Microencapsulated NaCl for Oral Salt-Replacement Therapy in Infants

Hyponatremia in patients with brain tumors, cerebral injury, or after brain surgery is frequently caused by inappropriate secretion of antidiuretic hormone, requiring therapy by fluid restriction (1,2). Cerebral salt wasting, another cause of hyponatremia, requires, however, substitution of fluid and sodium (3). Prolonged application of NaCl via intravenous lines is of limited practicality, and oral replacement of concentrated NaCl solution may cause nausea and emesis. The unpleasant salty taste may require a nasogastric tube for application, especially in pediatric patients. Repetitive placements maneuvers are stressful for patients, parents, and the medical staff. In this correspondence, we present an alternative for oral NaCl replacement, sustained-release, microencapsulated NaCl.

A 10-month-old girl presented with an incompletely resectable brain tumor (pilocytic astrocytoma) from the third ventricle to the pituitary gland, with infiltration of the optic chiasma. The postoperative phase was complicated by polyuria and excessive natriuresis. Serum sodium, chloride, and osmolality were low, whereas potassium, calcium, creatinine, uric acid, and blood urea nitrogen were normal. Results of a cortisol-releasing hormone test suggested hypothalamic damage. Atrial natriuretic peptide and brain natriuretic peptide
were elevated. The presence of hypo-reninemic hypoaldosteronism confirmed diagnosis of cerebral salt wasting and ruled out inappropriate secretion of antidiuretic hormone. Treatment included substitution of thyroxine, hydrocortisone, and fludrocortisone and high doses of intravenous NaCl (up to 60 mmol/kg per day). With clinical stabilization, oral substitution with microencapsulated NaCl was started (maximal daily dose = 16 mmol/kg, equivalent to 0.85 g/kg) and was continued for 2.5 months before fatal tumor progression demanded intravenous substitution again (Fig. 1).

For retarded release, drug coating (microencapsulation) is established in pharmaceutical technology (e.g., for acetylsalicylic acid, dipyridamole, or theophylline) but has not yet been described for NaCl (4). For the microencapsulation of NaCl, crystalline NaCl (particle size = 100–700 μm) was coated with ammonium methacrylate copolymer type B (Eudragit™ RS 12.5; Röhm Pharma, Weiterstadt, Germany) (5). Film-forming copolymer (500 g) was dissolved in 4000 g of a mixture containing 2-propanol and acetone, 3 : 2 (vol/vol). The coating process was performed in a Kugelcoater HKC-5-TJ (Hütting, Steinen, Germany) equipped with a turbojet device and bottom-spray nozzles. NaCl (2870 g) was preheated in the Kugelcoater with an inlet air temperature of 40°C. The coating process was started at 35°C, with an average spray rate of 12 g/minute. During the spraying process, the temperature was kept below 30°C to prevent sticking. The atomizing air pressure was set to 0.1 megapascal (MPa); the microclimate pressure around each nozzle was 0.05 MPa. The air volume was 250 m³/hour in the beginning and decreased to 180 m³/hour. The product was vacuum-dried. The dissolution of coated granules was monitored in purified water by conductometric determination of NaCl concentration; 50% of the encapsulated NaCl was released after 60 minutes.

The flavorless microencapsulated granules can be mixed easily with yogurt, pudding, or mashed baby food because the adverse effects of NaCl solution, such as nausea and vomiting, can be overcome by the preparation described.

In conclusion, coating of NaCl appears to be a cheap, simple, and effective way to administer large doses of salt orally to pediatric patients.  

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REFERENCES


NOTES

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