

Safety and Efficacy of Long Term Nasobiliary Drainage to Treat Intractable Pruritus in Cholestatic Liver Disease

Appleby VJ¹, Hutchinson JM and Davies MH

¹Department of Hepatology, St James University, Beckett Street, Leeds, LS7 9TF, UK

*Corresponding author: Victoria Appleby, Department of Hepatology, St James University, Beckett Street, Leeds, LS7 9TF, UK, Tel: (0113) 2433144; E-mail: Victoria.Appleby@bthft.nhs.uk

Rec date: Apr 18, 2014, Acc date: May 26, 2014, Pub date: June 02, 2014

Copyright: © 2014 Appleby VJ et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

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 often suboptimal. A stepwise medical approach is usually employed, followed by a trial molecular adsorbents recirculation system (MARS) 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)-NBD in three patients with intractable pruritus. This case series test the hypothesis that long-term 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 PBC (n=2), and BRIC (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 hours of NBD placement. LT-NBD was stopped in the patient with BRIC after eight weeks due to complete resolution of pruritus. In one PBC patient, LT-NBD was undertaken over 12 months, with complete resolution of pruritus. In the second PBC patient, LT-NBD was carried out over 14 months, with complete resolution of pruritus.

Discussion: This case series supports the efficacy of long term 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.

Keywords: Cholestatic; Liver diseases; Pruritus; Nasobiliary drainage

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 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 anti-histamines. 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 United Kingdom 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 United Kingdom Model For End-Stage Liver Disease (UKELD) score, rendering transplant for improved quality of life virtually impossible. Currently at the tertiary referral liver transplant unit where this procedure was trialed, 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 long term as any drain in situ for longer than four 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 (Childs-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: PBC patient 1-Alanine transaminase (ALT) 65 µ/L, Alkaline phosphatase (ALP) 1406 µ/L, bilirubin 22 µmol/L, albumin 42 g/L, PBC patient 2 - ALT 94 µ/L, ALP 1917 µ/L, bilirubin 28 µmol/L, albumin 44 g/L, BRIC patient 1-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. Sphincterotomy was performed in one of the three cases. 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 hours of NBD placement all three cases were completely free of pruritus. In two cases, drain insertion was complicated by post procedure abdominal pain and rise in serum amylase, but neither case fulfilled Cotton criteria for post Endoscopic Retrograde Cholangiopancreatography (ERCP) 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 re-occlusion, a repeat ERCP and catheter change was carried out. LT-NBD was stopped in the patient with BRIC after eight 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 PBC patient, 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 PBC patient, 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. 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 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 long term 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.

References

1. O'Keefe C, Baird AW, Nolan N, McCormick PA (2004) Cholestatic pruritus - the role of cutaneous mast cells and nerves. *Aliment Pharmacol Ther* 19: 1293-1300.
2. Albert P, Manuel H, Juan A, Miquel S, Antoni M (2010) Treatment of resistant pruritus from cholestasis with albumin dialysis: Combined analysis of patients from three centers. *Journal of Hepatology* 53 : 307-312.
3. Ahmet BT, Füsün Ö, Hasan B, Nagehan DS (2012) A case report: Nasobiliary drainage inducing remission in benign recurrent intrahepatic cholestasis. *Turk J Gastroenterol* 23 : 75-78.
4. Stapelbroek JM, van Erpecum KJ, Klomp LW, Venneman NG, Schwartz TP, et al. (2006) Nasobiliary drainage induces long-lasting remission in benign recurrent intrahepatic cholestasis. *Hepatology* 43: 51-53.
5. Beuers U, Gerken G, Puhl T (2006) Biliary drainage transiently relieves intractable pruritus in primary biliary cirrhosis. *Hepatology* 44: 280-281.
6. Singh V, Bhalla A, Sharma N, Dheerendra PC, Agarwal R, et al. (2009) Nasobiliary drainage in acute cholestatic hepatitis with pruritus. *Dig Liver Dis* 41: 442-445.
7. Cotton PB, Lehman G, Vennes J, Geenen JE, Russell RC, et al. (1991) Endoscopic sphincterotomy complications and their management: an attempt at consensus. *Gastrointest Endosc* 37: 383-393.