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Evaluating photodynamic therapy with Protoporphyrin IX in the context of mitochondrial bioenergetics

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Protoporphyrin IX (PPIX) is an endogenous photosensitizer widely studied for its use in photodynamic therapy (PDT) in some types of skin cancer and dermatological diseases. (1) Administration of 5-aminolevulinic acid (ALA) induces the endogenous synthesis of PPIX in mitochondria, via the heme biosynthetic pathway, making mitochondria the primary target of PDT. (2) With that in mind, it is important to understand the effects and mechanisms of PDT with PPIX directly on mitochondria at the bioenergetic level. In this study, we isolated mitochondria from healthy C57BL/6 mice's livers and evaluated mitochondrial respiration and swelling after PDT treatment at 635 nm. We analyzed mitochondrial respiration using different PPIX concentrations (0.5, 1.0, 4.5, and 9.5 μM) and light doses (0.6, 1.2, and 1.8 $\text{J}\cdot\text{cm}^{-2}$) in the PDT treatment. At first, we tested the different PPIX concentrations with the lower light dose (0.6 $\text{J}\cdot\text{cm}^{-2}$) in respiration, and 0.5 μM was the only one we could not see any effect. Thus, we choose this PPIX concentration to test the different light doses. Overall, respiration after PDT treatment showed an increase in mitochondria proton leak, reducing the respiratory control ratio (RCR) and coupling efficiency, and promoting a partial loss of cytochrome c, proportionally higher as the PPIX concentration or light dose increased. Besides, it also promoted mitochondrial swelling due to the opening of the mitochondrial permeability transition pore. These results indicate that PDT using PPIX as a photosensitizer probably causes damage to mitochondrial membranes, impairing respiration, which can contribute to cell death afterward.

Palavras-chave: Terapia fotodinâmica. Bioenergética mitocondrial. Respiração mitocondrial.

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