CURCUMIN IMPROVES SYSTEMIC RESPONSES TO EXERTIONAL HYPERTHERMIA

BUT DOES NOT ALTER PROTEIN CONTENT OF CIRCULATING LEUKOCYTES

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INTRODUCTION

Exertional heat stress increases gastrointestinal (GI) barrier permeability and risk of exertional heatstroke (EHS) via a TLR4-mediated inflammatory pathway. Curcumin has been shown to inhibit the MyD88 & TRIF-dependent pathways of TLR4 signaling in vitro but has not been examined in a human exertional heat stress model. PURPOSE: This work investigated the effect of 3d of 500mg/d dietary curcumin supplementation on the cellular and systemic responses to exertional heat stress in non-heat acclimated humans.

METHODS: Subjects (N=6) ran (65%VO₂max) for 60min inside an environmental chamber (37°C; 35%RH) two times (CURCUMIN/PLACEBO). Core temperature (Tc), heart rate (HR), and physiological strain index (PSI) were measured throughout exercise. Peripheral blood mononuclear cells (PBMC) were isolated from blood samples that were taken before (PRE), after (POST), 1hr (1POST), and 4hr after (4POST) exercise. From these samples, Western Blot was used to analyze the protein content of markers along the TLR4 signaling pathway (TLR4, MyD88, pIKB, IKB, pNF-kB, NFKB), as well as indicators of cellular energy status (SIRT1 & AMPK) and mediators of the heat shock response (pHSF-1, HSF-1, HSP70). Group differences were determined with 2-Way (Condition x Time) RM ANOVA.

RESULTS: Tc rose less (0.23±0.15°C) under CURCUMIN (p=0.01) and both HR and PSI were lower (HR: 9±2 bpm; PSI: 12±8%) from 45-60min of exercise (p<0.05). In PBMC, the ratio of pNF-kB to NFKB at 1-POST had returned to baseline in both groups. There was a trend towards increased HSP70 in CURCUMIN, but this did not reach statistical significance (p=0.05). p-AMPK was reduced by 82% in PLACEBO and by 57% in CURCUMIN at 1POST (p<0.05), with no difference between groups. Likewise, at 1POST TLR4 was reduced by 29% in PLACEBO and by 17% in CURCUMIN (p<0.05), with no difference between groups. CONCLUSION: Despite robust improvements in system physiology responses to exertional heat stress under CURCUMIN (reported here) and improvements in circulating inflammatory markers (reported elsewhere), we did not detect any significant differences in the protein content of PBMCs collected under PLACEBO and CURCUMIN conditions. With regard to exercise, we did note a significant elevation in pNF-kB/NFKB at 1-POST, which (ironically) coincided with a significant reduction in TLR4 (but not MyD88). At present, our working hypothesis is that pAMPK was downregulated in an effort to maintain pro-inflammatory capacity of PBMC during the “open window”, as reductions in pAMPK have been shown to potentiate LPS-induced activation of leukocytes in select animal models.

CONCLUSIONS

1. Short term (3d) dietary curcumin supplementation improves systems-physiology responses to exertional heat stress (Figure 1).

2. While curcumin supplementation did reduce circulating markers of inflammation and gastrointestinal barrier permeability (data not shown), there were no differences in the protein content of PBMCs collected under curcumin and placebo conditions.

3. An elevation in the pNF-kB to NFKB ratio at 1-POST was observed in both conditions. Paradoxically, this coincided with a significant reduction in TLR4 (but not MyD88) (Figure 4).

4. We postulate that the downregulation of p-AMPK and SIRT 1 at 1-POST was a compensatory mechanism that allowed PBMCs to maintain their pro-inflammatory capacity during the “open window” that preceds an endurance exercise challenge. Reductions in these markers have been shown to potentiate LPS-induced activation of leukocytes in select animal models. (Figure 5).

REFERENCES