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| **Carnosine enhances pulmonary-rehabilitation for COPD: evidence from a preclinical model** |
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| **Introduction/Aim:** Pulmonary rehabilitation addresses critical aspects of COPD such as exercise intolerance, but may not adequately mitigate the heightened risk of cardiovascular disease (CVD). Oxidative stress is a common driver in both COPD and CVD, highlighting the necessity for antioxidant strategies in conjunction with rehabilitation.  Carnosine is a bioactive dipeptide, which may protect against oxidative stress and reduce exercise fatigue. This study investigates if carnosine supplementation can enhance exercise training benefits in a preclinical model of COPD.  **Methods:** Male BALB/c mice were exposed to either room air or cigarette smoke (CS; 9 cigarettes per day) for up to 8 weeks with or without carnosine supplementation (1 mg/mL dissolved in drinking water). Along with 30 minutes per day involuntary treadmill exercise training (50% of maximal speed). Exercise tolerance, airway inflammation and vascular function were assessed.  **Results:** ChronicCS exposure negatively impacted on body weight gain, exercise capacity, resting heart rate (p<0.0001, n=14), along with marked airway inflammation (p<0.0001, n=6). This was associated with a blunted acetylcholine-induced vasodilatation, marking endothelial dysfunction (p<0.0001, n=6). Immunofluorescence analysis revealed increase adhesion of platelets to the vascular endothelium, and CD62p surface maker denoting their activation (p<0.0001, n=6). No significant benefits were observed by exercise training alone. However, carnosine supplementation with exercise training lessened the negative impacts of chronic CS on body weight gain, exercise capacity and resting heart rate without detectable changes in airway inflammation. Carnosine and exercise training preserved endothelial function, minimised platelet adhesion to the vascular endothelium and their activation by CS exposure.  **Conclusion:** Exercise training alone may be insufficient in fully addressing the heightened CVD risk associating with CS-induced COPD. Carnosine supplementation appears to have synergistic benefits on the vasculature, which may offer a more comprehensive and tailored approach to the management of COPD.  **Grant Support:**  NHMRC project grant APP1138915 |