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Efficacy of hydroxyurea in reducing the erythropoietic stress of ineffective erythropoiesis in transfusion dependent beta thalassaemia: A randomised, double-blind placebo-controlled clinical trial

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The unbalanced synthesis and accumulation of α -globin chains due to impaired synthesis of β -globin results in the destruction of red blood cells (RBC) and erythroid precursors of patients with β -thalassaemia. This leads to an increased erythropoietic activity and ineffective erythropoiesis in the bone marrow of these patients. Hydroxyurea is a licenced medication that decreases the RBC destruction of patients with β -thalassaemia. However, its effect on erythropoietic stress is unclear. In this study, our objective was to evaluate the effect of hydroxyurea on erythropoietic stress of ineffective erythropoiesis in transfusion-dependent (TD) β -thalassaemia. This experimental study was carried out at the Thalassaemia Unit of Colombo North Teaching Hospital as part of a randomised, double-blind placebo-controlled clinical trial that evaluates the efficacy of hydroxyurea. We recruited 24 patients with TD β -thalassaemia who were taking hydroxyurea 10-20 mg/kg/day and 16 patients who were receiving a placebo. The erythropoietic stress of ineffective erythropoiesis was assessed by measuring serum soluble transferrin receptor (sTfR) levels before and six months after taking either hydroxyurea or placebo. Levels of sTfR were measured using a validated enzyme-linked immunosorbent assay. Paired t-test was used in the statistical analysis. Nineteen (79%) out of 24 patients who received hydroxyurea showed a reduction in sTfR level, of which 8 (33%) and 6 (25%) showed >25% and 10-25% reductions, respectively. A significant reduction in mean sTfR level was observed after hydroxyurea treatment ($72.3 \pm SD 25.9$) compared to pre-treatment levels ($89.6 \pm SD 22.9$), ($p < 0.01$). Conversely, no difference in sTfR levels was seen in patients who received the placebo pre- ($91.9 \pm SD 24.7$) and post-treatment ($96.4 \pm SD 19.4$), ($p = 0.17$). In conclusion, oral hydroxyurea significantly reduced the erythropoietic stress of ineffective erythropoiesis in patients with TD β -thalassaemia showing a promise as a treatment modality.

Keywords: β -thalassaemia, hydroxyurea, serum soluble transferrin receptors, ineffective erythropoiesis

Acknowledgement: Financial assistance by National Research Council Research grant 18-030

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