

OXIDATION FLUX CHANGE IN DIABETIC RETINOPATHY: DOES IT EXIST OR NOT?

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SUMMARY

The oxidation process is one of the most important natural processes. Oxidative change in retina is believed to be an important process in the pathogenesis of diabetic retinopathy. In the present study, the oxidation flux change was assessed in such cases. The simulation test to determine the oxidation flux change based on nanomedicine technique was used. Of interest, no flux change could be detected. The main pathogenesis should be direct injury of membrane structure by other processes. Therefore, study results support the concept according to which the oxidation flux change in basement membrane does not exist.

INTRODUCTION

Diabetic patients have a two- to four-fold increased risk for the development of microvascular (renal, neuronal and retinal) and macrovascular

complications. Mediators of vascular damage of diabetes include poor glycemic control, lipoprotein abnormalities, hypertension, oxidative stress, inflammation and advanced glycation end-products (AGEs), which are modified proteins formed by non-enzymatic glycation (1). Oxidative stress is increased in the retina in diabetes; the levels of oxidatively modified DNA and nitrosylated proteins are elevated, and antioxidant defense enzymes are impaired (2). The levels of superoxides are elevated in the retina, and the mitochondria become dysfunctional with proapoptotic protein, Bax, translocating from the cytosol into the mitochondria, and cytochrome c leaking out from the mitochondria (2).

Hyperglycemia *per se* or through the accumulation of AGEs, increased oxidative stress, leading to NOS uncoupling and nitric oxide (NO)-quenching by excess superoxide and peroxynitrite, and individual genetic background are thought to be responsible for this NO metabolism imbalance (3). There is substantial evidence from animal and clinical studies for both impaired antioxidant defenses and increased oxidative damage in the retina of diabetic subjects that were, in case of animal studies, reversible with antioxidant supplementation (4). Whether oxidative damage has a causative role in the pathology of diabetic retinopathy, and thus whether antioxidants can prevent or correct

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any retinal damage, has not been established, nor has the specific nature of any damaging species been characterized (4). Here, the author determined the oxidation flux change in such diabetic retinopathy cases.

MATERIALS AND METHODS

Basic information on retinal basement membrane in normal and diabetic retinopathy

Since there is no direct study on the human retinal basement membrane (*membrana limitans interna*) thickness in normal and diabetic retinopathy, the author used data from an experimental study in a cat model (5). According to the cat model, the thickness in normal and diabetic retinopathy is 72 nm and 114 nm, respectively. These values were used for further simulation study.

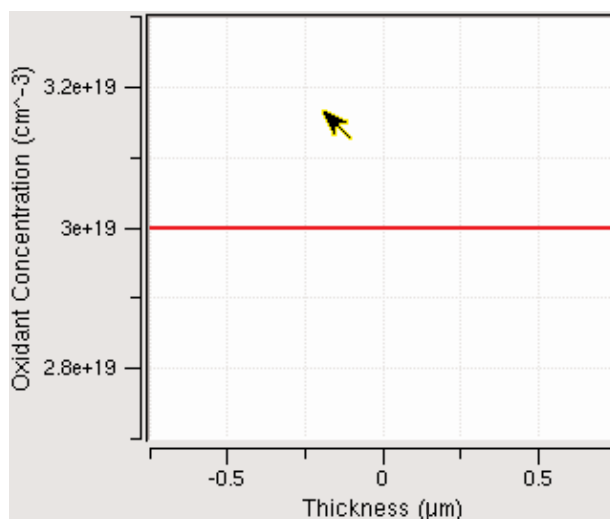
Simulation test to determine the oxidation flux

Basically, the operative definition of transmembrane flux means changes in ion movement across the membrane. The simulation test to determine the oxidation flux change based on nanomedicine technique was used employing the Process: Oxidation Flux technique. Briefly, this simulation technique integrates both the classic Deal-Grove's model and Massoud's model, which both describe the oxidation growth process (6). Specifically, this technique investigates the effects of different parameters and conditions on the oxidation process by looking into the oxidation flux (6). It gives the user freedom to adjust critical parameters and conditions in the process such as oxidant condition, time, initial oxide thickness, temperature, pressure, crystal orientation, as well as an opportunity to choose between Deal-Grove's or Massoud's model, or a combination of both (6). The primary condition in this study is wet condition, temperature 37°C, operated time 60 minutes and oxygen pressure 0.1 atmosphere according to the normal situation in the bloodstream. Difference in membrane thickness is used as a simulating condition. In this study, flux exchange data of a nondiabetic group was accepted as nonoxidation basement membrane.

RESULTS

According to the simulation test, the oxidant concentration for normal and diabetic retinopathy equals $3e+19/cm^3$ and $3e+19/cm^3$. Figure 1 shows the simulation results.

Figure 1. Oxidation flux across basement membrane



DISCUSSION

The oxidation process is one of the most important natural processes. It is implemented in the processes such as the gate dielectric growth. Oxidative change in retina is believed to be an important process in the pathogenesis of diabetic retinopathy. According to the recent study by Song *et al.*, most remarkable changes of vessels were observed in the group of experimental diabetic rats and included fragmental thickness, split of basement membrane, swelling and distortion of endothelial cells (7).

In this study, the author used a new technique in nanomedicine to determine the oxidation flux in diabetic retinopathy. Of interest, no change of flux could be detected. The main pathogenesis should be direct injury of membrane structure by other processes such as death of capillary cells and retinal neurons by a very near apoptosis process (8). Of interest, there is recent evidence that these findings suggest that oxidative damage, although probably involved, is unlikely to play a predominant role in the development of diabetic retinal microangiopathies (9). Therefore,

this study appears to support the concept according to which the oxidation flux change does not exist in diabetic retinopathy.

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