

# Bile Acid Induced Diarrhoea

## Pathophysiological and Clinical Aspects

Akademisk avhandling

Som för avläggande av medicine doktorsexamen  
vid Sahlgrenska Akademin  
kommer att offentligen försvaras i  
Arvid Carlsson salen  
Fredagen den 4:e april 2008 kl. 13

Av

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Leg. läkare

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Avhandlingen baseras på följande arbeten

- I. The bile acid turnover rate assessed with the <sup>75</sup>SeHCAT test is stable in chronic diarrhoea although it is slightly decreased in healthy subjects after a long period of time**  
A Bajor, A Kilander, H Sjövall, M Rudling, K-A Ung  
Submitted for publication
- II. Normal or increased bile acid uptake in isolated mucosa from patients with bile acid malabsorption**  
A Bajor, A Kilander, A Fae, C Gälman, O Jonsson, L Öhman, M Rudling, H Sjövall, P-O Stotzer, K-A Ung  
*Eur J Gastroenterol Hepatol* 2006;18(4):397-403.
- III. Enhanced motility-activated jejunal secretion is quantitatively related to reduced bile acid uptake in patients with bile acid malabsorption**  
A Bajor, K-A Ung, L Öhman, M Simren, H Sjövall  
In Manuscript
- IV. Budesonide treatment is associated with increased bile acid absorption in collagenous colitis**  
A Bajor, A Kilander, C Gälman, M Rudling, K-A Ung  
*Aliment Pharmacol Ther* 2006;24(11-12):1643-9

# Bile Acid Induced Diarrhoea

## Pathophysiological and Clinical Aspects

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A common cause for referral to gastroenterologists is chronic watery diarrhoea. Approximately 40% of these patients have idiopathic bile acid malabsorption (BAM) – a condition with unknown aetiology. The  $^{75}\text{SeHCAT}$  test, which correlates inversely with faecal excretion and hepatic synthesis of bile acids, is used to diagnose BAM.

The aims of the thesis were to study different mechanisms behind BAM. We investigated the stability of the  $^{75}\text{SeHCAT}$  test in diarrhoea patients having done the test twice, and in healthy controls. The  $^{75}\text{SeHCAT}$  values were stable over time, suggesting that in clinical practice there is no indication for a second test. There was also a strong negative correlation between the  $^{75}\text{SeHCAT}$  retention and the plasma marker for hepatic bile acid synthesis “C4” both in diarrhoea and in controls.

Impaired ileal absorption of bile acids may be secondary to a defective ileal reabsorption system. We assessed bile acid uptake in ileal biopsies from diarrhoea patients - both with normal and abnormal  $^{75}\text{SeHCAT}$  test- and compared with the bile acid uptake in ileal biopsies from patients with normal bowel habits. Our data suggest that BAM is not caused by impaired bile acid uptake in the ileum.

We also tested whether BAM is associated with increased active small intestinal chloride secretion as estimated from small intestinal potential difference (PD) measurements. We recorded PD during manometry in patients with abnormal  $^{75}\text{SeHCAT}$  test and compared the values with PD recording values in healthy controls. There was a higher PD in the fasting state in the BAM group and there was also a negative correlation between the  $^{75}\text{SeHCAT}$  test values and the estimated chloride secretion.

It is known that budesonide has effect on symptoms of diarrhoea both in Crohn’s disease and in collagenous colitis. We investigated whether the improvement in symptoms in collagenous colitis is associated with an enhancement of bile acid uptake and/or changes in bile acid synthesis. After 8 weeks of budesonide treatment the  $^{75}\text{SeHCAT}$  values increased significantly, synthesis rate decreased and the diarrhoea symptoms improved.

**Conclusions:** The  $^{75}\text{SeHCAT}$  test is stable over a long period of time. C4, the plasma marker for bile acid synthesis, may be used in clinical practice instead of the  $^{75}\text{SeHCAT}$  test. BAM does not seem to be caused by impaired absorption of bile acids in the ileum. A possible mechanism is increased small intestinal fluid secretion and motility, which in turn overrides the absorptive capacity of the colonic mucosa and leads to diarrhoea. The positive symptomatic effects of budesonide in collagenous colitis may in part be mediated by increased ileal absorption and lower colonic concentrations of bile acids.

**Keywords:** Diarrhoea, bile acid transport, bile acid synthesis,  $^{75}\text{SeHCAT}$  reproducibility, C4, budesonide, collagenous colitis, in vitro, malabsorption, ASBT, intestinal secretion, potential difference, manometry.

ISBN 978-91-628-7445-2