The role of endotoxin in critical illness myopathy and polyneuropathy

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Comment

Sirs: We read the article by Dr. Mohammadi and colleagues dealing with parameters that correlate with the severity of early stage critical illness polyneuropathy (CIP) with great interest [5]. The authors performed nerve conduction studies and electromyography in 20 consecutive patients with severe sepsis or septic shock from day 1 to day 14 after onset of sepsis. The essential finding was a reduction in the amplitude in the compound action potential of the median and/or peroneal nerve which was reduced in 75% of patients already at day 1, and in 88% of patients at day 7. Remarkably, the reduction in the amplitude of the compound motor action potential correlated with the serum concentrations of endotoxin and interleukin-2-receptors. We have recently shown a direct interaction of endotoxin with heterologously expressed voltage-gated skeletal muscle sodium channels in vitro [4]. Endotoxin reduced sodium channel availability at depolarized membrane potentials during acute application of high concentrations (≥ 50 ng/ml) and after prolonged exposure (1 h) to a clinically relevant concentration (300 pg/ml). After 24 h of in vitro incubation with 300 pg/ml endotoxin, the reduction of

sodium channel availability was irreversible and independent from the membrane potential.

In septic patients, CIP and critical illness myopathy (CIM) often coexist [2, 3], and the incidence in patients with sepsis or septic shock varies between 70% and 80% [1]. Taken together, the results of the clinical study performed by Dr. Mohammadi and colleagues, and our in vitro study on the interaction of endotoxin with voltage-gated sodium channels suggest that endotoxin might be a crucial factor in the development of neuromuscular sequelae of sepsis already at a very early stage after onset of sepsis. This highlights the need for development of anti-endotoxin strategies to prevent CIM and CIP.

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