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Granulocyte-colony stimulating factor for mobilizing bone marrow stem cells in the sub acute stroke. How safe is the use of granulocyte-colony stimulating factor in sub-acute stroke? Is this stem cell trial of recovery enhancement beneficial?

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Efforts are being made to develop neuroprotective agents for recovery and prevention of further deterioration of brain tissues in patient with stroke.Granulocyte-colony stimulating factor (GCSF) is a glycoprotein hormone encoded by a single gene located on chromosome 17q 11-22. It functions in the regulation of granulopoiesis& terminal maturation of neutrophills. It is being used for the treatment of neutropenia for the production of CD34+ haematopoietic stem cell (HSC) for bone marrow transplant patients. Neuroprotective effect of GCSF is being studied in various experimental studies but its mechanism of action is not well understood and appears to be multimodal.

What is this study?

This was a randomized, double blind, placebo-controlled phase IIB trial for the assessment of safety of use of GCSF in patients with recent stroke, and also to study its effect on mobilization of bone marrow derived haematopoietic stem cells and their fate in brain tissue.

Who were the participants?

A total of 60 patients were included from 205 screened participants between 3-30 days after ischaemic and haemorrhagic stroke from July 2007 to January 2010 from a single center. They were divided into two groups in a ratio of 2:1 in treatment vs. placebo group. Both groups were well matched for their base line characters and prognostic factors.

What was the intervention?

Patients were randomly assigned into treatment and placebo group. Treatment group was given Granulocyte- colony stimulating factor (GCSF)10ug/kg of against a matched saline in placebo group subcutaneously for 5 days in a double blinded fashion. All the patients were given an opportunity for haematopiietc stem cell labeling for another substudy. Volumetric analysis of infracted tissue in the brain was also performed in both groups for patients in whom it was possible.

What was the outcome?

There was no statistical difference between the two groups in terms of primary outcome e.g. severe adverse event (SEA) at 90 days, GCSF 37.5% vs. 35%in placebo group.. There was no difference in the vascular events in two groups. GCSF increased CD34+ and total white cell count by 9.5 and 4.2 folds respectively.

Only one participant showed migration of iron labeled CD34+ cell in the ischaemic stroke lesion. There was a reduction in the volume of ischaemic lesion in the MRI of the GCSF treated patients. A subgroup analysis showed functional improvement in the GCSF treated group as appeared by improved NIHSS score.

Why is this study important and noteworthy?

The author concluded that GCSF administration was safe in patients with sub-acute stroke. Improvement in the functional status of GCSF treated patients along with the stroke lesion volume also favours some neurorepair properties of GCSF but needs further evaluation. Mobilization of CD34+ cells to the ischaemic brain lesion opens future molecular level research question for further studies.

This trial had avery small sample size which limits the interpretation of results for a larger group of population but this provides a solid ground for future studies in evaluating the efficacy of GCSF as neuroprotective and repair agent for stroke patients. Many Phase III trials are required before the implication of GCSF as neuroprotective agent in the treatment of

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stroke opening a new era for the treatment of this devastating disease.

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Recommended Reading

1. Granulocyte-colony stimulating factor for mobilizing bone marrow stem cells in subacute stroke: the stem cell trial of recovery enhancement after stroke 2 randomized controlled trial. England TJ, Abaei M, Auer DP, Lowe J, Jones DR, Sare G, Walker M, Bath PM. Stroke 2012; 43: 405-11.