

Rectal lactulose: Getting to the bottom of it

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Background

Hepatic encephalopathy is a syndrome of neuropsychiatric symptoms that can develop in severe liver disease due to the build up of toxins in the blood such as ammonia. It negatively impacts patient survival as encephalopathy severe enough to lead to hospitalisation is associated with a survival probability of 42% at 1 year and 23% at 3 years¹.

Role of lactulose

Lactulose is used as a first-line agent in the management of hepatic encephalopathy. When given orally, lactulose is not absorbed and reaches the colon virtually unchanged, where colonic bacteria metabolise it to low molecular weight acids thereby acidifying the pH of the colon².

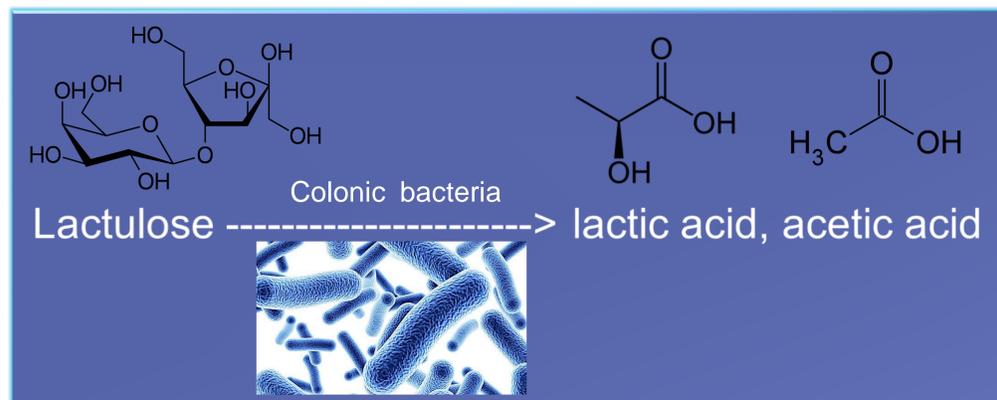


Figure 1 Conversion of lactulose in the colon by bacteria

The acidification of the colon results in the conversion of ammonia to the ammonium ion (NH_4^+). The reabsorption of ammonia into the bloodstream leads to the symptoms of hepatic encephalopathy. Ammonium ions are not reabsorbed and are excreted from the body.

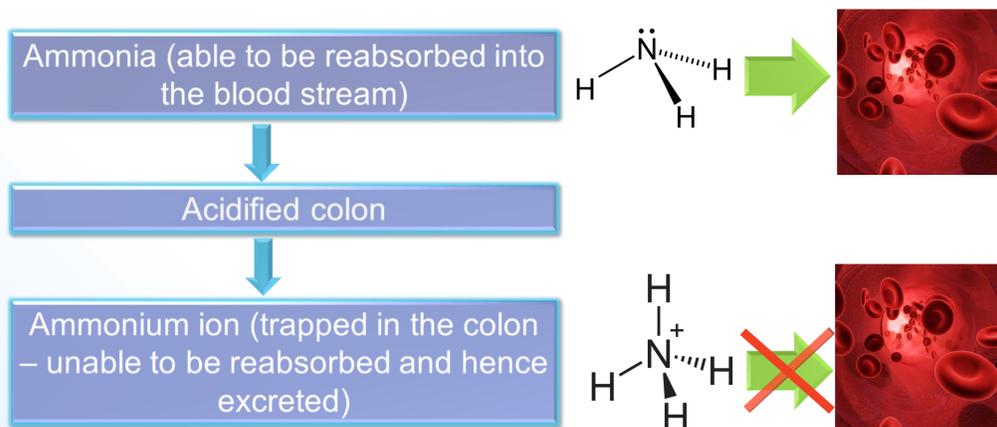


Figure 2 Removal of ammonia from the blood

Dosage

- When administered orally or enterally, large doses of lactulose are required:
 - 30-45mL every 1-2 hours until a laxative effect is achieved, then reduce frequency to 3 to 4 times a day³.
- In those unable to tolerate oral or enteral doses, lactulose may be diluted and given rectally.

There is a general lack of awareness that the oral and rectal lactulose doses are not the same. The following prescription is common, but is incorrect:

~~PO/PR lactulose 30mL q4h~~

THE ORAL AND RECTAL DOSE OF LACTULOSE FOR HEPATIC ENCEPHALOPATHY IS NOT THE SAME. THERE IS NO DIRECT CONVERSION BETWEEN THE ORAL AND RECTAL DOSE.

There is also no standardised way in which lactulose is prepared and administered for rectal administration at Westmead Hospital.

Getting to the bottom of the rectal dose

When given rectally, an adequate volume must be administered in order for the lactulose to reach the ascending colon where colonic bacteria can convert it to low molecular weight acids. Administration of a small volume (e.g. 30mL) results in the solution remaining in the rectum where there is insufficient bacteria to convert it and it would therefore have no therapeutic effect.

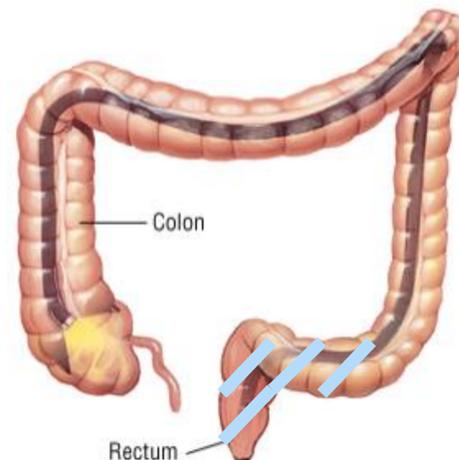


Figure 3 Colon after administration of smaller volume (e.g. 30mL)

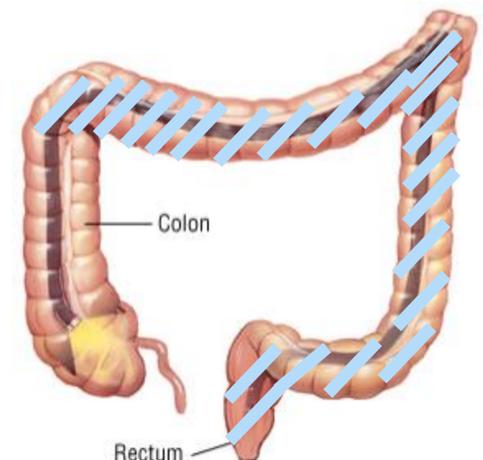


Figure 4 Colon after administration of a larger volume (e.g. 200mL)

Clinical studies demonstrating efficacy used large volumes of rectal lactulose (1 litre or more) as a retention enema, usually in the ratio of 300mL lactulose syrup to 700mL water or normal saline⁴. However, it may be problematic to administer such large volumes to a patient.

How do you administer 1 litre of fluid to patient rectally??

Administration of a volume less than 200mL of lactulose solution would probably not be adequate to reach the ascending colon, and would therefore be ineffective⁵.

Hospital wide guideline

It has become apparent there is a need for a hospital guideline to standardise the prescribing and administration of lactulose for the management of hepatic encephalopathy. A multidisciplinary meeting was held between pharmacy, gastroenterology and nursing to discuss the creation of a hospital lactulose guideline.

Based on the available evidence, practicalities, and experience, consensus was to suggest a dose of 60mL of lactulose syrup diluted with 140mL of water to make a total volume of 200mL. Feedback was obtained from other clinical specialties including intensive care and medical high dependency units.

PR lactulose syrup 60mL + 140mL water (total volume=200mL) every 4 to 6 hours

To the future

Further investigations are planned to demonstrate that 200mL of rectal lactulose is effective in the treatment of hepatic encephalopathy as there is currently no published evidence which demonstrates the effectiveness of a volume less than one litre.

References

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