URIC ACID EFFECTS IN INFLAMMATORY RESPONSE

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Introduction and objectives: Uric acid is the main antioxidant that accumulates in plasma (200–500 μM). Its mono-anion form, urate (pKa 5.4), chelates transition metals ions, reacts with hydroxyl radical, singlet oxygen and repairs protein radicals. Despite its antioxidant potential, the release of urate from dying cells initiates inflammatory response. Urate also primes immune cells and induces cytokine production. Here, we investigated the effects of urate in superoxide, hypochlorous acid (HOCl) and cytokines release to understand the redox mechanisms by which urate modulate inflammatory response.

Materials and methods: HL-60 cells were differentiated into neutrophils (dHL-60; 5 days, 1.3 % dimethylsulfoxide) and activated with phorbol myristate acetate (PMA; 100 ng/mL). Superoxide production was detected using dihydroethidium probe (DHE). The products of DHE oxidation, 2-hydroethidium (2-OH) and ethidium were separated in a HPLC and quantified by fluorescence. The consumption of oxygen was evaluated by polarography using Clark electrode. Hypochlorous acid was measured by taurine chloroamine-DTNB assay. Tumor necrosis factor alpha (TNF-α) was quantified by Enzyme-Linked Immunosorbent Assay (ELISA).

Results and discussion: At low concentration (50 μM) urate decreased in 15% the levels of superoxide. However, at 500 μM, urate increased in 51% the levels of superoxide. Urate slightly increased oxygen consumption in cells activated with PMA. The incubation with PMA increased five times the levels of HOCl by dHL-60. Urate (0.5 to 2 mM) decreased HOCl concentration. The PMA also induced a hundred fold increase in TNF-α release (98.8 ± 1.2 pg/mL). Urate (2 mM) caused a significant decreased in TNF-α release (88.9 ± 3.2 pg/mL).

Conclusion: These results demonstrate that urate could have a dual effect in the redox balance during the inflammatory oxidative burst. Additional studies are being performed to understand the modulatory mechanisms of urate upon immune cells.

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Kew words: uric acid, inflammation, immune cells.