

# Levodopa plus carbidopa before physiotherapy increased motor recovery after stroke

Scheidtmann K, Fries W, Müller F, Koenig E. Effect of levodopa in combination with physiotherapy on functional motor recovery after stroke: a prospective, randomised, double-blind study. *Lancet*. 2001 Sep 8;358:787-90.

## QUESTION

In patients who had a stroke, is levodopa more effective than placebo, when given before physiotherapy sessions, for enhancing motor recovery?

## DESIGN

Randomized (unclear allocation concealment\*), blinded (participants, health care providers, and outcome assessors),\* placebo-controlled trial with 6-week follow-up.

## SETTING

A rehabilitation hospital in Germany.

## PATIENTS

53 patients who had a stroke 3 weeks to 6 months before randomization and a radiologically verified thromboembolic brain infarction. Exclusion criteria were depression according to *Diagnostic Statistical Manual IV* criteria or treatment with selective serotonin-reuptake inhibitors or tricyclic antidepressants. 47 patients (89%) (mean age 62 y, 55% men) were included in the analysis.

## INTERVENTION

Patients were allocated to levodopa, 100 mg, plus carbidopa ( $n = 26$ ) or to placebo

( $n = 27$ ) given daily in the morning  $\geq 30$  minutes before the physiotherapy session for 3 weeks. For the next 3 weeks, both groups had 1 hour of daily physiotherapy from Monday to Friday without the allocated treatment, 1 week before and during the study, all patients stopped receiving any drugs that affected norepinephrine concentrations.

## MAIN OUTCOME MEASURE

Motor function assessed with the Rivermead Motor Assessment scale.

## MAIN RESULTS

Levodopa plus carbidopa before physiotherapy was more effective than placebo before physiotherapy for increasing overall motor function at 3 ( $P < 0.004$ ) and 6 weeks ( $P < 0.02$ ) (Table). Levodopa plus carbidopa

before physiotherapy was more effective than placebo for increasing arm function at 3 ( $P < 0.015$ ) and 6 weeks ( $P < 0.008$ ).

## CONCLUSION

In patients who had a stroke, levodopa plus carbidopa before physiotherapy sessions increased motor recovery more than did placebo.

Source of funding: In part, DuPont Pharma (Germany).

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\*See Glossary.

## Levodopa plus carbidopa vs placebo before physiotherapy sessions after stroke†

Outcomes	Levodopa	Placebo	Difference in score between groups (95% CI)‡
Overall motor function (3 wk)	13.6	9.7	3.9 (0.55 to 7.2)
Overall motor function (6 wk)	15.4	11.3	4.1 (0.59 to 7.6)

†Outcomes assessed with Rivermead Motor Assessment scale.

‡CI calculated from data provided by author.

## COMMENTARY

The study by Scheidtmann and colleagues describes a novel approach to rehabilitation after stroke, assessing the effects of 3 weeks of treatment with levodopa plus carbidopa (Sinemet) on responses to physical rehabilitation. The findings show a statistically significant increase in motor function with the short-term use of levodopa in patients with hemiplegic ischemic stroke. The magnitude of improvement in impairment and disability is potentially clinically relevant. If these findings are correct, they would have major implications for the treatment of stroke.

Although the study design was good, some methodologic limitations exist. Patients who were recruited varied greatly in their degree of impairment at baseline, including those who were early in the recovery phase after stroke and those late after the period of maximal motor recovery. This small trial has differences between groups at baseline: Patients in the levodopa group were younger, recruited later after stroke onset, and less impaired or disabled at study entry and had a lower proportion of right hemispheric strokes than did those in the placebo group. Any of these factors could result in bias of the study outcome. No attempt was made to correct for these baseline differences by using

a multivariate analysis, as recommended in a previous authoritative article (1). The study was relatively short term, and gains would need to be sustained over a longer period to show a clinically important effect on impairment and disability after stroke.

Anecdotal case reports exist claiming that drug therapy with levodopa or dopaminergic agonists may also enhance recovery in traumatic brain injury (2). However, at the present time, insufficient evidence exists to recommend this treatment in routine clinical practice.

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## References

- Assmann SE, Pocock SJ, Enos LE, Kasten LE. Subgroup analysis and other (mis)uses of baseline data in clinical trials. *Lancet*. 2000;355:1064-9.
- Karli DC, Burke DT, Kim HJ, et al. Effects of dopaminergic combination therapy for frontal lobe dysfunction in traumatic brain injury rehabilitation. *Brain Inj*. 1999;13:63-8.