Internet Journal of Medical Update

Journal home page: http://www.akspublication.com/ijmu

Editorial

Insights into the management of diabetic neuropathy

Vidushi S Neergheen-Bhujun

Department of Health Sciences, Faculty of Science and ANDI Centre of Excellence for Biomedical and Biomaterials Research, University of Mauritius, Reduit, Republic of Mauritius

Diabetes mellitus is a metabolic disease affecting approximately 387 million people worldwide[1]. Type II diabetes mellitus (T2DM) is characterised by hyperglycaemia, altered lipid metabolism and insulin resistance[2]. Over 90% of patients with diabetes suffer from this type of clinical disorder[1].

Under normal physiological conditions, plasma glucose concentrations are maintained within a narrow range, despite wide fluctuations in supply and demand, through a tightly regulated and dynamic interaction between insulin secretion and tissue sensitivity to insulin[3]. The main underlying defect in T2DM, responsible for the deterioration of glycemic control is the progressive decrease in β-cell function that results in inadequate insulin secretion, a consequence of diabetogenic genes and acquired factors responsible for the etiopathogenesis[4].

Recent findings indicate that defects in β-cell function and increased insulin resistance occur early in the natural history of T2DM and can be present for 3 to 6 years before diagnosis. Insulin resistance can be described as impairment in the way glucose, lipids, protein metabolism, and vascular endothelium respond to the physiologic effects of insulin, characterized by the inability of insulin to activate its tyrosine kinase receptor and downstream signaling pathways in target tissues[5]. Insulin resistance eventually leads to a loss of functional pancreatic beta cell mass that results in an actual insulin deficiency[6].

Amongst the clinical problems that T2DM entails, diabetic complications that emanate from uncontrolled hyperglycemia are very prevalent. Diabetic neuropathy (DN) is one of the most common and severe manifestations that may affect sensory, motor and autonomic nerves[7]. Problems with digestion, urination, impotence and many other functions can result, but the most commonly affected area is the feet and legs contributing to diabetic peripheral neuropathy. Nerve damage may manifest itself in many ways including loss of feeling in the feet and toes, which is a particular risk which may lead to major infections and even amputation as a last resort treatment. People with diabetes in fact carry a risk of amputation that is more than 25 times greater than that seen in those without diabetes[1].

Although the mechanisms leading to diabetic neuropathy have not yet been fully elucidated, hyperglycemia or the loss of insulin-dependent regulation has been identified as the major culprit. A number of pathophysiological mechanisms have been proposed, inter alia: the polyol pathway and the subsequent induction of intracellular oxidative stress[8], the glycosylation of proteins that cause an abnormal function in the nerve[9], a reduction in neurotrophic factors and circulating hormone[10] as well as mitochondrial dysfunction[11].

Current understanding of the aberrant pathways involved in DN can lead to identification of important drug targets. Despite the availability of existing therapies such as medications against neuropathic pain and immunotherapy for the management of DN, achieving optimal treatment remains elusive. It seems that the only disease modifying treatment remains addressing the underlying diabetes via enhanced glucose control[12].

Although the cornerstone of DN treatment involves primarily glycemic control, medications that target the initiation of neuropathy are of significance and the quest for potential therapeutic agents is ongoing with considerable focus on natural products. In this vein, Patel *et al*[13] demonstrated the promising effects of scopoletin rich extracts of *Urtica dioica* in experimental models of diabetic neuropathy. The extracts had hypoalgesic effects and significantly increased the density of granule cells in the diabetic rat dentate gyrus, which can improve cognitive impairment in diabetics. Similarly, vitamin A may increase the local production of nerve growth factor and elicit the expression of the receptor for retinoic acid beta thereby restoring some functional changes induced by DN[14]. These findings encourage further pharmacological research to define the mechanism of actions of these bioactive constituents.

The IJMU December 2014 issue presents a mix of original work that focuses on biomedical research. The level of leptin and adiponectin as biomarkers in gestational diabetes is addressed followed by a randomized, non-interventional, observational study which evaluated the antihypertensive efficacy and tolerability of ramipril versus telmisartan in stage 1 hypertensive patients with diabetes mellitus. In addition, the neuroprotective effects of the co-administration of *Rauwolfia vomitoria* and *Gongronema latifolium* in experimental rats is described. Two case reports that highlight the application of yoga and prosthetic valve in clinical research are also included in this issue.

REFRENCES

1. International Diabetes Federation. 2014. Retrived from http://www.idf.org (accessed 4th December 2014)
2. Nolan CJ, Damm P, Prentki M. Type 2 diabetes across generations: from pathophysiology to prevention and management. *Lancet*. 2011;378(9786):169-81.
3. Holt RI. Diagnosis, epidemiology and pathogenesis of diabetes mellitus: an update for psychiatrists. *Br J Psychiatry Suppl*. 2004;47:S55-63.
4. Freeman JS. A physiologic and pharmacological basis for implementation of incretin hormones in the treatment of type 2 diabetes mellitus. *Mayo Clin Proc*. 2010;85(12 Suppl):S5-S14.
5. Aziz A, Wheatcroft S. Insulin resistance in Type 2 diabetes and obesity: implications for endothelial function. *Expert Rev Cardiovasc Ther*. 2011;9(4):403-7.
6. Scollan-Koliopoulos M, David B. The evaluation and management of childhood type 2 diabetes mellitus. *Prim Care Diabetes*. 2011;5(3):151-8.
7. Fowler MJ. Microvascular and macrovascular complications of diabetes. *Clin Diabet*. 2008;26(2):77-82.
8. Wilson DK, Bohren KM, Gabbay KH, Quiocho FA. An unlikely sugar substrate site in the 1.65 A structure of the human aldose reductase holoenzyme implicated in diabetic complications. *Science*. 1992;257(5066):81-4.
9. Degenhardt TP, Thorpe SR, Baynes JW. Chemical modification of proteins by methylglyoxal. *Cell Mol Biol (Noisy-le-grand)*. 1998;44(7):1139-45.
10. Fernyhough P, Tomlinson DR. The therapeutic potential of neurotrophins for the treatment of diabetic neuropathy. *Diabetes Rev*. 1999;7:300-11.
11. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. *Nature*. 2001;414(6865):813-20.
12. Calabek B, Callaghan B, Feldman EL. Therapy for diabetic neuropathy: an overview. *Handb Clin Neurol*. 2014;126:317-33.
13. Patel SS, Udayabanu M. Effect of Urtica dioica on memory dysfunction and hypoalgesia in an experimental model of diabetic neuropathy. *Neurosci Lett*. 2013;552:114-9.
14. Hernández-Pedro N, Granados-Soto V, Ordoñez G, Pineda B, et a. Vitamin A increases nerve growth factor and retinoic acid receptor beta and improves diabetic neuropathy in rats. *Transl Res*. 2014;164(3):196-201.

Vidushi S Neergheen-Bhujun
Associate Editor
Email: v.neergheen@uom.ac.mu

 DOI: http://dx.doi.org/10.4314/ijmu.v10i1.1