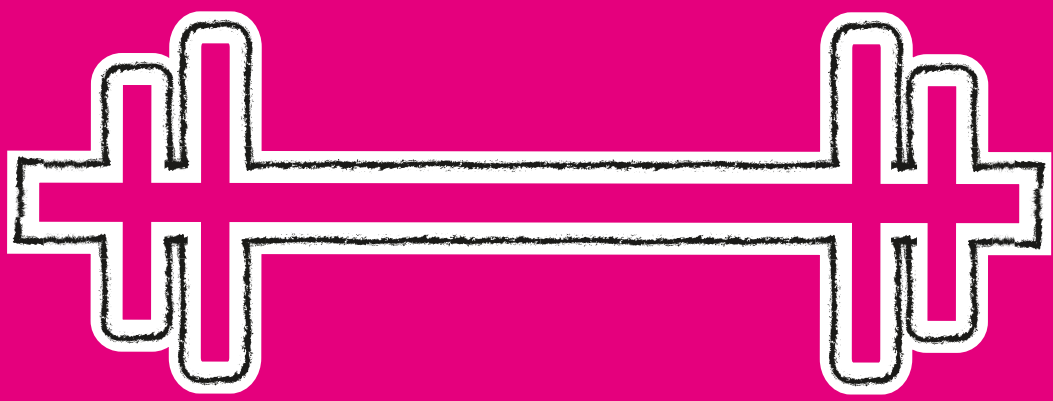
SCIENCE

THE MULTI-DIMENSIONAL BURDEN OF CIRRHOSIS AND HEPATIC ENCEPHALOPATHY ON PATIENTS AND CAREGIVERS



Bajaj JS, Wade JB, Gibson DP, Heuman DM, Thacker LR, Sterling RK, et al. Am J Gastroenterol. 2011;106:1646-1653.

Hepa-Merz®
L-ornithine-L-aspartate

EVALUATING THE IMPACT AND BURDEN OF HE

Introduction

- Hepatic encephalopathy (HE) is associated with cognitive deficits and waning mental status.
- The impact of liver cirrhosis and HE on the financial status of the patients and the burden on their caregivers have not previously been evaluated.

Study

Objective

To study the emotional and socioeconomic impact of liver cirrhosis and HE on patients and their caregivers.

Design

- Cross-sectional study in 104 cirrhotic patients with or without HE and their caregivers
- Patients and caregivers were interviewed separately at a one time study visit

Patient population

Causes of liver cirrhosis were chronic hepatitis C (44%), non-alcoholic steato-hepatitis (23%), alcohol consumption + hepatitis C (11%), alcohol consumption (7%) and other causes (15%). Only cirrhosis patients with resolved HE (minimal health status exam >25) and no cancer patients were included.

Tests performed

- Patients: Cognitive test battery, sociodemographic and financial questionnaire
- Caregivers: Caregiver burden and Zarit Burden Interview (ZBI)-Short Form

Results

- Only 12.5% of patients with previous HE were currently working vs. 81% of those without previous HE
- Previous HE decreased yearly family income

Previous HE negatively affects cognitive function, as well as employment capability and financial status of the patients.

- The degree of caregiver burden was highly correlated with the patient's cognitive impairment
- Control of HE by reducing intracerebral ammonia level led to significantly improved Zarit burden and total perceived caregivers burden

Patients with previous HE are a significantly higher burden on their caregivers, especially with regard to schedule, personal health, and sense of entrapment.

SIGNIFICANT BURDEN OF PREVIOUS HE AND COGNITIVE DYSFUNCTION

Impact of previous HE on patients

Patients	No previous HE (n = 58)	Previous HE (n = 46)
Age (years)	58.6 (6.3)	57.1 (7.0)
Model-for-end-stage liver disease score	**10.7 (5.0)**	**15.5 (5.7)***
Diabetes mellitus	35%	37%
On chronic pain therapy	16%	15%
Depression requiring therapy	32%	14%
Anxiety requiring therapy	10%	10%
Currently working	**81%**	**12.5%***
Need to decrease hours	**39%**	**71%***
Worse off regarding job	**47%**	**74%***
Worse off regarding financial status	**61%**	**85%***
Median duration they would continue to live if all income stopped	**7–12 months**	**1–2 months***
Median longest period free of work	**21 days**	**365 days***
Dept from cirrhosis	36%	54%

Impact of preveoius HE on the patients' caregivers

Caregivers	No previous HE (n = 58)	Previous HE (n = 46)
Zarit burden interview	**11.5 (8.4)**	**16 (9)***
Total perceived caregivers burden	**65 (21.8)**	**75.4 (19.2)***
Impact on finances	9.3 (3.3)	10.6 (4.1)
Sense of abandonment	14.6 (7.2)	13.8 (3.3)
Impact on schedule	**11.9 (7.0)**	**16.1 (6.2)***
Impact on personal health	**15.6 (4.1)**	**17.8 (3.7)***
Sense of entrapment	**13.4 (6.5)**	**17.3 (8.3)***

* $p < 0.05$
Values represent means (± standard deviation).

Hepa-Merz®
L-ornithine-L-aspartate

CIRRHOSIS AND HE LINKED WITH HIGH EMOTIONAL AND SOCIOECONOMIC BURDEN

Conclusion

Hepatic encephalopathy and cognitive dysfunction are associated with worse employment and financial status, as well as increased caregiver burden.

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: Bajaj JS, Wade JB, Gibson DP, Heuman DM, Thacker LR, Sterling RK, et al. The multi-dimensional burden of cirrhosis and hepatic encephalopathy on patients and caregivers. Am J Gastroenterol. 2011;106:1646-1653.

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