



GALENIC PREPARATIONS AND RARE DISEASES: GUANIDINOACETATE METHYLTRANSFERASE DEFICIENCY: EXPERIENCE IN A LOCAL HOSPITAL

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BACKGROUND

Guanidinoacetate methyltransferase (GAMT) deficiency is a rare disorder (prevalence <1/1,000,000), inherited as autosomal recessive traits, characterised by an inborn error of creatine synthesis. Creatine deficiency results in a combination of symptoms such as intellectual disability, autistic behaviour, seizures, speech delay and hypotonia. Magnetic resonance is used at diagnosis and follow-up. The treatment goal is an increase in creatine levels in the brain with oral creatine supplements, ornithine and sodium benzoate. On-the-market benzoate medicinal products do not exist and dietary supplements of ornithine and creatine do not satisfy the needs of the paediatric population in constant growth. Galenic preparations are the unique way to succeed in treating this rare disease (Figure 1: GAMT metabolic pathway).

PURPOSE

The objective was to report our experience, in order to focus on the importance of galenic preparations, unique resources to treat paediatric patients and orphan diseases.

MATERIALS AND METHODS

The best regimen was established by a multidisciplinary approach in a function of patients' weight and laboratory data (creatine and guanidinoacetate levels). An appropriate formulation was chosen according to active substance solubility and mucous membranes irritancy. Follow-up data were recorded retrospectively through medical records.

RESULTS

Two Egyptian patients, 13 and 19 years' old, weight 56 and 94 kg respectively, in 2012 were diagnosed with GAMT deficiency by the Paediatric Unit. We chose unitary solid formulation (Table 1): ornithine maps of 5 g for the first patient (10 g/die), maps of 2 g for the second (7 g/die) (106 mg/kg/die). Creatine had been given as powder, with a specific doser, considering high daily amount: 11 gx2/die for the first patient and 12 gx3/die for the second patient (382 mg/Kg/die). Concerning sodium benzoate, an irritant for mucosa, a 20% liquid formulation was chosen, to be administered with fruit juice. Clinicians decided a posology of 59 mg/kg/die, so 9 mLx2/die were administered to the first patient, and 14 mLx2/die were administered to the second patient. Patients since 2012 have not manifested adverse drug reactions and therapy has brought a stable clinical picture: optimal creatine level, measured as peak at MR, and low levels of guanidinoacetate on spot (8.3 mcM/L), indicative of good metabolic control.

CONCLUSIONS

GAMT deficiency is a rare cerebral disorder, with a high impact on patients' quality of life. A palliative approach is possible only through galenic preparations. Personalised therapies allow these patients to manage intellectual and movement disability in a better way, contributing to improving and/or stabilising the clinical picture.

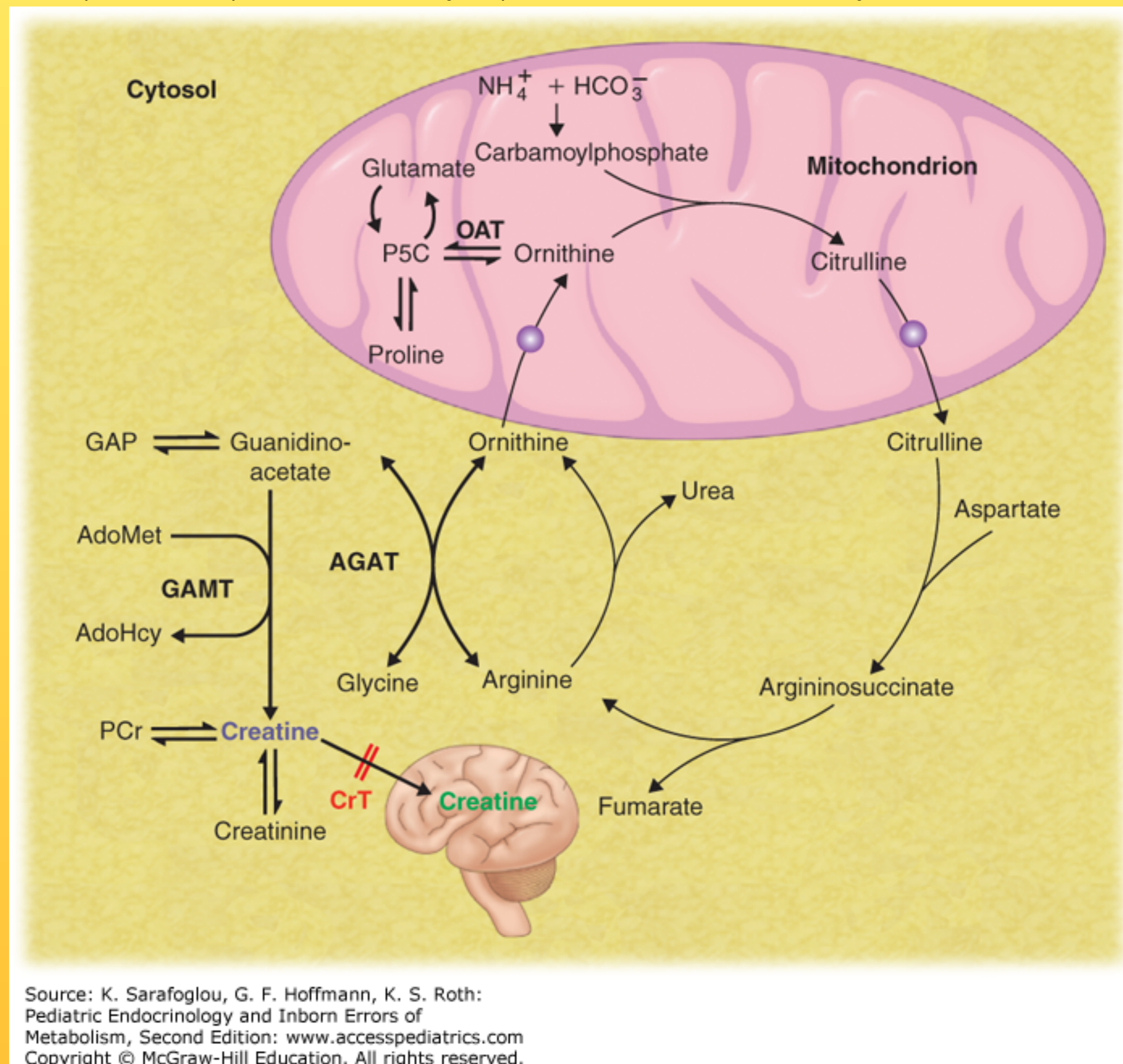


Table 1	FORMULATION	FIRST PATIENT	SECOND PATIENT
ORNITHINE powder	MAPS	10 g/die	7 g/die
CREATINE	POWDER with doser	11 g x 2/die	12 g x 3/die
SODIUM BENZOATE	LIQUID, 20% (20 mg/100 mL)	9 mL x 2/die	14 mL x 2/die

