SAFETY AND EFFICACY OF HYDROXYUREA IN CHILDREN AND ADOLESCENTS WITH SICKLE/BETA-THALASSEMIA: THE GREEK EXPERIENCE

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BACKGROUND

Hydroxyurea is a cytotoxic, antimitabolite and myelosuppressive drug that has been used over the last years in adult patients with sickle cell disease (SCD), resulting in reduction in pain crises, hospitalizations and need for transfusions. Hydroxyurea has also been used, during recent years, in the treatment of children with severe SCD. However, data on young patients with a mild clinical course, such as usually present in sickle/beta-thalassemia, is limited.

AIM

The aim of the present study was to evaluate the safety and efficacy of hydroxyurea in Greek children and adolescents with S/beta-thalassemia.

PATIENTS-METHODS

13 patients (8 girls and 5 boys) with S/beta-thalassemia, aged 9.42±4.5 years (3.5-18), were included in the study.
- Hydroxyurea’s daily dose ranged from 15-25 mg/kg, with a mean of 18.6 mg/kg.
- Treatment was given for 12 months.

Laboratory and clinical follow-up consisted of:
- White blood cell count, hemoglobin, hematocrit, red blood cell indices, reticulocyte count and platelets count measured every 2 weeks.
- Biochemistry measured every 2 months.
- Hemoglobin F measured every 2 to 3 months.
- Patients were clinically evaluated on every visit.
- Clinical course and adverse events were reported for the study period.

RESULTS

- A reduction of pain crises as compared to the year before treatment (median:2, 0-5 vs median:0, 0-3, p=0.003) as well as of hospitalizations (median:1, 0-3 vs median:1, 0-1, p=0.014) was noted.
- None of the patients presented with a severe clinical event (acute chest syndrome, avascular bone necrosis, stroke, splenic sequestration crisis) during the study period.
- An increase in hemoglobin, fetal hemoglobin, mean corpuscular volume and mean corpuscular hemoglobin and a decrease in reticulocyte count, white blood cell count, platelet count, total bilirubin and indirect bilirubin level was noted (Table 1).
- With regards to adverse events, 2 patients had mild transaminasemia, 2 had mildly elevated serum creatinine levels, one transient thrombocytopenia and one transient leukopenia with neutropenia. All of the above mentioned toxicities were short-term and dose-dependable.

| Table 1. Laboratory parameters (mean ± SD) during HU treatment. |
|-------------------------|-----------------|-----------------|
|                         | Entry 12 months | p-value         |
| Hb (g/dl)               | 9.2 ± 0.7       | 9.7 ± 0.8       | 0.048           |
| HB (%)                  | 9.1 ± 5.9       | 23.4 ± 8.9      | <0.001          |
| MCV (fl)                | 66.5 ± 3.7      | 86.5 ± 9.5      | <0.001          |
| MCH (pg)                | 21 ± 1.1        | 27.5 ± 2.9      | <0.001          |
| WBC (/μL)               | 9854 ± 3402     | 7607 ± 3401     | 0.013           |
| PLT (/μL)               | 382153 ± 184509 | 290307 ± 135675 | 0.005          |
| Reticulocyte count (%)  | 9.4 ± 4.5       | 4.2 ± 2.3       | <0.001          |
| Total bilirubin (mg/dl) | 2.2 ± 1.4       | 1.3 ± 0.6       | 0.019           |
| Indirect bilirubin (mg/dl) | 1.8 ± 1.2     | 1 ± 0.5         | 0.016           |

CONCLUSIONS

To the best of our knowledge, this is the first study to specifically assess the effect of hydroxyurea therapy in young patients with S/beta-thalassemia and of the same ethnic origin. The study shows that hydroxyurea treatment is safe and efficacious in this patient cohort, however, long-term follow up and evaluation of possible protective effect on organ dysfunction is warranted.

REFERENCES