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**ELEVATED CREATINE KINASE SUGGESTS BETTER PROGNOSIS IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS**

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**Background** Creatine kinase (CK) is an enzyme found in skeletal muscles, myocardium and brain (CK-MM, CK-MB, and CK-BB isoenzymes respectively). In these tissues with high energy requirements, CK catalyses conversion of phosphocreatine to creatine, generating adenosine triphosphate. Elevated CK-MM is considered a marker of muscle damage. In the past, CK has been used to differentiate between myopathic and neurogenic disease, higher CK being associated with myopathic disease. It is now recognised that CK may be mildly to moderately elevated in patients with amyotrophic lateral sclerosis (ALS). An obvious explanation of raised CK in ALS is striate muscle atrophy resulting from degeneration of the subserving motor neurons. Another possible explanation is upregulation of this enzyme to provide an energy substrate in a hypercatabolic condition. The reason that CK elevation occurs in only a proportion of ALS cases, the precise cause and its behaviour with disease progression is unknown.

**Objectives** To determine:

1. Are ALS patients with raised CK any different from patients with normal CK?
2. What are the implications of raised CK on disease outcome or prognosis?
3. Does CK mirror disease progression or activity and, if so, can it be used to monitor disease progression or response to therapeutic interventions?
4. Can the magnitude of muscle enzyme release be used to predict the magnitude of muscle functional impairment?

**Methodology** This is an observational cohort study, using the clinical database from the Olesoxime (TRO19622) investigational medicinal product trial. This trial involving 512 patients with ALS was conducted across 15 European centres (2009–2011). The patients were followed up at 3 monthly intervals for 18 months while monitoring various biochemical and haematological parameters, including CK. The steering committee of TROPHOS (the pharmaceutical company developing Olesoxime) kindly provided the database from the Olesoxime trial to conduct this study.

**Results** Baseline CK was raised in 52% of the participants with mean CK±SD being  $257\pm 239$  IU/L. Mean CK in male participants was significantly higher than in females ( $p<0.001$ ). Mean CK was significantly higher amongst participants with limb onset ALS compared to participants with bulbar onset ALS ( $p<0.001$ ). There was no significant difference in CK levels between upper limb and lower limb onset disease ( $p=0.746$ ). Higher CK was associated with significantly better survival, even when adjusted for prognostic co-variants ( $P=0.005$ ).

**Conclusions** CK level is a prognostic factor for survival in ALS, independent of its association with site of disease onset. This finding suggests that CK may be involved in a defence mechanism. CK levels cannot be used to predict the disease severity or manual muscle scores at any time point. This study highlights the usefulness of CK as a prognostic marker in ALS.



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