Importance of erythropoietin in brain protection after cardiac surgery-the role of diffusion weighted magnetic resonance imaging

Poster No.: C-0516
Congress: ECR 2012
Type: Scientific Exhibit
Authors: K. Surlan Popovic¹, N. Lakic¹, S. Andrej¹, A. Kravanja¹, M. Lenarcic², A. Savandic¹, Ljubljana/SI, Ljubljana, SI/SI
Keywords: Neuroradiology brain, MR-Diffusion/Perfusion, Surgery, Ischaemia / Infarction
DOI: 10.1594/ecr2012/C-0516

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Purpose

Among the most serious and frequent complications of cardiac surgery are neurologic complications that might increase morbidity, mortality, and length of hospital stay.

The current protocols for perioperative brain protection against ischemic events are not optimal. Hypothermia during cardiac surgery protects against brain ischemia; however, some alterations of the coagulation cascade and the inflammatory response occur during hypothermia. Furthermore, although arterialline filters prevent passage of particles larger than 20 to 40 µm, smaller particles produced by embolization in distal vessels may still cause transient or permanent neurologic disorders. A steadily growing body of evidence indicates that the therapeutic benefits of recombinant human erythropoietin (rHuEpo) could extend far beyond the treatment of anemia [Rath 2009]. Several mechanisms of rHuEpo neuroprotection have been recognized, including (1) decreasing glutamate toxicity, (2) inducing the generation of neuronal antiapoptotic factors, (3) reducing inflammation.

In a multicenter double-blinded placebo-controlled study of patients with ischemic stroke, Ehrenreich et al [2002] found a reduction in infarct size and a better clinical outcome in patients treated with rHuEpo. According to the evidence, erythropoietin functions as a multipotent tissue protector in the heart [ Parsa 2003, van der Meer 2005] and in the central nervous system [Sakanaka 1998; Wang 2004; Noguchi 2007].

The purpose of the present study was to find out whether pre-, peri- and postoperative intravenous administration of rHuEpo has any influence on the development of transient or permanent neurologic dysfunction in patients undergoing open heart surgery by using DW MRI in erythropoietin-treated and control groups of patients.
Methods and Materials

In this study, we included 20 patients who were older than 18 years and required surgical revascularization of the heart with the use of the HLM. Table 1 summarizes the characteristics of the study group.

The patient rHuEpo protocol consisted of 3 consecutive doses (24,000 IU) of epoetinum alfa (Eprex; Janssen-Cilag, Turnhout, Belgium) administered intravenously. The first dose was given 1 day before the procedure, the second dose was administered on the day of operation, and the third dose was given 1 day after completion of the surgery.

After the operation, patients were transferred to the intensive care unit ward, where the anesthesiologist on duty closely monitored the patient's neurologic status. All deviations were recorded. A clinical neurologist performed neurologic examination before the operation and on the first and second postoperative days.

A magnetic resonance imaging (MRI) examination was performed in all patients of the study group 24 hours before surgery and a median of 4 days (range, 2-5 days) after surgery. MRI studies were obtained on a 3T instrument (Magnetom Trio TIM; Siemens, Erlangen, Germany) with standardized protocols [Knipp 2004; Stolz 2004; Barber 2008]. Scans were always performed in the same order with a T1-weighted 3-plane localizer, a diffusion-weighted imaging (DWI) sequence, and a fluid-attenuated inversion recovery (FLAIR) sequence. DW images were obtained with a multislice, single-shot spin-echo echo planar image sequence. Slice thickness was 5 mm with a 0.5-mm gap, with the number of slices set to include the entire brain. The matrix size was 128 x 128, the field of view was 230 mm, and the repetition/echo time (TR/TE) was 4000/83 milliseconds. The diffusion gradient strength was varied between 0 and 45 mT/m, resulting in 2b values of increasing magnitude from 0 to 1000 seconds/mm. FLAIR images were obtained with a slice thickness of 5 mm with a 0.5-mm gap, with the number of slices set to include the entire brain. The matrix size was 204 x 256, the field of view was 220 mm, the TR/TE was 9000/94 milliseconds, and the inversion time, TI, was 2500 milliseconds. The images were presented to one of the investigators blinded to the results of the clinical assessments, and the postoperative MRI scans were analyzed for the presence and number of ischemic lesions. These results were compared with those for preoperative MRI scans.
Results

Twelve male and eight female patients, aging from 64-86 years (median 75.5) were included in the study. None of them had significant carotid lesions. All patients underwent complete coronary artery revascularization.

The baseline characteristics of the rHuEpo-treated and nontreated groups were comparable. The outcomes of the 2 groups were comparable for all observed parameters: the number of coronary artery bypass grafts, anesthesia duration, blood pressure, and transfusion volume. All of the patients survived open heart surgery. No patient showed neurologic dysfunction before the operation, and only 2 of the patients in the untreated group experienced delirium. Both patients had MRI-detectable brain changes. MRI evaluations performed 24 hours before surgery revealed multiple ischemic lesions in all of the patients. The lesions were all small, 2 to 5 mm in diameter. Some of the lesions in the border zone between the middle cerebral artery and the anterior cerebral artery were confluent. Only 1 patient had a large ischemic region in the left middle artery circulation.

Four (40%) of the 10 participants without rHuEpo therapy showed new cerebral infarction in the postoperative DWI sequence (Figure 1,2,3,4). Two of 4 patients with postoperative ischemia had small lesions (approximately 2 mm in diameter); the other 2 patients had ischemic lesions larger than 5 mm (Figure 1,2,3,4). The distribution of the DWI lesions was as follows: the middle cerebral artery (61%), the border zone between the middle cerebral artery and the anterior cerebral artery (31%), and the posterior circulation (8%); 76% of the ischemic lesions were on the left. DWI lesions occurred in more than 1 vascular territory in all patients with multiple lesions. We observed no fresh ischemic lesions on DWI images in the 10 patients treated with rHuEpo prior to surgery.
Fig. 1: Diffusion-weighted magnetic resonance imaging of a 72-year-old man. A postoperative scan performed 3 days after surgery revealed 5 new diffusion-weighted lesions. One lesion was located in the white matter of the left occipital lobe (5 mm), 3 lesions (2 mm) were located in the left frontal lobe, and 1 lesion (2 mm) was located in the gray matter of the right occipital-parietal region. These lesions were consistent with small embolic infarctions.
Fig. 2: Diffusion-weighted magnetic resonance imaging of a 72-year-old man. A postoperative scan performed 3 days after surgery revealed 5 new diffusion-weighted lesions. One lesion was located in the white matter of the left occipital lobe (5 mm), 3 lesions (2 mm) were located in the left frontal lobe, and 1 lesion (2 mm) was located in the gray matter of the right occipital-parietal region. These lesions were consistent with small embolic infarctions.
**Fig. 3:** Diffusion-weighted magnetic resonance imaging of a 72-year-old man. A postoperative scan performed 3 days after surgery revealed 5 new diffusion-weighted lesions. One lesion was located in the white matter of the left occipital lobe (5 mm), 3 lesions (2 mm) were located in the left frontal lobe, and 1 lesion (2 mm) was located in the gray matter of the right occipital-parietal region. These lesions were consistent with small embolic infarctions.
Fig. 4: Diffusion-weighted magnetic resonance imaging of a 72-year-old man. A postoperative scan performed 3 days after surgery revealed 5 new diffusion-weighted lesions. One lesion was located in the white matter of the left occipital lobe (5 mm), 3 lesions (2 mm) were located in the left frontal lobe, and 1 lesion (2 mm) was located in the gray matter of the right occipital-parietal region. These lesions were consistent with small embolic infarctions.

© Clinical Institute of Radiology, Clinical Centre Ljubljana Neuroradiology - Ljubljana/SI
Conclusion

The results regarding brain protection with rHuEpo are encouraging and rHuEpo is a promising neuroprotective agent. Evaluation of brain with DW MRI prior and after heart surgery may help in the development of new strategies to reduce postoperative brain damage. The effects on long-term clinical outcome are to be followed up.
References


Personal Information

Katarina Šurlan Popović MD, PhD
Neuroradiology department
Clinical institute of radiology
University medical center Ljubljana
Zaloška 7, 1000 Ljubljana
Slovenia
katarina.surlan@guest.arnes.si