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Ischemic Preconditioning in Cardiac Cells: from Bench to Bedside

Since 1986 that Dr Charles E. Murry and his colleagues published their discovery about the protective effects of ischemic preconditioning (IPC), a large number of Pro- and Con- studies have been published (1). Besides the protective effects of ischemia itself, a number of pharmaceutical agents may have protective effects against ischemia known as pharmacologic preconditioning. Having a long list of agents, these have been under examinations both clinically and/or in lab setting. Some disease states have been proposed to have a relationship with effects of IPC; including diabetes or high altitude diseases (2, 3). Another variety of IPC is remote IPC which has been acting at remote organ tissues (4-6)

How does IPC with such a wide range of effects work? In fact, IPC works both in cardiac and neurologic cells; two cell types that are highly "ischemia-sensitive"; more interestingly, volatile anesthetics-induced preconditioning (part of a larger phenomenon known as Anesthetic Preconditioning: APC) has protective effects in both cell types; i.e. myocardial cells and brain neurons (7). The underlying mechanisms for IPC and APC are mainly similar; the following items being the most important common mechanisms:

- ATP-sensitive potassium channels in mitochondria (mK_{ATP}): being one of the most important mechanisms in both IPC and APC, leads to intracellular protective mechanisms; including but not limited to PKCε phosphorylation (a subgroup of Protein Kinase C: PKC); among the main mitochondrial related mechanisms, inhibition of mitochondrial permeability transition pore (mPTP) opening, also, " the content of nitric oxide (NO) and also, inhibition of nitric oxide synthase (NOS)" and the role of mitochondrial connexins could not be neglected (7, 8)
- Reactive Oxygen Species (ROS): when mitochondria release small amounts of ROS, both APC and IPC could be triggered, leading to their cardio- and neuro-protective effects (7, 9, 10)
- Inflammatory cytokines: a cascade of inflammatory cytokines are inhibited due to the protective effects of IPC and APC; mainly through attenuated activity of NF-κB and the downstream of NF-κB-inflammatory cytokines (7, 11-13)
- Apoptosis: increased anti-apoptotic effects of protein Bcl-2, leading to decreased expression of caspase-3 are the main mechanisms considered as IPC effects through inhibition of apoptosis (7, 14-16)

Considering the discovered mechanisms of IPC and APC, it seems reasonable that both cardiomyocytes and brain neurons are benefited from volatile anesthetics-induced preconditioning.

However, the above lines are not the complete picture of IPC and further studies, especially regarding the clinical aspects of the issue are under way. In this issue of the *Journal of Cellular and Molecular Anesthesia*, Anvaripour A, et al. have published their study demonstrating that 4% Sevoflurane could not have a protective effect on myocardial cells as an anesthetic with APC effects (17); a finding in controversy with some of the other previous studies. These results again confirm the delicate path from bench to bedside, which is not always a straight forward one. This time, the path goes through precondition effects of volatile anesthetics.

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