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| **Creatine supplementation attenuates pathogen-induced airway inflammation in pediatric primary airway epithelial cells** |
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| **Introduction/Aim:** Airway inflammation and oxidative stress are hallmarks of airway disease, and pathogen infection may worsen the disease condition. Creatine is a nutritional supplement with anti-inflammatory and antioxidant properties. We investigated whether creatine supplementation mitigates pro-inflammatory and oxidative stress host responses in a model of pathogen-induced airway inflammation.**Methods:** Primary nasal airway epithelial cells (AEC) were sampled from non-wheezing, non-atopic infants undergoing elective surgery for non-respiratory related conditions (n=8, 3.2±1.0 years, 4 males). Primary AECs were established as air-liquid interface (ALI) cultures and pre-treated with PneumaCultTM-ALI growth media supplemented with 0, 1 and 10mM creatine monohydrate for 24 hours (h) before stimulation with 50 µg/mL lipopolysaccharide (LPS; O55:B5). Trans-epithelial electrical resistance (TEER) was measured at 6, 12, 24 and 72h post-LPS exposure, and supernatants and RNA were analysed for cytotoxicity, inflammatory markers, and gene expression. Statistical analyses were conducted using linear mixed-effect modelling.**Results:** LPS reduced TEER (p=0.031) and increased cellular cytotoxicity (p=0.020), *TLR4* (p=0.024), and mitochondrial antioxidant *SOD2* (p<0.0001) gene expression. Gene expression of *ICAM1*, *NF-κB1* and *Nox4* were unchanged after LPS stimulation, and there was no effect of creatine. Instead, treatment with 10mM creatine reduced cellular cytotoxicity (p=0.018), creatine transporter gene expression (*SLC6A8*, p=0.002), and increased cytosolic antioxidant *GPx1* expression (p=0.024). Creatine treatment (10mM) also reduced IL-6 (p=0.001) and IL-8 (p<0.001) in the supernatant following LPS stimulation.**Conclusion:** Treatment of pediatric primary AECs with creatine demonstrated anti-inflammatory effects against LPS-induced inflammation. Further investigation is warranted to investigate anti-inflammatory effects of creatine against live bacterial infections.G**rant Support:** RTP Scholarship; GNT1196188 |