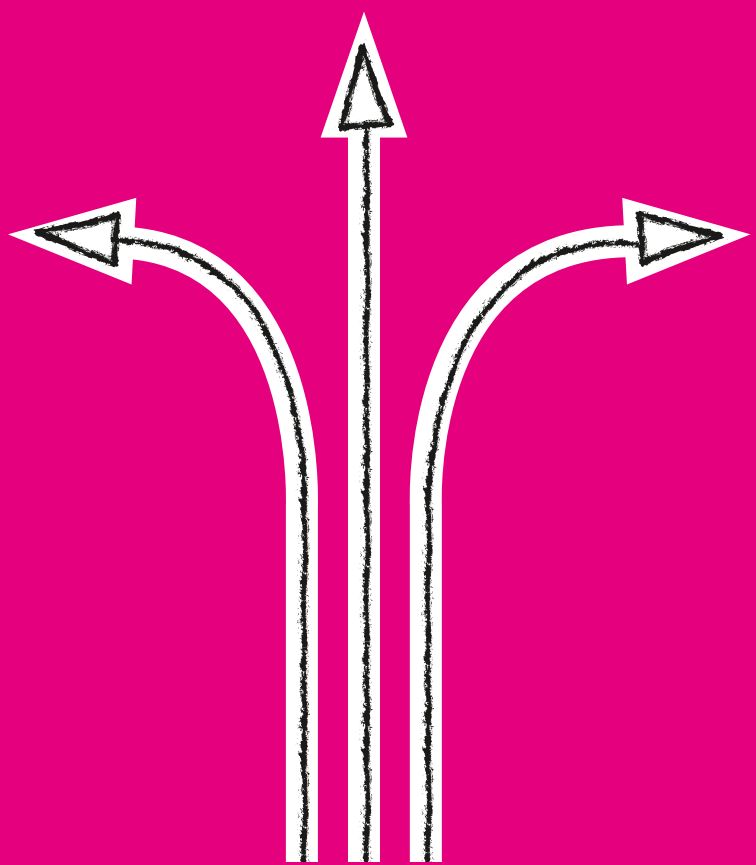
SCIENCE

RANDOMIZED CONTROLLED TRIAL COMPARING LACTULOSE, PROBIOTICS AND LOLA IN MINIMAL HEPATIC ENCEPHALOPATHY (MHE)



Mittal VV, Sharma BC, Sharma P, Sarin SK. Eur J Gastroenterol Hepatol. 2011;23(8):725-732.

FIRST RANDOMIZED TRIAL OF HEPA-MERZ® IN MHE

Introduction

- Although MHE represents the mildest form of HE, daily functioning and quality of life are impaired.
- Due to similar pathophysiology of MHE and HE, treatment options based on reducing intracerebral ammonia levels are the same for both conditions.
- This represents the first randomized trial with Hepa-Merz® in patients with MHE.

Study

Objective

To evaluate the effect of 3 MHE treatments on disease improvement and change in health-related quality of life (HRQOL).

Design

Three-month, randomized, 4-arm study in 160 patients with liver cirrhosis and MHE.

Patient population

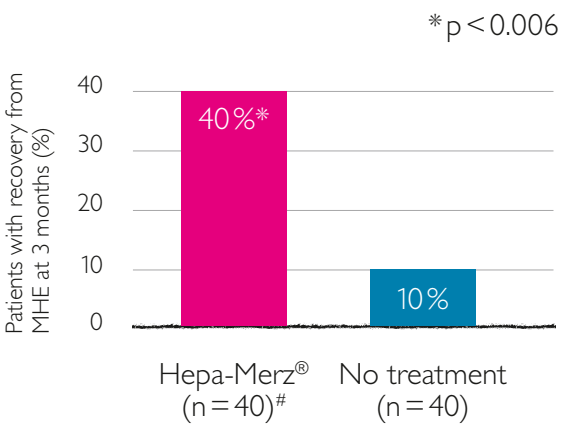
- Causes of liver cirrhosis were alcohol consumption (n = 66), chronic hepatitis B (n = 32), and chronic hepatitis C (n = 23); other causes (n = 39)
- Treatment groups were balanced with regard to patient population size and baseline parameters

Treatment

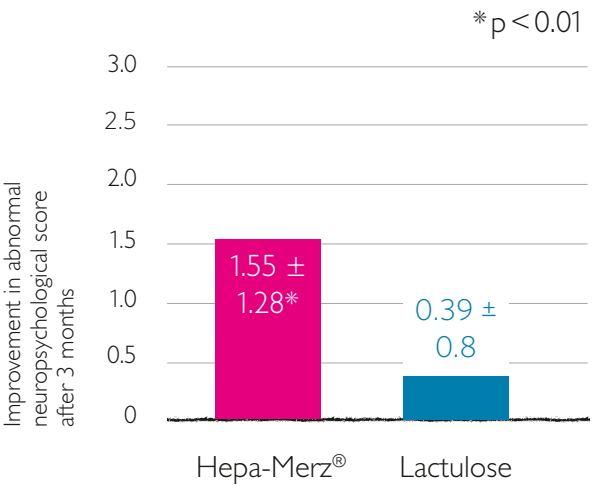
- Group A: Standard care for liver cirrhosis (no treatment)
- Group B: Lactulose 30 – 60 ml per day
- Group C: Probiotics 110 billion colony-forming units twice daily
- Group D: Hepa-Merz® 6 g 3-times per day

HEPA-MERZ® SIGNIFICANTLY IMPROVES PATIENT FUNCTIONING

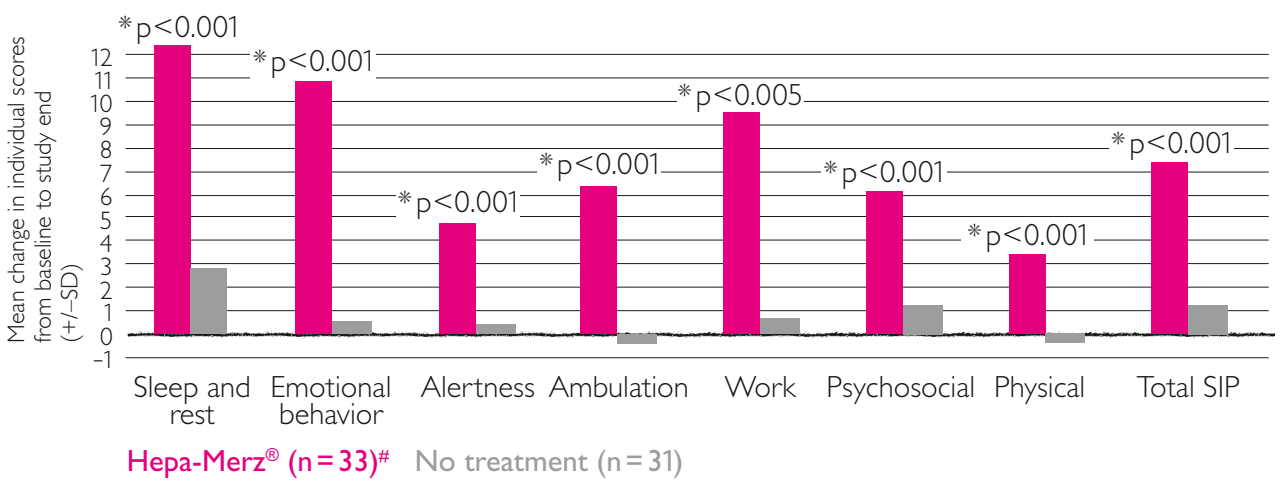
Treatment with Hepa-Merz® resulted in signigicantly more recoveries from MHE than no treatment



Hepa-Merz® significantly improved cerebral function compared with no treatment



Improved daily functioning with Hepa-Merz® compared to no treatment



Safty

- All treatments were well tolerated.
- There were no major adverse drug reactions. Mild abdominal symptoms were recorded in 7 patients receiving lactulose.

No significant difference between Hepa-Merz® and the other 2 treatment options

Hepa-Merz®
L-ornithine-L-aspartate

HEPA-MERZ® SIGNIFICANTLY IMPROVES MHE AND PATIENTS' HRQOL

Conclusion

The study illustrated that treatment of MHE with Hepa-Merz® improves the disease state as well as health-related quality of life and is well tolerated.*

* No significant difference between the 3 tested treatments.

Hepa-Merz® Prescribing Information

Hepa-Merz® Granules. Active substance: L-ornithine-L-aspartate. **Composition:** One sachet with 5 g of Granules contains: **Active substance:** 3 g L-ornithine-L-aspartate. **Excipients:** citric acid, saccharin sodium, sodium cyclamate, povidone 25, fructose, flavorings, orange yellow S (E110). Note for diabetics: One sachet of Hepa-Merz® Granules contains 1.13 g of fructose (corresponds to approx. 0.11 BU). **Therapeutic indications:** Treatment of concomitant disease and sequelae due to impaired detoxification activity (e.g. in cirrhosis of the liver) with the symptoms of latent and manifest hepatic encephalopathy. **Contraindications:** Absolute: Hypersensitivity to L-ornithine-L-aspartate, orange yellow S or any of the other excipients. Severely impaired renal function (renal insufficiency). A serum creatinine value over 3 mg/100 ml can be used as a guideline value. Relative: Pregnancy and lactation: No clinical data are available relating to intake of Hepa-Merz® Granules during pregnancy. No exhaustive animal studies have been performed for L-ornithine-L-aspartate, to investigate its toxicity in relation to reproduction. Administration of Hepa-Merz® Granules during pregnancy should therefore be avoided. If, however, treatment with Hepa-Merz® Granules is considered necessary, careful consideration should be given to the benefit versus risk ratio. It is not known whether L-ornithine-L-aspartate is excreted into the breast milk. Administration of Hepa-Merz® Granules should therefore be avoided during lactation. If, however, treatment with Hepa-Merz® Granules is considered necessary, careful consideration should be given to the benefit versus risk ratio. **Undesirable effects:** Uncommon (≥ 1/1000 to < 1/100): Nausea, vomiting, stomach ache, flatulence, diarrhea. Very rare (< 1/10000): Pain in the limbs. These undesirable effects are usually transient and do not require withdrawal of the medicine. Orange yellow S (E110) can trigger allergic reactions. **Warnings:** Hepa-Merz® Granules contain fructose. Patients with rare hereditary problems of fructose intolerance should not take this medicine. **Further precautions:** As a result of the disease, the ability to drive and operate machinery may be impaired during treatment with L-ornithine-L-aspartate.

Hepa-Merz® Infusion concentrate. Active substance: L-ornithine-L-aspartate. **Composition:** One ampoule of 10 ml contains: **Active substance:** 5 g L-ornithine-L-aspartate. **Excipients:** Water for injections. **Therapeutic indications:** Latent and manifest hepatic encephalopathy. **Contraindications:** Absolute: Hypersensitivity to L-ornithine-L-aspartate. Severe renal impairment (renal failure). A serum creatinine level in excess of 3 mg/100 ml can be taken as a guide. Relative: Pregnancy and lactation: There are no clinical data available on the use of Hepa-Merz® Infusion concentrate in pregnancy. L-ornithine-L-aspartate has been investigated for reproduction toxicity only to a limited extent in experimental animal studies. The administration of Hepa-Merz® Infusion concentrate in pregnancy should therefore be avoided. If treatment with Hepa-Merz® is nevertheless thought to be necessary, the benefits and risks should be carefully assessed. It is not known whether L-ornithine-L-aspartate passes into breast milk. Administration of Hepa-Merz® should therefore be avoided during lactation. If treatment with Hepa-Merz® is nevertheless thought to be necessary, the benefits and risks should be carefully assessed. **Undesirable effects:** Uncommon (≥ 1/1000 to < 1/100): Nausea. Rare (≥ 1/10000 to < 1/1000): vomiting. Frequency not known (frequency cannot be estimated from the available data): hypersensitivity, anaphylactic reaction. Generally however, the gastrointestinal symptoms are transient, and do not necessitate discontinuation of treatment. They disappear on reduction of the dose or the infusion rate. **Further precautions:** Hepa-Merz® concentrate for solution for infusion can be mixed with the usual infusion solutions. So far no peculiarities have been observed with regard to miscibility. However, the ampoules should be admixed to the infusion solution only immediately before application. At high doses of Hepa-Merz® Infusion concentrate, serum and urine urea levels should be monitored. If liver function is substantially impaired, the infusion rate must be adjusted to the individual patient in order to prevent nausea and vomiting. Depending on the underlying disease, the ability to drive and operate machines may also be impaired on treatment with L-ornithine-L-aspartate. Hepa-Merz® Infusion concentrate must not be injected into an artery. Status: January 2013. Merz Pharmaceuticals GmbH, 60048 Frankfurt.

Reference: Mittal VV, Sharma BC, Sharma P, Sarin SK. A randomized controlled trial comparing lactulose, probiotics, and L-ornithine L-aspartate in treatment of minimal hepatic encephalopathy. Eur J Gastroenterol Hepatol. 2011;23(8):725-732.

For more information, visit **www.merz.com**