

MEETING ABSTRACT

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Endotoxin-induced microparticle formation is subject to tolerance development in humans

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Background

Microparticles (MP) are small membrane vesicles expressing tissue factor and staining positive for annexin V which are released from different cell types during cell activation and apoptosis. MP are considered to promote coagulation and impair vascular function. Circulating concentrations of MP are elevated in patients with systemic inflammatory conditions.

Methods

Formation of MP was studied in 8 healthy male subjects exposed to intravenous *E. coli* endotoxin (LPS; 2 ng/kg body weight) who were re-challenged after 17 ± 11 days. In addition, intravenous vitamin C (25 g) or placebo was administered 3.5 hours after LPS on alternate trial days in random order. Venous blood samples were taken before, 3 h and 6 h after LPS administration. MP were detected using FACS analysis. Leukocyte count and body temperature were measured as positive control. All results are expressed in medians in the unit 10^3 MP/ μ L plasma.

Results

MP formation was increased 3 h and 6 h after LPS administration. However, this effect was only demonstrable after the first LPS challenge with an increase of MP from baseline 596 units [range 399–1704 units] by a factor of 1.05 at 3 h and 3.87 at 6 h after LPS, and abolished after the second LPS exposure with a decrease from 874 units [430–1404 units] by a factor of 1.17 at 3 h and 1.25 at 6 h. This increase was independent of vitamin C administration. In contrast, reactivity of body

temperature and leukocytosis 3 h and 6 h after LPS was similar between the study periods.

Conclusions

Our results demonstrate rapid and marked formation of MP in healthy men after systemic LPS challenge. The development of tolerance to LPS is observed in the absence of mitigated systemic inflammatory responses. This suggests that MP formation follows different pathways than those of inflammatory mechanisms.

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