compared to the recommended daily allowance of folic acid; and (v) the proposed competition of folic acid with methotrexate for renal excretion may in fact increase the exposure of leukemic cells to methotrexate in presence of adequate folic acid [1].

Nutritional deficiency of folate and its further depletion with chemotherapy is common in children with ALL, especially in countries with high prevalence of malnutrition and lack of folate fortification [2]. Despite a documented higher infection-related deaths during induction, and interruption of maintenance chemotherapy in folate deficient children, the theoretical concern of increased relapse has prevented us from supplementing with folic acid. Developed countries with mandatory folate fortification have not encountered increased relapses in the post-fortification era; this is further supported by data from adults where routine folate use during chemotherapy helps in improving the chemotherapy tolerance without compromising efficacy [3].

We propose that careful consideration should be given towards folic acid supplementation in deficient children undergoing chemotherapy for ALL, especially in countries without mandatory folate fortification.

NIRMALYA ROY MOULIK AND ARCHANA KUMAR
Division of Pediatric Hematology-Oncology, Department of Pediatrics, King George’s Medical University, Lucknow, India.
archanakumar53@yahoo.co.in

REFERENCES

Low Dose of Carglumic Acid for Treatment of Hyperammonemia due to N-Acetylglutamate Synthase Deficiency

N-acetylglutamate synthase (NAGS) deficiency is an autosomal recessive disorder of the urea cycle. N-carbamylglutamate (NCG) is a structural analogue of human N-acetylglutamate and is licensed for the treatment of hyperammonemia due to NAGS deficiency [1,2].

A 5-day-old boy – first child of a consanguineous Turkish couple – had an elevated ammonia level of 328 mmol/L. Treatment with intravenous glucose, oral sodium benzoate (200 mg/kg/day) and arginine (200 mg/kg/day) was started and enteral feeding was stopped. Despite this, his ammonia level remained elevated. Carglumic acid was started with a dose of 100 mg/kg/day, and the ammonia level was normalized. His clinical and laboratory findings were consistent with NAGS deficiency. Mutation analysis revealed classical mutation of the NAGS gene (Exon6: c.1450T>C (p. Trp484Arg)). The patient was discharged with carglumic acid (100 mg/kg/day) and a protein-restricted, high-calorie diet.

The patient was not brought to our outpatient clinic for the following 6 months. At 8 months of age, he was not using protein-restricted diet, and the carglumic acid dose was reduced to 12.5 mg/kg/day as the child was now heavier. Carglumic acid dose was raised to 25 mg/kg/day. The patient did not attend to our clinic for another 7 months, and he was taking carglumic acid at the dose of 10 mg/kg/day when he was 15 months of age. Carglumic acid dose was again raised to 20 mg/kg/day, and a protein-restricted diet was continued. At 27 months, reported to emergency unit with an elevated ammonia level of 228 mmol/L along with an upper respiratory tract infection. The carglumic acid dose was raised to 50 mg/kg/day, and ammonia level
returned to normal within 6 hours. After hyperammonemia resolved, carglumic acid dosage was reduced to 30 mg/kg/day and protein-restricted diet was discontinued. The patient’s ammonia levels remained within normal limits. At 3 years of age, the patient has no neurodevelopmental abnormalities.

The initial NCG dosage for treatment of acute hyperammonemia ranges between 100 to 250 mg/kg/day [2,3]. After the acute episode, the lowest reported effective daily dosage is 15 mg/kg/day [4]. Our patient had no hyperammonemia episodes under NCG treatment with a dose of 10 mg/kg/day. However, it seems that a lower dose is not enough during illness, as he was using a dose of 20 mg/kg/day when he developed hyperammonemia along with an infection. NCG therapy appears to correct the metabolic defect; therefore, dietary protein can be increased to 2-3 g/kg/day in some patients [2,5]. In our child – after the NCG dosage was raised to 30 mg/kg/day – protein restriction was totally removed but the ammonia levels remained normal. We conclude that NCG is effective for controlling hyperammonemia in NAGS deficiency; at a much lower dose, except during acute infections.

**Steroids in Celiac Crisis: Doubtful Role!**

Celiac crisis is characterized by severe diarrhea, dehydration, hypokalemia, hyponatremia, hypomagnesaemia, hypocalcaemia, and hypoproteinemia. Although seen in all ages, it is most often seen in children younger than two years [1]. Apart from the usual supportive care, glucocorticoid therapy is usually required to achieve a successful recovery [2-4]. We present three patients who presented with celiac crisis. Despite adequate care and early institution of steroids the outcome was unfavourable in two of them.

First was a 9-year-old boy, and second a 4-year-old boy; both presented with history of recurrent diarrhea, weight loss and abdominal pain. Both patients were lethargic, emaciated, dehydrated and hypotensive. Serum level of tissue transglutamase (TTG) IgA antibodies was >200 IU/mL in both children. Endoscopy in second patient revealed flattened duodenal folds with scalloped margins, and partial villous atrophy. Both these patients received full supportive care, including intravenous hydro-cortisone. First patient died due to disseminated intra-vascular coagulation, and second did not improve; the parents got him discharged against medical advice.

Third patient was a 5-year-old girl, known case of celiac disease, who presented with worsening diarrhea, and weight loss, pedal edema. TTG levels were 190 IU/mL. This child received full supportive care; she gradually improved and was discharged after 3 weeks.

The reason why some patients with celiac disease have a much severe course is unclear. A combination of varied mucosal inflammation, immune activation and disruption of normal patterns of motility is likely [5]. The possible precipitating cause of crisis in our patients were severe malnutrition, hypoproteinemia, infection and late diagnosis. Corticosteroids are indicated in celiac crisis to reduce the mucosal inflammation, restore brush border epithelium enzymes and cause positive influence on the bowel epithelium maturation [1,3,4]. However, two of our patients deteriorated on steroids; third improved despite receiving no steroids. Use of steroids, especially with a probability of underlying sepsis, could be counterproductive. Further, steroids can exaggerate hypokalemia by causing kaliuresis. The role of steroids in celiac crisis needs further evaluation.

---

**References**