Cerebrolysin in traumatic brain injury – A pilot study of a neurotrophic and neurogenic agent in the treatment of acute traumatic brain injury

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Results
The patients’ disposition analysis showed a difference in the average age between the Cerebrolysin (younger patients) and control group. Vital parameters and lab values did not differ significantly between the two groups with the exception of increased blood loss in the control group. The change in severity over time for the study shows a significantly more prominent and faster remission in the Cerebrolysin group (Fig. 1). Figure 2 shows a change of the GCS item “eye opening”, beginning in the first week in the Cerebrolysin group. Also, the item “best verbal response” (Fig. 3) showed a statistically significant difference between Cerebrolysin and placebo for all weeks of treatment. Again, for the GCS item “motor response”, the difference to placebo was significant for the first two weeks of treatment with Cerebrolysin (Fig. 4). The change in consciousness/ise is recorded in figure 5, showing the statistically highly significant remission under Cerebrolysin therapy. This is corroborated by the reduction of the GCS global score as shown in figure 6. The differences between the two groups (weeks and placebo) in the different weeks of treatment attain high significance (p<0.0001) and also in the same phase p<0.0006. Figure 7 shows GCS scores of all patients in the course of treatment during the first weeks. Cerebrolysin patients score better than placebo-treated patients. The change in the individual patient's orographic performance was rated with IFT. Figure 8 shows a statistically significant difference between Cerebrolysin and placebo for the whole duration of the study, but most prominently in week 2. In figure 9 the change is given as percent of change; positive results are opposed to negative ones. In both samples, the positive results are mostly found in the Cerebrolysin group: the negative results in placebo-treated patients except for week 4.

Conclusions
Optimal treatment of brain trauma should ideally attain several goals: in acute treatment, a reduction of increased blood loss in the control group. The change in severity over time for the study shows a significantly more prominent and faster remission in the Cerebrolysin group (Fig. 1). Figure 2 shows a change of the GCS item “eye opening”, beginning in the first week in the Cerebrolysin group. Also, the item “best verbal response” (Fig. 3) showed a statistically significant difference between Cerebrolysin and placebo for all weeks of treatment. Again, for the GCS item “motor response”, the difference to placebo was significant for the first two weeks of treatment with Cerebrolysin (Fig. 4). The change in consciousness/ise is recorded in figure 5, showing the statistically highly significant remission under Cerebrolysin therapy. This is corroborated by the reduction of the GCS global score as shown in figure 6. The differences between the two groups (weeks and placebo) in the different weeks of treatment attain high significance (p<0.0001) and also in the same phase p<0.0006. Figure 7 shows GCS scores of all patients in the course of treatment during the first weeks. Cerebrolysin patients score better than placebo-treated patients. The change in the individual patient's orographic performance was rated with IFT. Figure 8 shows a statistically significant difference between Cerebrolysin and placebo for the whole duration of the study, but most prominently in week 2. In figure 9 the change is given as percent of change; positive results are opposed to negative ones. In both samples, the positive results are mostly found in the Cerebrolysin group: the negative results in placebo-treated patients except for week 4.

Related references
1 Original article: J Neurol Neurochirurgie Psychiatrie 2006;7:12-20

Introduction
Numerous in vitro studies have documented the neuroprotective, neurotrophic and neurogenic properties of Cerebrolysin, a standardized protein brain-derived, stabilized, aqueous protein solution, various protein molecules of which can pass the blood–brain barrier. We conducted a double-blind, placebo-controlled, add-on study of Cerebrolysin in the treatment of traumatic brain injury.

Methods
The study was conducted in 5 centers comparing 44 patients, 33 in each group: Vital parameters and laboratory values were controlled. Half of the patients received Cerebrolysin together with 50ml of 5% NaCl solution i.v. drip. The placebo group had 100 ml of 5% NaCl solution i.v. drip each for 15 minutes for a period of three weeks (21 days). We included patients of both sexes after receiving informed consent signed by the patient or the legal representative. The patients were between the ages of 19–60 years with a degree of severity from>4 to<11 in Go web-scope. The patients were randomly allocated to receive a placebo infusion at a rate of 5 ml/kg body weight per dose on days 7, 14, 21, 42 and 63. On days 7, 21 and 63, version B of the SKT and on days 14 and 42, rating instruments we applied the Glasgow-Coma-Scale (GCS) and the Clinical-Global-Impression (CGI) rated by blinded experienced staff, cognitive capacities were assessed by qualified blinded neuropsychologists using the “Short Synthemat Scale” (Symptom-Questionnaire (SSQ)). Adverse effects were documented with the DOUTE/PBS scale. These assessments were performed at inclusion and on days 7, 14, 21, 42, 52 and 63. On days 7, 21, 31, versions of the DCS and in days 14, 42, version C were applied to prevent possible learning or habitation effects. Statistical computations were based on the intent-to-treat principle under application of the non-parametric Mantel-Haenszel Test and multiple non-parametric u-tests for independent samples, controlled by t-tests. For intra-individual comparisons, the non-parametric Wilcoxon test was applied and categorical variables were calculated by chi-square test, the statistics following the EU Guidelines for Statistics.

TBI: clinical data

Fig. 1. Severity of illness in CGI during the course of the study
Statistically, the Mantel-Haenszel Test showed a non-significantly greater difference between placebo and Cerebrolysin (p = 0.058) for the severity of illness in the whole study period, indicating a trend and faster improvement with Cerebrolysin.

Fig. 2. GCS I – item “eye opening”
Analyzing effects of treatment over time with the Mantel-Haenszel Test showed a statistically significant difference of p = 0.029 and analysis of variance 3.85 points and occurred in week 1. Also, the item “on eventual” only, in week 1.

Fig. 3. GCS I – item “best verbal response”:
The Mantel-Haenszel Test showed a statistically significant difference of p = 0.0001 on the two-tailed 5% level. Similar distribution ratios were calculated for Cerebrolysin and placebo in.

Fig. 4. GCS I – item “best motor response”:
Also, for this item Mantel-Haenszel analysis of differences showed a significant difference of p = 0.0001 on the two-tailed 5% level. The scores show a different pattern than the previous ones: If reaction, localization and answer to commands are taken into account.

Fig. 5. Level of consciousness
Statistical analysis showed no significant group difference at any time but trend towards a significant neurogenic of results over time. These results do not confirm the hypothesis that Cerebrolysin might have a neurotrophic effect. However, Mantel-Haenszel analysis of effects of treatment over time showed a statistically significant treatment difference (p =< 0.0001) on the two-tailed 0.1% level, indicating a better recovery under Cerebrolysin.

Fig. 6. GCS scores for overall level of consciousness
Reduction of increased blood loss in the control group. The change in severity over time for the study shows a significantly more prominent and faster remission in the Cerebrolysin group (Fig. 1). Figure 2 shows a change of the GCS item “eye opening”, beginning in the first week in the Cerebrolysin group. Also, the item “best verbal response” (Fig. 3) showed a statistically significant difference between Cerebrolysin and placebo for all weeks of treatment. Again, for the GCS item “motor response”, the difference to placebo was significant for the first two weeks of treatment with Cerebrolysin (Fig. 4). The change in consciousness/ise is recorded in figure 5, showing the statistically highly significant remission under Cerebrolysin therapy. This is corroborated by the reduction of the GCS global score as shown in figure 6. The differences between the two groups (weeks and placebo) in the different weeks of treatment attain high significance (p<0.0001) and also in the same phase p<0.0006. Figure 7 shows GCS scores of all patients in the course of treatment during the first weeks. Cerebrolysin patients score better than placebo-treated patients. The change in the individual patient's orographic performance was rated with IFT. Figure 8 shows a statistically significant difference between Cerebrolysin and placebo for the whole duration of the study, but most prominently in week 2. In figure 9 the change is given as percent of change; positive results are opposed to negative ones. In both samples, the positive results are mostly found in the Cerebrolysin group: the negative results in placebo-treated patients except for week 4.

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