**Megadose sodium ascorbate attenuates splanchnic sympathetic nerve activity in Gram-negative rodent sepsis.**

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**Introduction.** There is evidence that the brain can suppress innate immune responses to infections via the splanchnic sympathetic nerves. Bilateral splanchnic denervation can accelerate bacterial clearance and improve clinical state in established ovine sepsis. As splanchnic denervation is an unacceptable treatment for sepsis, it is critical to assess potential pharmacological approaches.

**Aims.** To assess, if megadose sodium ascorbate reduces splanchnic sympathetic nerve activity (SpSNA) during rodent Gram-negative sepsis and if cerebrospinal fluid (CSF) levels of ascorbate increase with treatment.

**Methods.** Male and female Sprague-Dawley rats were randomised to receive iv *E. coli* (4 × 109 CFU/mL, n = 14) or lipopolysaccharide (LPS, 60 µg/kg, n = 14; control for infection). After 1-h, these groups were randomised to receive iv megadose sodium ascorbate (n = 7/group) or sodium and fluid-matched control (placebo, n = 7/group) for 3-h. The left SpSNA was continuously recorded via silver wire electrodes. Plasma and CSF samples were collected to measure ascorbate concentrations.

**Results.** During infection, sodium ascorbate treatment, blunted the rise in SpSNA compared with the placebo-treatment (131±68.2 vs. 227±122 % of baseline, PGroup×Time=0.041). This effect was not observed in the LPS groups. Plasma ascorbate levels increased in the *E. coli* and LPS groups treated with sodium ascorbate compared with placebo (16.2±3.48 vs. 0.21±0.06 mM and 21.9±7.68 vs. 0.11±0.07 mM, P<0.0001 P<0.0001, respectively). This was accompanied by increases in CSF ascorbate concentrations in the *E. coli* and LPS groups treated with sodium ascorbate compared with placebo (0.66±0.24 vs. 0.14±0.09 mM and 2.51±1.11 vs. 0.09±0.05 mM; P=0.001 and P<0.0001, respectively).

**Discussion.** Sodium ascorbate treatment attenuated the increase in splanchnic sympathetic nerve activity in rats with live *E. coli* infection but not with LPS. The reduction in splanchnic sympathetic nerve activity with sodium ascorbate during live Gram-negative infection might be due to enhanced bacterial clearance from the bloodstream.