Gamma Aminobutyric Acid Receptor Agonists for Acute Stroke

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Gamma aminobutyric acid (GABA) receptor agonists have shown to be effective in reducing infarct size and improving functional outcome in animal models of cerebral ischemia. However, the sedation effects of GABA receptor agonists limited the application in acute stroke patients because of the potential risk of stupor.

Materials and Methods

Objective
The aim of this study is to determine the efficacy and safety of GABA receptor agonists in the treatment of acute stroke.

Types of Studies
Randomized controlled trials.

Types of Participants
Acute stroke patients within 12 hours after stroke onset.

Types of Interventions
GABA receptor agonists in comparison with placebo.

Primary Outcomes
Death or dependency, defined as a Barthel Index score of ≤60, or the modified Rankin Scale graded 3 to 5, and adverse events.

Secondary Outcomes
Functional independence, defined as Barthel Index score >60, or modified Rankin Scale <3, and neurological function measured by other stroke scales.

Results
We included 5 trials with 3838 randomized patients. The methodological quality of the included trials was generally good, with low risk of bias. Four trials measured death and dependency at 3 months in chlormethiazole versus placebo without significant difference (2909 patients; risk ratio [RR], 1.03; 95% confidence interval [CI], 0.95–1.11). One trial measured this outcome between diazepam and placebo (849 patients; RR, 0.94; 95% CI, 0.82–1.07). In the subgroup analysis of total anterior circulation syndrome, a higher percentage of functional independence was found in the chlormethiazole group (635 patients; RR, 1.33; 95% CI, 1.09–1.64). The frequent adverse events related to chlormethiazole were somnolence (2527 patients; RR, 4.56; 95% CI, 3.50–5.95) and rhinitis (2527 patients; RR, 4.75; 95% CI, 2.67–8.46).

Conclusions
The results demonstrated no benefits from GABA receptor agonists for acute stroke patients compared with placebo.
(ie, no decreases in death or dependency were found; Figure). The subgroup analysis in total anterior circulation syndrome illustrated a positive result in functional independence. The most frequent adverse events caused by chlormethiazole were somnolence and rhinitis.

**Implications for Practice**
No evidence was found to support the use of GABA receptor agonists for the treatment of patients with acute stroke.

**Implications for Research**
Well-designed, double-blind randomized controlled trials would be required to test the efficacy of chlormethiazole in a large group of patients with total anterior circulation syndrome.

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**Disclosures**
None.

**Reference**

**KEY WORDS:** acute stroke ■ chlormethiazole ■ diazepam
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