Short report

Trial of ganglioside GM1 in acute stroke

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SUMMARY Ganglioside GM1 (100 mg) was given daily by intramuscular injection for 28 days in a double-blind placebo controlled trial of acute stroke. No significant difference was detected in a 6 month follow-up period between well matched control and active groups. Although the number of patients studied was small the findings are believed to indicate that GM1 is unlikely to be of value in the treatment of acute stroke in the dose and route of administration used.

Brain gangliosides are natural components of neuronal membranes and play a role in neuronal development, differentiation and regeneration probably by acting synergistically with endogenous nerve growth factors. Two studies have shown evidence that GM1, a component of the ganglioside series, may have a beneficial effect on recovery from stroke. In both trials the final evaluation was at only 6 weeks and was by neurological, electrophysiological and computed tomographic (CT) assessment. We have conducted a double-blind placebo controlled single centre study in acute stroke using a larger dose of GM1, earlier treatment and final assessment at 6 months.

Methods

All patients aged 35 to 85 years presenting within 72 hours of the onset of a cerebral hemisphere stroke with limb weakness were assessed. Patients were excluded if they were premenopausal, in poor general health, had a history of previous stroke, or a condition, neurological or otherwise, that would interfere with clinical assessment and rehabilitation. After stratification based on initial examination there was random double blind allocation of patients to treatment with GM1 100 mg intramuscularly or matching saline placebo daily for 28 days. Standard rehabilitation and physiotherapy was conducted by staff unassociated with the trial and all other medication was continued and altered as indicated by the physicians concerned. Neurological and functional assessment by the Barthel index was made by PB, SO or CS at entry, and one week, one, 3 and 6 months after entry. Haematological and biochemical examinations were made at entry to the study and repeated at the end of treatment. CT of the head was done as soon as possible and generally 5–6 days after stroke onset. Between-group comparisons were made using unpaired t tests or Mann-Whitney tests, on both raw data and within group changes from baseline. Confidence intervals 95% for the difference between the group means were calculated for the Barthel index scores which appeared normally distributed. The trial was conducted under terms of permission granted by the Committee on Safety of Medicines and was approved by the Islington Health District Ethical Committee. Patients or their relatives gave informed consent.

Results

The table shows that the GM1 and placebo groups were very similar in clinical state, underlying pathology and risk factors for stroke. Only one in five of those assessed (54 out of 257) proved eligible for entry, the major exclusions being due to coma, poor general health, previous neurological disease and aged over 85 years. There was one secondary exclusion due to tumour. The GM1 withdrawals were due to epilepsy 5 months after entry, and neurosurgery for a haematoma. The placebo withdrawals were due to a second stroke and lost records. There were no significant differences between the two groups at any assessment time in deaths, clinical neurology scores (not shown) or Barthel index scores (table). The 95%
confidence intervals of the difference between the
means (GM1—placebo) were +16·8 to −21·0 and
+23·2 to −7·4 at 1 and 6 months respectively. There
were no adverse reactions or significant change in
laboratory investigations in either group.

Discussion

A major problem in the assessment of the new treat-
ments in acute stroke is the beta error inherent in trials
with relatively small numbers of cases. Trials of ade-
quate statistical power generally require multicentre
studies which introduce their own problems and are
extremely costly. Confidence intervals analysis pro-
vides a method of more precise evaluation of results
obtained.5

Although there was a lower mortality rate in the
patients receiving GM1, our findings make it evident
that only a larger study with either higher doses
and/or a different route of administration (intra-
venous) may show a worthwhile clinical effect. From
the sample we studied, we could not detect differences
in responses between haemorrhagic and ischaemic
stroke patients so that it is difficult to predict whether
selecting cerebral infarction alone would be more
effective. Results from on-going multicentre inter-
national studies on administration of GM1 in the
early stages of stroke (D Massari, personal commu-
nication) are awaited with interest.

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