Metoclopramide nanoparticles modulate immune response in a diabetic rat model: association with regulatory T cells and proinflammatory cytokines

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Abstract:

Background: The inflammatory basis of diabetes mellitus directed the researchers’ attention to the immune system for better management and prevention of complications. Metoclopramide (MCA; the only US Food and Drug Administration-approved for gastroparesis) has the ability to restore immune function through increasing prolactin secretion. This study aimed to test the effect of BSA/MCA nanoparticles (NPs) on modulating immune response. Methods: BSA/MCA NPs were fabricated by desolvation and evaluated in vitro via measuring loading efficiency, particle size, and surface charge. The selected formula was further evaluated via differential scanning calorimetry and release behavior. Then, NPs were injected into rats (25 mg MCA/kg/week) for 3 weeks to be evaluated histopathologically and immunologically via measuring proinflammatory cytokines, such as IL1β, IL6, and TNFα, in addition to measuring regulatory T-cell frequency. Results: MCA was successfully loaded on BSA, achieving high encapsulation efficiency reaching 63±2%, particles size of 120–130 nm with good polydispersity, and a negative surface charge indicating that entire positively charged drug was encapsulated inside NPs. Differential scanning calorimetry thermography of selected NPs showed an obvious interaction between components and cross-linking of BSA molecules using glutaraldehyde, resulting in sustained release of MCA (around 50% within 3 days). MCA NPs significantly restored the immune response via decreasing proinflammatory cytokines and increasing regulatory T-cell frequency when compared to control and free MCA (drug not loaded in NPs)-treated groups. Histopathological examination of this MCA NPs-treated group did not show the characteristic lesions of diabetes, and apoptosis nearly disappeared. Conclusion: BSA/MCA NPs could be considered a new modality for treatment of gastroparesis, in addition to management of diabetes itself and preventing its complications via an MCA-immunomodulatory effect.

Keywords:

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