TARGETING MITOCHONDRIA WITH METHYLENE BLUE IN HUMAN EPICARDIAL ADIPOSE TISSUE

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Coronary heart disease (CHD) is the leading cause of mortality due to myocardial infarction and of morbidity due to heart failure. Epicardial adipose tissue (EAT) is considered a biologically active organ that has been extensively studied in the past decades in relation with CHD. Monoamine oxidases (MAOs) are mitochondrial enzymes that have been unequivocally recognized as sources of cardiovascular oxidative stress. Mitochondrial dysfunction and the related oxidative stress are central pathomechanisms in CHD, thus targeting mitochondria has emerged as promising therapeutic approach. Methylene blue (MB) is a redox agent reported to protect cardiac mitochondria, yet no data are available about its effects on adipose tissue. The present study, performed in EAT harvested from patients subjected to cardiac surgery (n=25), was aimed to assess the effects of MB in preventing the bioenergetic failure and oxidative stress by modulating ETC and MAOs expression. EAT samples incubated with MB (0.1 µM for 24h) were used for the assessment of MAO gene and protein expression (RT-PCR and immune-fluorescence) and ROS production (spectrophotometry and confocal microscopy). High-resolution respirometry was also performed on fresh EAT samples in the presence *vs.* absence of MB (0.1 µM). We report that MAO-A is the predominant isoform in the EAT. MB was able to reduce MAO expression and ROS generation and to increase all mitochondrial respiratory parameters. In conclusion, methylene blue is a potential candidate for drug repurposing by alleviating oxidative stress and mitochondrial stress in human epicardial adipose tissue in patients with coronary heart disease.

Keywords: methylene blue; epicardial adipose tissue; mitochondria; monoamine oxidase; oxidative stress.

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