The Immunomodulatory Properties of 2-Hydroxyethyl Methacrylate are Mediated by the NLRP3 Inflammasome.

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Abstract

PURPOSE: The methacrylate monomer 2-hydroxyethyl methacrylate (HEMA), commonly used in dentistry, has multiple effects on the immune system. This study examined whether HEMA affects the immune system by inducing formation of the NLRP3 inflammasome.

MATERIALS AND METHODS: Human peripheral blood mononuclear cells (PBMCs) and the human monocyte cell line THP1 were cultured with or without 1000 μM HEMA. To block NLRP3 inflammasome activation, 130 mM KCl was also added to some of the cultures. For the in vivo studies, two different experimental setups were used. In the first experimental setup, mice were injected subcutaneously at the base of the tail with 20 μmol HEMA with or without 100 mM KCl. After 3 weeks, the animals were given an identical booster injection. Two weeks after the last injection, the mice were sacrificed and splenectomized. In the second experimental setup, HEMA (20 μmol), with or without 100 mM KCl, was injected subcutaneously into the tails of BALB/c mice. The mice were given two similar injections at 3-week intervals to allow evaluation of the local inflammation induced by HEMA. After the last inoculation, the injection site was examined daily for 4 days, after which the mice were sacrificed.

RESULTS: Cultures of PBMCs and THP1 cells exposed to HEMA in vitro produced more IL-1β and IL-18 than did control cells. Increased extracellular concentration of KCl inhibited the secretion of IL-1β. HEMA exposure did not induce cytokine
production in variants of the THP1 cell line unable to form the NLRP3 inflammasome. For the first experimental setup, the level of unstimulated basic splenocyte proliferation in vitro was significantly higher in cultures from mice exposed in vivo to HEMA only than in cultures from mice injected with HEMA plus KCl. In the second experimental setup of the in vivo studies, the HEMA-treated mice developed more pronounced inflammation at the site of injection compared to the group of mice given HEMA plus KCl.

CONCLUSION: HEMA affects the immune system by inducing formation of the NLRP3 inflammasome.

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