Fluoroscopy-associated oxidative stress and cellular damage in patients with atrial fibrillation or ventricular arrhythmias undergoing transcatheter ablation: prevention by N-acetylcysteine pre-treatment.

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Background/Aims. Transcatheter ablation (TCA) is a highly effective and safe electrophysiological procedure for the treatment of atrial fibrillation or ventricular arrhythmias.1,2 However, for the positioning of the cardiac catheter and navigation through the heart cavity, the ablation procedure requires the use of fluoroscopy. Although it is widely accepted that: 1) there is no threshold dose of ionizing radiations below which there is no risk for the patient and the operator3-5, and 2) especially in DNA nucleobases, a single exposure to low-dose ionizing radiations may trigger oxidative damage6-8, presently there are no clear data on potential risks resulting from the exposure to ionizing radiations in subjects undergoing TCA. To evaluate the extent and the implications of the cellular damage resulting from low-dose ionizing radiations in patients undergoing TCA, we have measured the urinary excretion of 8-hydroxy-2-deoxyguanosine (8-OHdG) -a reliable index of oxidative DNA damage in vivo- both before and at different time intervals after the ablation. At the same time intervals, the oxidative stress status of each patient was measured by evaluating the reduced glutathione disulfide/glutathione (GSSG/GSH) ratio in blood.

Patients and Methods. In 34 patients with atrial fibrillation and in 15 patients with ventricular arrhythmias undergoing TCA the urinary excretion of 8-OHdG, was evaluated before (t0), 3hrs (t1), 24hrs (t2) and 48hrs (t3) after the ablation. Urinary 8-OHdG was determined by a very specific and sensitive previously validated LC-MS/MS method9. GSSG/GSH ratio was measured in whole blood employing a previously validated LC-MS/MS method as well 10. Based on the results achieved in the initial 49 patients, 600 mg N-acetylcysteine (NAC) were intravenously administered to 10 additional consecutive patients, 1 hr prior to carrying out the ablation for arrhythmias correction. Urinary 8-OHdG and blood GSSG/GSH ratio were determined at the same time intervals as above.

Results. 8-OHdG levels were higher 24hrs following ablation procedures (T2) if compared with baseline levels (T0) ($p=0.0261$). On the other hand, T2 was significantly higher than T3 ($p=0.0528$), T3 levels being comparable to those observed at T0 ($p=0,8522$). A similar trend of statistical significance was also observed for GSSG/GSH ratio. There was a significant burst between T0 and T1 ($p<0.0001$); a slight reduction between T1 and T2 ($p<0.054$) and between T2 and T3 ($p=0.42$), T3 levels being comparable to those observed at T0 ($p=0.08$). In the 10 patients that were pre-treated with NAC, as expected, no changes in urinary 8-OHdG levels were found at the different times of observation in comparison with 10 no treated matched patients. With respect to GSSG/GSH ratio, there was no difference between T0 and T1 ($p=0.39$); between T1 and T2 ($p=0.85$) and between T2 and T3 ($p=0.72$), and between T3 vs T0 ($p=0.23$). In addition, significantly lower

GSSG/GSH levels at T1 and at T2 in the 10 subjects pre-treated with NAC versus the untreated ones was found (p=0,02; p=0,04 respectively).

Conclusions. A statistically significant, short-term oxidative damage takes place in patients with atrial fibrillation or ventricular arrhythmias undergoing TCA. Such fluoroscopy-associated oxidative stress but not cellular damage is prevented by pre-treating patients with low-dose/high-dose NAC administered orally/intravenously. The present pilot study provides the groundwork and the rationale for identifying potential preventive interventions to minimize the damage from ionizing radiations in subject with atrial fibrillation or ventricular arrhythmias undergoing TCA.

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