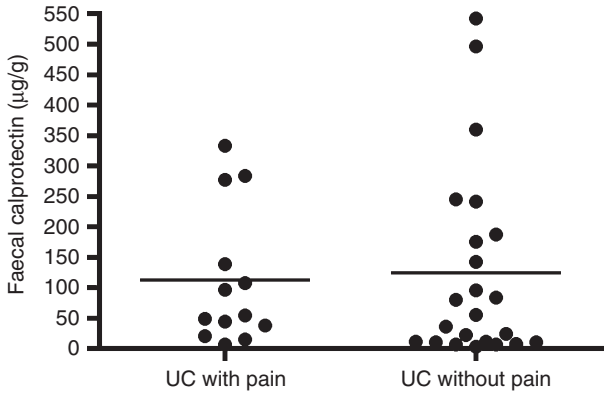

Figure 1 | Faecal calprotectin levels in ulcerative colitis (UC) patients in remission with and without abdominal pain.

indicators of mucosal inflammation, were comparable in IBD patients with or without IBS-like symptoms.

A recent study by Jonefjäll *et al.*[2] investigating 94 patients with ulcerative colitis (UC) in remission came to the same conclusion. These findings are in contrast to the findings of Keohane *et al.*, who observed significantly higher calprotectin levels in IBD patients with IBS-like symptoms.[3]

In support of the findings of Berrill *et al.* and Jonefjäll *et al.*, we were also unable to demonstrate a significant difference in calprotectin levels among 36 UC patients in remission, both with and without abdominal pain, reflecting IBS-like symptoms (see Figure 1). However, in UC patients with abdominal pain, faecal calprotectin levels significantly correlated with pain scores ($r = 0.80$, $P = 0.002$).

Furthermore, we demonstrated increased transcription of the nociceptive signalling molecule TRPV1 in this group, which also correlated with pain scores.[4] This is in line with the findings of Akbar *et al.*[5], who demonstrated that UC patients in remission complaining of abdominal pain had significantly higher numbers of TRPV1-positive nerve fibres in the rectosigmoid mucosa.

We therefore hypothesise that the potential cause of IBS-like symptoms in UC patients in remission is not the sub-clinical inflammation *per se*, but rather the secondary changes induced during the acute inflammatory phase, which persist during remission. Upregulation of TRPV1 could represent one of these secondary alterations in mucosal neurobiology responsible for increased peripheral nociceptive discharge and subsequent pain symptom development. The reason why this occurs in only a fraction of UC patients in remission remains to be elucidated.

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Letter: antibiotic dose adjustment in patients with advanced liver disease

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Sirs, We read with great interest the careful review article by Lewis and Stine on the use of medications in patients with advanced liver disease.[1] This is a complete practical guide for clinicians, but some data are lacking. Here, we will add information about newer antimicrobial agents utilised in the treatment of antibiotic-resistant bacterial infections in cirrhotic patients.[2]

Linezolid (LNZ) is metabolised by non-enzymatic chemical oxidation mainly into two inactive metabolites, an aminoethoxyacetic acid and a hydroxyethyl glycine. Excretion in urine is the dominant route of elimination. The pharmacokinetics (PK) are not altered in patients with mild-to-moderate hepatic impairment (Child-Pugh class A or B); therefore, no dosage adjustments are necessary. PK data are not available for patients with severe

hepatic impairment (Child-Pugh class C). However, no dosage adjustments are required because it is metabolised by a non-enzymatic process.[3-5]

Daptomycin (DAP) is a cyclic lipopeptide derived from *Streptomyces roseosporus* as a fermentation product. It has a minimal hepatic metabolism and it is excreted primarily unchanged in urine. The PK of DAP are not altered in subjects with mild-to-moderate hepatic impairment, compared with healthy volunteers, whereas the PK in patients with severe hepatic impairment have not been studied; therefore, caution is advised in the patient with severe hepatic impairment.[6, 7]

Tigecycline (TGC) is a derivative of minocycline. The two major metabolic pathways of TGC consist of glucuronidation, and amide hydrolysis to t-butylamino-acetic acid and 9-aminominocycline. The major route of elimination of TGC is faecal, likely via biliary excretion. Dose adjustment is required for patients with severe hepatic impairment. In this setting, the initial dose should be 100 mg followed by a reduced maintenance dose of 25 mg every 12 h. No dosage adjustments are necessary in patients with mild-to-moderate hepatic impairment.[8, 9]

Finally, dosage adjustments are not required for doripenem and ceftaroline in patients with hepatic impairment.[4, 10]

In conclusion, we hope that this additional information can be included in this practical guide and can be useful to clinicians in the management of antibiotic-resistant bacterial infections in cirrhotic patients.

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Letter: antibiotic dose adjustment in patients with advanced liver disease – authors' reply

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We appreciate the additional specific information provided by Dr Leone and colleagues[1] on the use of these five antimicrobials in patients with hepatic impairment, in their letter concerning our recent review.[2] The pharmacokinetic data they provide along with their specific dosing recommendations should assist clinicians using these agents in patients with advanced liver disease. We encourage Dr Leone and others to publish their clinical experience with these, as well as other, drug classes and disorders in order that the database for using drugs in cirrhosis can continue to be expanded.

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