or delay the need for liver transplantation, relieving the burden on an already scarce resource, as well as avoiding the risks associated with complex surgery, and side effects associated with immunosuppression.

transplantation in all three cases. LT-NBD could therefore be used as an accessible modality that could potentially avoid or delay the need for liver transplantation, thus relieving the burden on an already scarce resource, as well as avoiding the risks associated with complex surgery, and side effects associated with immunosuppression. Furthermore if LT-NBD is effective at treating medication resistant pruritus then surgical biliary diversion may also be a potential LT option, in suitable patients. We support the use of LT-NBD in all patients with intractable itch secondary to cholestatic liver disease who have failed stepwise medical therapy and MARS.

Contributors MHD conceived the idea of trialling nasobiliary drainage to relieve the symptom of intractable itch secondary to cholestasis. VJA and JMH performed a literature search to establish previous experience of using nasobiliary drainage, and the duration of therapy. MHD was responsible for selecting the patients to trial the therapeutic intervention. VJA was responsible for collecting data on itch and its effect on quality of life as well as permission from each patient to write up their case. MHD performed the procedures and was responsible for the aftercare and subsequent outpatient contact with the patients. VJA and JMH prepared the initial draft of the manuscript which was subsequently distributed to MHD for comments and revisions which were then made by VJA and JMH. VJA has been responsible for liaising with Frontline Gastroenterology and informing the other team members of results.

Competing interest None.

Patient consent Obtained.

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REFERENCES

1 Imam MH, Gossard AA, Sinakos E, *et al*. Pathogenesis and management of pruritus in cholestatic liver disease. *J Gastroenterol Hepatol* 2012;27:1150–8.
2 Parés A, Herrera M, Avilés J, *et al*. Treatment of resistant pruritus from cholestasis with albumin dialysis: Combined analysis of patients from three centers. *J Hepatol* 2010;53:307–12.
3 Toros AB, Özerdenen F, Bektas H, *et al*. A case report: Nasobiliary drainage inducing remission in benign recurrent intrahepatic cholestasis. *Turk J Gastroenterol* 2012;23:75–8.
4 Stapelbroek JM, Van Erpecum KJ, Klomp LW, *et al*. Nasobiliary drainage induces long-lasting remission in benign recurrent intrahepatic cholestasis. *Hepatology* 2006;43:51–3.
5 Beuers U, Gerken G, Pusl T, Biliary drainage transiently relieves intractable pruritus in primary biliary cirrhosis. *Hepatology* 2006;44:280–1.
6 Singh V, Bhalla A, Sharma N, *et al*. Nasobiliary drainage in acute cholestatic hepatitis with pruritus. *Dig Liver Dis* 2009;41:442–5.
7 Cotton PB, Lehman G, Vennes J, *et al*. Endoscopic sphincterotomy complications and their management: an attempt at consensus. *Gastrointest Endosc* 1991;37:383–93.