Understanding tissue oxygenation

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Safeguarding adequate oxygen supply to tissues is one of the cornerstones of anaesthesiologic and intensive care. Understanding the determinants of tissue oxygenation and the cellular consequences of alterations in oxygen supply is mandatory for optimizing patient care. Over the last decade the microcirculation has gained more and more attention both from scientific and clinical perspective. Microcirculatory dysfunction in the critically ill has become a target for therapeutic interventions. In this respect it is important to realize that recent preclinical findings have changed the view on both oxygen transport at the microcirculatory level and the cellular response to altered oxygenation.

Classically, the capillaries were regarded as the exclusive place for oxygen to diffuse from the microcirculation into the tissue cells [1]. Based on measurements with tissue oxygen electrodes it was derived that large diffusion gradients were present and intracellular PO_2 should be low (typically between 1 and 10 mmHg). Low intracellular PO_2 was not regarded as a problem, because mitochondrial respiration had been shown to be independent on oxygen levels well below 1 mmHg [2]. This led to the idea that oxygen was no regulator of metabolism [3]. Therefore, in the classical view, it was irrelevant how much oxygen was exactly available to tissue cells, as long as some level of oxygenation was maintained. Much of our clinical thinking is based on these concepts, like the "better too much than too little oxygen" approach.

More recently, it has become evident that oxygen can diffuse from any small vessel and that even oxygen shunting between arterioles and venules takes place [1]. In the mean time, technical advances in methods for measuring oxygen in tissues led to the understanding that intracellular oxygen levels are much higher than always anticipated. For example, we demonstrated mitochondrial PO_2 in vivo to be in the range of 30-50 mmHg in vivo using a novel optical technique [4-6]. Nowadays, we also know that cellular oxygen metabolism [7] and gene expression [8] are oxygen-dependent over a broad range. Not only do cells respond to hypoxia, but also cellular defence mechanisms come into action in response to hyperoxia [9]. While the clinical consequences of these findings remain unknown, they do hint in the direction that "optimizing" oxygen delivery to tissue might have a negative downside.

In this presentation I will discuss the recent changes in our understanding of tissue oxygenation. Furthermore, I will explain how we measure mitochondrial oxygen tension by means of delayed fluorescence of protoporphyrin IX.

References

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