



SKIN PRICK TEST WITH ORAL STREPTOCOCCAL ANTIGEN AS A NEW DIAGNOSTIC TEST FOR BEHÇET'S DISEASE

Thesis

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List of Abbreviations

| | |
|----------------|--------------------------------------|
| μm | micrometer |
| 95% CI | 95% Confidence Interval |
| AIDS | Acquired Immune Deficiency Syndrome |
| ANA | Anti-Nuclear Antibody |
| ATP | Adenosine Triphosphate |
| AUC | Area under the ROC Curve |
| BD | Behçet's Disease |
| C3 | Complement 3 |
| CBC | Complete Blood Count |
| CMV | Cytomegalovirus |
| CNS | Central Nervous System |
| CT | Computed Tomography |
| DNA | Deoxyribonucleic Acid |
| EBV | Epstein - Barr Virus |
| EN | Erythema Nodosum |
| ESR | Erythrocyte Sedimentation rate |
| FNR | False Negative Rate |
| FPR | False Positive Rate |
| FS | Filter-Sterilized |
| FSS SPT | Filtered Self-Saliva Skin Prick Test |
| GI | Gastrointestinal |
| GU | Genital Ulcers |
| h | hour |
| HCl | Hydrogen Chloride |
| HIV | Human Immunodeficiency Virus |
| HLA | Human Leukocyte Antigen |

List of Abbreviations (Continued)

| | |
|-------------------------------|--|
| HSP | Heat Shock Protein |
| HSV | Herpes Simplex Virus |
| ICBD | International Criteria for Behçet's Disease |
| IFNα | Interferon Alpha |
| Ig | Immunoglobulin |
| IL | Interleukin |
| ISG | International Study Group |
| LR- | Negative Likelihood Ratio |
| LR+ | Positive likelihood ratio |
| M/F | Male/Female |
| MAGIC | Mouth and Genital Ulcers with Inflamed Cartilage |
| mm | millimeter |
| MRI | Magnetic Resonance Imaging |
| MS | Mitis-Salivarius |
| n | number |
| NAD | No Abnormality Detected |
| nm | Nano Meter |
| NPV | Negative predictive value |
| NSAIDs | Non-Steroidal Anti-Inflammatory Drugs |
| NSS SPT | Non-Filtered Self-Saliva Skin Prick Test |
| OR | Odds Ratio |
| PBMCs | Peripheral Blood Mononuclear Cells |
| PFAPA | Periodic Fever, Aphthosis, Pharyngitis, and Adenitis |
| PPV | Positive Predictive Value |

List of Abbreviations (Continued)

| | |
|--------------------------------------|-----------------------------------|
| PT | Pathergy Test |
| PTX | Pentoxifylline |
| RAS | Recurrent Aphthous Stomatitis |
| ROC | Receiver-Operating Characteristic |
| RR | Relative Risk |
| S. mitis | Streptococcus Mitis |
| S. sanguis | Streptococcus Sanguis |
| SE | Standard Error |
| SpxB | Pyruvate Oxidase |
| Th1 | T-lymphocyte helper 1 |
| TLC | Total Leucocytic Count |
| TLR | Toll Like Receptor |
| TNF-α | Tumor Necrosis Factor Alpha |
| USA | United States of America |
| VZV | Varicella-Zoster Virus |

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ABSTRACT

Background: Behçet's disease (BD) is a rare systemic vasculitis disorder of unknown etiology characterized by recurrent attacks of oral aphthous ulcers, genital sores and ocular lesion (triple-symptoms complex). Although the actual aetiology of BD is still unclear, the pathogenesis has been generally clearer by the etiological research based on the genetic intrinsic factors and immunological reactions to the extrinsic triggering factors in environmental agents.

Aim of the Work: To determine the reliability of skin prick test using streptococcal antigen extracted from saliva of Behçet patient, for in vivo diagnosis of Behçet disease in comparison to the usual pathergy test.

Patients and Methods: The study is a cross sectional study that was carried out from July 2017 to April 2019 at inpatient and outpatient clinic.

Results: All these results showed that skin prick test using streptococcal antigen extracted from saliva of Behçet patient could be a new diagnostic test for Behçet's disease. The diagnostic accuracy of skin prick using streptococcal antigen extracted from saliva of Behçet patient in Behçet's disease is 81.7%%, with sensitivity = 63.3%, specificity = 100%, positive predicted value = 100% and negative predicted value = 73.17%.

Conclusion: Skin prick test using streptococcal antigen extracted from saliva of Behçet patient showed a good diagnostic value in Behçet's disease

Keywords: Behçet disease, skin prick test using streptococcal antigen extracted from saliva of Behçet patient, recurrent oral aphthosis, pathergy reaction.

INTRODUCTION

Behçet disease is a rare vasculitic disorder that is characterized by a triple-symptom complex of recurrent oral aphthous ulcers, genital ulcers, and uveitis (*Alpsoy, 2016*). Although the actual aetiology of BD is still unclear, the pathogenesis has been generally clearer by the etiological research based on the genetic intrinsic factors and immunological reactions to the extrinsic triggering factors in environmental agents (*Altenburg et al., 2006*).

As one of the triggering factors, the oral unhygienic condition may be suspected, because periodontitis, decayed teeth and chronic tonsillitis are frequently noted in the oral cavity of BD patients (*Mumcu et al., 2004*). The infectious triggering factors are suspected to be many organisms including streptococci and herpes simplex viruses (HSVs) (*Galeone et al., 2012*).

The proportion of *Streptococcus sanguinis* (*S. sanguinis*), which was previously recognized as species of the genus *Streptococcus* named “*S. sanguis*,” was significantly high in the oral bacterial flora of BD patients in comparison with those of healthy controls (*Kaneko et al., 2008*). Most of the patients tend to acquire hypersensitivity against streptococci in their oral bacterial flora, as much stronger cutaneous reactions were seen by

-Introduction-

the prick with streptococcal antigen than those by “Pathergy test” (*Kaneko et al., 2014*). In vitro system, inflammatory cytokines, interleukin (IL)-6, and interferon (IFN)- γ were produced from peripheral blood mononuclear cells (PBMCs) of BD patients, which were stimulated by streptococcal antigen, and the serum-antibody titers against streptococci were also elevated in BD patients (*Kaneko et al., 2016*).

The diagnosis of BD is not thought to be difficult for the clinically typical cases who are based on the diagnostic criteria by Japanese and/or International Study Group (*Krokawa and Suzuki, 2004*), except for the atypical cases without the main mucocutaneous symptoms including recurrent Aphthous ulceration.

Pathergy test has been thought to be helpful for making a diagnosis of BD for long time (*Kaneko et al., 2014*), Pathergy was regarded as pathognomonic of BD because it was absent in control groups with recurrent aphthous stomatitis and systemic lupus erythematosus. It is used to describe hyper-reactivity of the skin that occurs in response to minimal trauma. A positive skin pathergy test (SPT), characterised by erythematous induration at the site of the needle stick with a small pustule containing sterile pus at its centre, and is among the criteria required for a diagnosis of Behçet’s disease (*Varol et al., 2010*).