Enhanced superoxide release and elevated protein kinase C activity in neutrophils from diabetic patients: association with periodontitis

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Abstract: Inflammation and oxidative stress are important factors in the pathogenesis of diabetes and contribute to the pathogenesis of diabetic complications. Periodontitis is an inflammatory disease that is characterized by increased oxidative stress, and the risk for periodontitis is increased significantly in diabetic subjects. In this study, we examined the superoxide (O_2^-)-generating reduced nicotinamide adenine dinucleotide phosphate-oxidase complex and protein kinase C (PKC) activity in neutrophils. Fifty diabetic patients were grouped according to glycemic control and the severity of periodontitis. Neutrophils from diabetic patients with moderate [amount of glycated hemoglobin (HbA_{1c}) between 7.0% and 8.0%] or poor (HbA_{1c} >8.0%) glycemic control released significantly more O_2^- than neutrophils from diabetic patients with good glycemic control (HbA_{1c} <7.0%) and neutrophils from nondiabetic, healthy individuals upon stimulation with 4p-phorbol 12-myristate 13-acetate or N-formyl-MetLeu-Phe. Depending on glycemic status, neutrophils from these patients also exhibited increased activity of the soluble- and membrane-bound forms of PKC, elevated amounts of diglyceride, and enhanced phosphorylation of p47-*phox* during cell stimulation. In addition, we report a significant correlation between glycemic control (HbA_{1c} levels) and the severity of periodontitis in diabetic patients, suggesting that enhanced oxidative stress and increased inflanunation exacerbate both diseases. Thus, hyperglycemia can lead to a novel form of neutrophil priming, where elevated PKC activity results in increased phosphorylation *ofp47-phox* and O_2^- release.]. *Leukoc. Biol.* 78: 862-870; 2005.