Erythropoietin in traumatic brain injury: The “golden bullet” on the horizon?

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The study by Liao and colleagues investigated the cellular and molecular events of erythropoietin (EPO)-mediated neuroprotection in traumatic brain injury (TBI).\textsuperscript{[1]} Using the “classic” Feeney cortical contusion model, the authors performed an experimental study on 130 Wistar rats, designed to elucidate in more detail the established anti-apoptotic effects of recombinant human EPO (rhEPO). Animals were randomly assigned to either a treatment group with rhEPO, applied by intraperitoneal injection once a day for seven days after TBI, or a vehicle-injection control group managed under identical conditions. Outcome parameters consisted of quantification of neuronal cell death by TUNEL histochemistry and assessment of gene (RT-PCR) and protein (Western blot) expression of the pro-apoptotic molecule Bax. The data revealed that the treatment with rhEPO led to a decrease of TUNEL-positive neurons, associated with attenuated Bax mRNA and protein expression after TBI, compared to the vehicle control group. The authors concluded that EPO represents an effective neuroprotective treatment in experimental TBI by reducing Bax expression and associated apoptotic neuronal cell death. These findings confirm a previous report from the same group\textsuperscript{[2]} and shed some further light onto the EPO-mediated regulation of the molecular events leading to neuronal cell death and secondary brain injury.

Until now, no specific pharmacological therapy for severe TBI is available to reduce the incidence of secondary brain injury and adverse outcome.\textsuperscript{[3,4]} It is now becoming apparent that the role of EPO reaches far beyond the physiological regulation of erythropoiesis in the bone marrow. In fact, multiple experimental studies in recent years have revealed that EPO represents a potent endogenous mediator of neuroprotection in a variety of central nervous system disorders, including head trauma.\textsuperscript{[5,6]} Based on its potent neuroprotective effects, EPO was recently proclaimed as one of the emerging new therapeutic strategies for TBI.\textsuperscript{[4,7]} The data from the present paper support the notion of an anti-apoptotic role of EPO in experimental head injury.\textsuperscript{[1]} Nevertheless, care must be taken in the extrapolation of data derived from animal studies to clinical strategies in humans. As we painfully learned in recent years, multiple proven neuroprotective agents from animal models have failed in translation to a pharmacological approach in TBI patients.\textsuperscript{[3,4]} The main roadblock to the successful implementation of new therapeutic strategies is represented by the heterogeneity of head injury and the unique individual characteristics of each injury pattern, which renders the design of clinical trials designed for a generalized patient population extremely challenging. Carbamylated erythropoietin represents a modified pharmacological agent which exerts neuroprotective functions while not affecting hematocrit.\textsuperscript{[8]} This new molecule may be a prime candidate molecule for clinical investigations in TBI, under the prerequisite that the drawbacks and lessons learned...
from previously failed trials are taken into account for the design of potential future clinical trials.

References


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