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## The [<sup>13</sup>C]methacetin breath test: An alternative for monitoring valproic acid therapy in epilepsy during childhood?

### [<sup>13</sup>C]Methacetin Atemtest

#### Introduction

Valproic acid is a widely used antiepileptic drug which causes liver damage in up to 30% of patients undergoing treatment with this potent pharmacological agent. To detect early alteration of liver function during therapy with valproic acid, a valid and non-invasive method would be of great clinical interest.

#### Aim

The aim of this study was to prove the use of the [<sup>13</sup>C]methacetin breath test as a predictive method of detecting early liver dysfunction caused by valproic acid.

#### Materials and methods

In 4 patients with general epilepsy (age: 3.5 to 16 years, weight: 16.4 to 64.5 kg) valproic acid was therapeutically

introduced. Prior to and 6 weeks after introduction of valproic acid therapy the [<sup>13</sup>C]methacetin breath test was performed. An oral single-pulse-labeling of 4 mg/kg [<sup>13</sup>C]methacetin was administered. Thereafter, breath samples were collected every 15 minutes over a two-hour period, then every 30 minutes over a 6-hour period. Marked <sup>13</sup>CO<sub>2</sub> was measured by IRMS (Tracer mass 20 - 20, Europe Scientific, Crewe, U.K.).

#### Results

Prior to valproic acid therapy <sup>13</sup>CO<sub>2</sub> reached a maximum level of 31.0 DOB after 1.25 hours. The mean percentage of cumulative <sup>13</sup>CO<sub>2</sub>-exhalation was 31.4% after 8 hours. Six weeks after introduction of valproic acid therapy the maximum level of <sup>13</sup>CO<sub>2</sub> reached 19.9 DOB after 1.25 hours. The mean percentage of cumulative <sup>13</sup>CO<sub>2</sub> exhalation reached 29.3% after 8 hours. This was, however, not statistically significant compared to the data measured 6 weeks earlier.

#### Discussion

The metabolising mechanism of [<sup>13</sup>C]methacetin to <sup>13</sup>CO<sub>2</sub> is probably influenced by valproic acid which causes a liver alteration. One would assume to find a reduced <sup>13</sup>CO<sub>2</sub> exhalation as a result of a reduction of liver metabolising capacity.

#### Conclusion

At present, we cannot definitely state whether the presented data are reliable enough to detect early liver alteration induced by valproic acid.

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