Oxalate impacts macrophage metabolism and immune response to uropathogenic E. coli infection

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INTRODUCTION

• Urinary stones are suggested to be associated with oxalate and bacterial infection.
• Escherichia coli (E.coli) has been isolated from human urine and urinary stones composed of oxalate.⁴⁻⁵ It has also been shown to promote calcium oxalate (CaOx) crystallization.³
• Stone formers have a high incidence of urinary tract infection (UTI) and increased inflammation.⁴⁻⁵
• Oxalate and crystals have been shown to induce inflammation (i.e. Monocyte Chemotactic Protein-1 chemokine release) in renal epithelial cells⁶⁻⁷.
• The mechanisms leading to UTI in kidney stone patients are not well defined.
• We have previously determined that 1) monocyte cellular energetics is reduced in CaOx kidney stone formers, and 2) oxalate alters redox homeostasis and cellular energetics in monocytes (Figure 1).

OBJECTIVE

—to determine the impact of oxalate on macrophage metabolism, redox status, and anti-bacterial response to uropathogenic Escherichia coli (E. coli) infection.

METHODS

THP-1 Cells (Monocytes)
• Treated with sodium oxalate (NaOx) (50 μM, 48 hours)
• Differentiated into macrophages (PMA, 200 nM, 48 hours)

THP-1m (Macrophages)
• ± CaOx Crystals (50 μM, 24 hours)
• ± Uropathogenic E. coli strain (CFT073; 1:2, 1-8 hours)

Results

Figure 3: The effect of oxalate and CFT073 on THP-1 macrophage (A) mitochondrial membrane potential, (B) mitochondrial superoxide, and (C) total reactive oxygen species (ROS) levels. Positive controls: FCCP, LPS, and Menadione. n=0.05, *p<0.01, ***p<0.001.

Figure 4: The effect of oxalate on the anti-bacterial response of THP-1 macrophages over time. *p<0.05, **p<0.01, ***p<0.001.

Figure 5: The effect of oxalate and CFT073 on THP-1 macrophage cellular energetics. Results are presented as mean ± se; n=5-6 replicates per group.

Figure 1: Cellular energetic profiles in (A) monocytes isolated from healthy subjects (HL; black circles) and CaOx SF (white circles) and (B) monocytes from HS (black circle) treated with sodium oxalate. Results are presented as mean ± se; n=5-6 replicates per group.

Discussion

• These findings show oxalate impacts macrophage redox status, metabolism, and anti-bacterial response.
• Elucidating the role of CaOx crystals on macrophages during KS disease is critical and should provide new insight to the field since stone formers have increased KS recurrence and associated UTIs.

References


Support & Contact

• NIH grants: K01 DK106284 & R03 DK123542 (TM) and the O’Brien Center P30 DK079337.
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