Spinal muscular atrophy: Etiology and pathogenesis

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Spinal muscular atrophy (SMA) is a common fatal autosomal recessive disorder characterized by degeneration of lower motor neurons. The survival of motor neuron (SMN) gene has been identified as the determining gene of SMA. SMN encodes a protein located within a novel nuclear structure and interacting with RNA binding proteins. These results suggested that SMN might have a role in nuclear post-transcriptional mechanism of RNA metabolism.

The SMN protein analysis showed a strong correlation of the amount of the SMN protein encoded by the homologous gene copy (SMNC) with the clinical severity of the disease in a large cohort of patients (n = 52), independent of the race. The differences among symptoms at the onset, clinical progression and outcome allowed us to define some phenotypical sub-groups of the disease.

The complete clinical picture was observed only in 20% of the cases; the neurological symptoms were always present, while the signs of androgen insensitivity (gynecomastia, impotence, testicular atrophy) occurred in 30% of the whole sample. The muscular atrophy showed a proximal distribution in 86% of cases. Tremor was usually of postural type, sometimes with a kinetic component. Resting tremor was anodatically described (1%), without other symptoms and signs of extrapyramidal disorders. Phenotypical differences and clinical severity of the disease appeared to be influenced by the race: in the yellow race the neurological symptoms and the disease progression were more severe. The endocrinological pattern was more pronounced in the white race. No reports were recorded on KD in the black race.

Measurement of colonic transit time in patients with amyotrophic lateral sclerosis


Background: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder, characterized by progressive loss of motor neurons. However, ALS has been recognized to involve subclinically several non-motor systems. Cardial and autonomic motor involvement in ALS has been described. Delayed gastric emptying of solids as a gastrointestinal autonomic involvement was reported recently. Measurement of colonic transit time using radiopaque markers has been proved as a noninvasive and reliable test.

Methods: We have investigated 10 patients with ALS and 12 healthy age-matched volunteers. None of the patients has had diabetes or other disorders combined with autonomic dysfunction, none had known gastrointestinal disorders. The patients swallowed a gelatine capsule which contained 20 radio-opaque pellets on each of 6 consecutive days at the same time. On day seven a single abdominal x-ray was obtained. Segmental and colonic transit times were calculated from the number of retained pellets.

Results: 9 of 10 patients with ALS showed markedly delayed colonic transit times whereas healthy controls all had normal colonic transit times. Colonic transit was delayed in all colonic segments of ALS patients.

Interpretation: Delayed colonic transit times in patients with ALS encourage the theory of possible gastrointestinal autonomic involvement in ALS.