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Adjunct host-directed therapies: low-dose aspirin to treat tuberculosis (TB).

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Background: Host-directed therapies to eliminate *M.tuberculosis* (Mtb) in the host by limiting the inflammation associated to the disease as ibuprofen have been lately validated in mice. However, new experiments are needed before entering clinical trials. The aim of this study was to evaluate the usefulness of low-dose aspirin (LDA) in a recently developed murine model of active TB involving Kramnik-mice.

M&M: The Cardona's murine model of active TB was used[1]. The effect of LDA on survival was evaluated in 2 different experiments, after infecting intravenously (IV) C3HeB/FeJ mice at day 0 with $4x10^4$ CFU of Mtb H37Rv Pasteur strain. Ibuprofen (Dalsy®, as positive control) or LDA (Bayer, 3mg/kg) were administered ly for 2 weeks (w) from day 21. N=12 mice were included per group. Experiment 1 included a) non-treated b) ibuprofen-treated and c) LDA-treated mice. Experiment 2 evaluated synergy with human standard antituberculous treatment (RIMSTAR (Sandoz), 6 weeks (5 doses/week) from w4, dose adjusted to mice weight): a) RIMSTAR alone (control), b) RIMSTAR plus ibuprofen and c) RIMSTAR plus LDA.

Results: The administration of LDA, as ibuprofen, achieved a statistically significant survival compared to the untreated mice (p=0.0032). LDA did achieve synergy with RIMSTAR when added as coadjuvant treatment (although not significantly).

Conclusions: The study shows the potential usefulness of LDA as adjunct therapy for TB when evaluated in an active TB murine model. We are now preparing a CT to confirm these results in humans.

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References: [1] PMID: 24291066