Effects of Hemoadsorption with CytoSorb during Severe Rhabdomyolysis

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Dear Editor,

Severe rhabdomyolysis occurs due to various causes and injuries and can result in several potentially life-threatening complications [1, 2], of which acute kidney injury (AKI) is one of the most important adverse events. The pathomechanism of AKI in rhabdomyolysis is complex, and different mechanisms such as direct tubular damage by oxidative injury, tubular obstruction by precipitated Tamm-Horsfall protein-myoglobin complexes, and hypovolemia-associated renal vasoconstriction play a role [3, 4]. Of note, in most of these processes, myoglobin released by injured muscle is essentially and directly involved [3, 5]. In contrast, creatine kinase (CK) probably plays no mechanistic role in AKI, and its value as a marker for AKI remains controversial [6, 7]. In addition, other factors contribute to renal damage in patients with rhabdomyolysis, such as surgery, the underlying condition, or trauma. Beyond AKI, potassium and calcium disturbance, metabolic acidosis, and disseminated intravascular coagulation may arise, also depending on the cause of muscle injury [1].

Management of rhabdomyolysis intends to increase the clearance of myoglobin, to treat hypovolemia, and to balance electrolyte and pH changes, for preventing the complications mentioned above [2]. In addition to myoglobin, there may be other currently unknown mediators of damage released from muscle to peripheral blood, which could be removed by extracorporeal therapies. In contrast, the therapeutic value of removing CK during rhabdomyolysis is unclear. Dialysis with high cutoff membranes is frequent-

ly used in the management of rhabdomyolysis [8, 9]. However, in clinical practice, this approach is often not sufficient, and may be associated with unwanted loss of other molecules from the circulation. In this context, we read the report of Dilken et al. [10] with great interest.

The authors describe the case of a 56-year-old male patient who experienced a severe crush injury to the lower extremities and the abdominal wall, which led to traumatic rhabdomyolysis. Continuous veno-venous hemodialysis was initiated with a high cutoff membrane (EMIC-2, Fresenius Medical Care, Bad Homburg, Germany). This was associated with stabilization of myoglobin levels in peripheral blood in the presence of further increasing CK activity. The authors added a CytoSorb[®] hemoadsorption device to the hemodialysis circuit and observed a rather rapid decrease of CK activity and slowly decreasing myoglobin levels. This observation raised questions to us.

Hemoadsorption with CytoSorb[®] is increasingly used as stand-alone hemoperfusion, with various renal replacement circuits or with extracorporeal membrane oxygenation [11]. It adsorbs small hydrophobic molecules up to a size of around 55–60 kD. Myoglobin has a mass of 17 kD [12–14] and is effectively adsorbed by CytoSorb[®], which resulted in approval of the device for conditions with increased myoglobin levels such as rhabdomyolysis [15]. CK in its dimeric form, however, is certainly too large to be adsorbed by CytoSorb[®] and to be dialyzable even with a high cutoff membrane. CK is a dimer of two 43-kD subunits [14, 16, 17], and the predominant type in peripheral blood is the

MM-isoenzyme, in particular during rhabdomyolysis [18]. Although we cannot exclude that circulating CK-M monomers are adsorbed by the device, this would very likely not explain the rapid decrease of CK activity, which was observed already 4 h after initiation of hemoadsorption. Moreover, myoglobin initially increased and then only slowly decreased after installation of CytoSorb[®], further arguing against the hypothesis that CytoSorb[®] was responsible for the strong drop of CK activity during that phase. It would be helpful to know when exactly surgical procedures were performed, as it appears likely that dialysis and hemoadsorption were interrupted by surgery and that surgery modified rhabdomyolysis burden. Furthermore, we were wondering if and when the dialysate and membranes were replaced during the time period displayed in the graphs. For interpretation of the results, it would be important to know if a new dialysis unit was used with installation of CytoSorb[®]. The authors further state that saturation of the adsorber was noticed, and we are curious how saturation of the device was determined. Moreover, did the authors observe changes in other factors known to be adsorbed by CytoSorb[®], such as interleukin-6?

In summary, CytoSorb[®] adsorbs myoglobin with reportedly high efficacy. In addition, the device may adsorb other known and unknown molecules, which potentially play a role during pathogenesis of rhabdomyolysis. We fully agree with the authors that hemoadsorption is a potentially attractive adjunctive treatment for this condition, in addition to volume therapy, forced diuresis, and dialy-

sis if indicated. However, we doubt that CytoSorb[®] lowers CK activity by adsorbing the enzyme, at least in its dimeric form, and that lowering CK per se is of clinical importance. To the best of our knowledge, there is no publication directly proving adsorption of CK by CytoSorb[®]. Therefore, we suggest measuring levels of target molecules before and after the adsorber also in clinical settings, in order to provide definitive evidence of substance removal.

Disclosure Statement

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Author Contributions

H.C.D. drafted the manuscript, B.M.W.S. revised the manuscript for important intellectual content, and L.C.N. designed, supervised, and revised the manuscript.

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