Editorial

Reconsidering markers of oxidative stress

Looking into our own journal and in international literature about oxidative stress, we observe that not only markers and assays have become questionable but the whole concept of oxidative stress must be reconsidered.[1] It was common to use malondialdehyde (MDA) levels as marker for oxidative stress; MDA is a byproduct of lipid peroxidation (LPO) which is certainly closely related with oxidative stress but not identical.[2] Furthermore, the method mostly used is thiobarbituric acid (TBA) reaction measuring TBA reactive substances (TBARS) and not specifically MDA.[3] Discrepancy was reported in biomarkers of LPO and oxdative stress between vascular dementia with much higher MDA levels than in Alzheimer patients.[4] However, McGrath, et al had already clarified that increased LPO and oxidative stress in Alzheimer's disease could be assessed with 4-hydroxynonenal[5] but not MDA, either substance reacting with TBA. Moreover, markers of oxidative stress in the brain are widely measured in the blood stream, which is a different compartment and the farther the measurement of the marker is distant from the origin, the more questionable becomes its relevance and the more it is essential to standardize the measurement.[6] Lipid peroxidation is a very complex dynamic process and if we intend to evaluate LPO we ought to determine the kinetics of the reaction phases. But we normally measure one (more or less) arbitrary point of this process, because clinical studies are often not primarily designed to measure LPO but to determine clinical parameters, which are then compared to the outcome of the LPO measurement as marker for oxidative stress. Why should we expect that the time course of clinical parameters coincides with the development of LPO and the kinetics of marker assays? LPO and oxidative stress have their own dynamics. No wonder that many results from MDA measurements are considered random, very often insignificant and if statistically significant, clinical relevance is still questionable – as mentioned above, not only in the environment of our own journal but worldwide.

In similar way, we even could continue with other markers of oxidative stress and antioxidant capacity, from dithionitrobenzoate (DTNB) measurement of glutathione, which does not differentiate between glutathione (GSH) and other thiols (including membrane thiols, except different thiols are separated carefully before measurement) or determinations of superoxide dismutase (SOD) activity,[7] which are indirect conventional methods (except for direct electron paramagnetic resonance (EPR) measurement of the kinetics of the superoxide anion radical). Recently, other marker tests, such as total antioxidant capacity (TAC), trolox-equivalent antioxidant capacity (TEAC), and total radical-trapping antioxidant parameter (TRAP) have also been reconsidered critically.[8]

Last year, we investigated prognostic factors of neuroinflammation and oxidative stress in patients with brain injury. Consistent with the above remarks, we found stronger correlation of clinical scoring with neuroinflammation than with oxidative stress markers, especially MDA and GSH.[9]

In this issue there is a report on histopathology of the rat myocardium under physical exercise.[10] Histology was examined to see damages in myocardium instead of measuring LPO and TBARS as indicators of membrane damage in myocytes. Perhaps, the latter parameters can be interpreted more easily, but conventional histology may (at least under certain conditions) be more useful and relevant.

In the light of many questions raised about the relevance of measurements of oxidative stress and antioxidant capacity and in line with recent findings we should be careful with the interpretation of our own results.

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