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ORIGINAL ARTICLE

Effect of sublingual immunotherapy on platelet activity in children with allergic rhinitis☆

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KEYWORDS
Allergic rhinitis;
Platelet activation;
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Beta-Thromboglobulin

Abstract
Introduction: The role of platelet activation in allergic inflammation received increasing attention. Sublingual immunotherapy (SLIT) for allergic rhinitis (AR) can modify the immunological process to an allergen, rather than treating symptoms simply.
Objective: The aim of this study was to explore the role of platelet activation during SLIT in children with AR.
Methods: Forty-two House Dust Mite (HDM) – sensitized children with AR were enrolled and received HDM allergen extract for SLIT or placebo. Serum of different time points during treatment was collected and used for detection of Platelet Factor-4 (PF4) and Beta-Thromboglobulin (BTG) concentration by Enzyme-Linked Immuno Sorbent Assay (ELISA).
Results: Our data showed decreased expression of PF4 and BTG protein after one year's SLIT. Besides, the decrease of symptom scores and serum PF4 and BTG protein concentrations were positively related.
Conclusion: During SLIT, platelet activation was inhibited significantly. Our results might indicate that inhibition of platelet activation within the systemic circulation is an important mechanism during SLIT.

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PALAVRAS CHAVE
Rinite alérgica;
Ativação plaquetária;
Imunoterapia sublingual;
Fator 4 plaquetário;
Beta-tromboglobulina

Efeito da imunoterapia sublingual sobre a atividade plaquetária em crianças com rinite alérgica

Resumo
Introdução: O papel da ativação de plaquetas na inflamação alérgica recebeu atenção crescente. A imunoterapia sublingual (ITSL) para rinite alérgica (RA) pode modificar o processo imunológico a um alergeno, em vez de tratar os sintomas simplesmente.
Objetivo: O objetivo deste estudo foi explorar o papel da ativação plaquetária durante a ITSL em crianças com RA.
Método: Quarenta e duas crianças com RA sensibilizadas por Ácaros de Poeira Domiciliar (APD) foram inscritas e receberam extrato de alergeno de APD para ITSL ou placebo. O soro de diferentes pontos no tempo durante o tratamento foi recolhido e utilizado para a detecção de fator 4 plaquetário (F4P) e concentração de beta-tromboglobulina (BTG) por Ensaio Imunoenzimático (ELISA).
Resultados: Nossos dados mostraram diminuição da expressão de F4P e proteína BTG após ITSL de um ano. Além disso, a diminuição dos escores de sintomas e o F4P sérico e concentrações de proteína BTG foram relacionados de maneira positiva.
Conclusão: Durante ITSL, a ativação plaquetária foi inibida significativamente. Os nossos resultados podem indicar que a inibição da ativação de plaquetas dentro da circulação sistêmica é um mecanismo importante durante ITSL.

Introduction

Sublingual immunotherapy (SLIT) is the only treatment that regulates the immunological process during development of allergic rhinitis (AR), rather than treating symptoms simply.[1,2] However, the underlying mechanisms in the process and potential biomarkers are still not fully characterized.

Platelet activation occurs during antigen-induced airway reactions in allergic and asthmatic subjects. Raised levels of platelet-derived mediators, such as the chemokines, Beta-Thromboglobulin (BTG) and Platelet Factor-4 (PF4), are observed in plasma and bronchoalveolar lavage fluid of atopic individuals. These mediators have the ability to activate eosinophils, increase expression of Fc-IgG and Fc-IgE receptors, stimulate basophils to release histamine, and so on.[3–6] Since SLIT can inhibit allergic inflammation significantly, we suppose that SLIT may affect platelet activation in AR children.

In the current study, we aimed to clarify the effect of SLIT on platelet activation of AR children by detecting changes of serum PF4 and BTG concentration.

Methods

Patients

Forty-two children aged 6–12 years with a clinical history of House Dust Mite (HDM) induced AR for at least one year were enrolled. Skin Prick Test (SPT) was performed to screen children allergic to HDM. Those with chronic diseases (e.g. asthma, malnutrition, anatomic malformation of the respiratory system, chronic lung disease, heart disease, gastro-oesophageal reflux disease, cystic fibrosis) and those with a history of chronic drug use (e.g. oral or nasal corticosteroids, antiepileptics, immune suppressives) were excluded from the study. The study was performed with the approval of local ethics committee and with the parent's written informed consent.

Sublingual immunotherapy and grouping

The HDM allergen extract for SLIT was manufactured by Wolwopharma Biotechnology Company (Zhejiang, China) and used in the form of drops (n° 1, 1 mg/mL; n° 2, 10 mg/mL; n° 3, 100 mg/mL and n° 4, 333 mg/mL). According to the manufacture's instruction, the patients were asked to take increasing doses (from n° 1 to n° 3) during the first three weeks' up-dosing phase, and then were instructed to have 3 drops of n° 4 solution once daily during the maintenance phase. Drops were instructed to be kept under the tongue for 2–3 min before swallowed. Children in the placebo group received diluents containing 50% glycerol and 50% saline buffer. All the children were grouped as SLIT (21 children) and placebo (21 children) group randomly. The drugs were labeled with patient code numbers, and the investigator assigned patients in a sequential randomized fashion to a study code number. Individual drug bottles were identity masked such that both patients and researchers were blind to treatment assignment. Study blinding was preserved at the study sites until all subjects completed the study. Compliance with medications was assessed both by the parent questionnaire and by measurement of drug weight administered every second week.