

Oxidative Stress in Diabetic Neuropathy: Strategies for Treatment

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Diabetes

Diabetes is a major public health problem. In 2014, the global prevalence of diabetes was estimated to be 9% among adults aged 18 years old and above [1]. The incidence of diabetes has increased immensely in the past 10 years. The World Health Organization (WHO) projects that diabetes will be the seventh leading cause of death in 2030 [2]. This alone makes it an epidemic disease. Diabetes is associated with a number of metabolic risk factors that contribute to a high rate of micro and macrovascular events. One of the most common and debilitating complications associated with diabetes is Diabetic Neuropathy (DN); it affects about 10% of patients newly diagnosed with diabetes and more than 50% of patients with longstanding diabetes [3].

Diabetic neuropathy

Diabetic neuropathy can be classified as peripheral, autonomic, proximal, or focal. Each affects different parts of the body in various ways [4]. Diabetic Peripheral neuropathy (DPN), the most common type of diabetic neuropathy is associated with impaired nerve conduction, abnormal thermal perception, axonal atrophy, demyelination, blunted regenerative potential, and loss of nerve fibers [5]. Additionally, DN can lead to autonomic dysfunction, which manifests as orthostatic hypotension, fainting, arrhythmias, gastrointestinal dysmotility, bloating, diarrhea, etc [6]. Patients diagnosed with DN experience an increased sensitivity to pain (hyperalgesia), as well as an increased responsiveness to non-painful stimuli (allodynia) [7-11]. With the progression of the disease, pain is replaced with complete numbness followed by serious foot problems, ultimately resulting in ulcerations and leading to foot amputation [12-14]. Although DPN has long been viewed as neurocentric, it is now widely accepted that the rate of peripheral nervous system deterioration is intimately correlated with the significant pathological interactions between neurons, Schwann cells, and microvascular endothelium [15-17]. In the last decade, much attention has been focused on the role of hyperglycemia in the progression of DPN. Clinical studies have established that intensive glycemic control and improved blood glucose levels reduce the incidence and slow the progression of DPN, thus clearly implicating hyperglycemia in the initiation of distal neuropathy [18-21]. However, the underlying mechanisms leading to diabetic peripheral neuropathy are not well described and need further investigations.

Diabetic neuropathy and oxidative stress

In recent studies, we and others have shown that high glucose/hyperglycemia is associated with increased systemic and cellular oxidative stress, now considered as a common pathway of cellular injury leading to diabetic complications [22-27]. It has been suggested that antioxidant treatment prevents or slows the development of neuropathy in animal models of diabetes, signifying a major pathogenic role of reactive oxygen species (ROS) in the pathology of DN [28-30]. However the sources of ROS as well as the mechanistic pathways that are altered by the production of these radicals are still unknown (Figure 1).

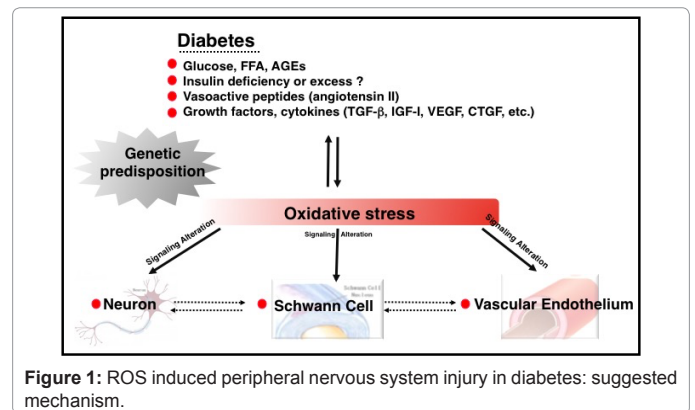


Figure 1: ROS induced peripheral nervous system injury in diabetes: suggested mechanism.

Conclusion

Understanding the cellular and molecular signaling mechanisms altered by ROS production in the onset and development of DPN is fundamental in developing new intervention strategies that would benefit diabetic patients and stop the progression or block the onset of DPN.

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