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FMLP-, thapsigargin-, and H_2O_2-evoked changes in intracellular free calcium concentration in lymphocytes and neutrophils of type 2 diabetic patients

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Abstract Type 2 diabetic (T2DM) patients are immune-compromised having a higher susceptibility to infections and long-term complications in different parts of the body contributing to increased morbidity and mortality. A derangement in the homeostasis of intracellular free calcium concentration $[Ca^{2+}]_i$ is known to be associated with several diseases in the body including T2DM. Both neutrophils and lymphocytes play active protective roles in host immune response to infection showing impairment in microbicidal functions including phagocytosis and chemotaxis which are calcium-dependent processes. This study evaluated the process of $[Ca^{2+}]_i$ mobilization from both neutrophils and lymphocytes taken from blood of both T2DM patients and healthy age-matched control subjects investigating the effect of *N*-formyl-methionyl-leucyl-phenylalanine (fMLP), thapsigargin (TG), and hydrogen peroxide (H_2O_2) on $[Ca^{2+}]_i$ homeostasis. This study employed isolated peripheral blood neutrophils and lymphocytes from 24 T2DM patients and 24 healthy volunteers. Either neutrophils or lymphocytes were stimulated separately with fMLP, TG, or H_2O_2. Induced changes in $[Ca^{2+}]$ in both neutrophils and lymphocytes were evaluated using spectrofluorometric methods. Stimulation of human neutrophils and lymphocytes with fMLP, TG, or H_2O_2 in the presence of $[Ca^{2+}]_o$ resulted in significant decreases in $[Ca^{2+}]_i$ mobilization from T2DM patients compared with healthy controls. These data indicate that neutrophils and lymphocytes from T2DM patients are less responsive to calcium mobilizing agents compared with granulocytes from healthy controls and this is possibly due to the hyperglycemia. The results suggest that agonist-evoked decrease in $[Ca^{2+}]_i$ in immune cells might be one of the possible mechanisms of impaired immunity in diabetic patients.

Keywords Type 2 diabetes mellitus · Lymphocytes · Neutrophils · Cytosolic calcium · Agonists

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Introduction

Type 2 diabetes mellitus (T2DM) is a major metabolic disorder where the host defense mechanism is highly compromised [1]. Impaired functions of granulocytes and lymphocytes and several other immunological dysfunctions have been reported in studies relating to diabetic patients and animals [2, 3]. There are many ongoing studies trying to elucidate the association between diabetes and leukocyte functions. Calcium plays a very important physiological role as a second messenger in mediating cellular regulation [4]. A disturbance in the intracellular free calcium concentration ($[Ca^{2+}]_i$) is a major cause of metabolic disorders, and there is much evidence that Ca^{2+} plays an

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