

Editor's note

Alpha-lipoic acid and stem cell approach for chronic diseases

As a sign of recent joint cooperation between MJI and *Deutsch Indonesische Gesellschaft für Medizin (DIGM)* or German Indonesian Medical Association, two articles written by the DIGM members are published in this issue.

One article reports the use of α -Lipoic acid (LA) for various pathoneurological cases different from peripheral diabetic neuropathy. Other article reviews the recent findings and stands of stem cell therapy in diabetic foot that is still a great burden for diabetic patients and healthcare providers despite all advancement pharmacotherapies of diabetes.

Lipoic acid is one of the endogenous antioxidant substances, which works hand-in-hand with mitochondria to produce energy.¹ One of the most studied roles of LA is as a cofactor in aerobic metabolism, specifically the pyruvate dehydrogenase complex (PDC or PDHC). This hypothesis has been revealed in a recent study by Sun et al.² They studied the effect of LA enriched nutrient combinations on physical performances, oxidative stress and mitochondrial biogenesis in rats after exhaustive exercise. They found out that nutrient supplementation increased the protein expression of mitochondrial complexes I, II and III, mtDNA number and transcription factors. Dehydro lipoic-HisZn (DHL-HisZn), a new LA derivative has been studied to inhibit ROS and to prevent renal ischemia-reperfusion injury in rats. DHL-HisZn reduced serum levels of blood urea nitrogen and creatinine, and decreased MDA levels in the kidneys of rats with ischemia-reperfusion injury.³

In brain and cognitive research area, LA together with other "mitochondrial nutrients" such as carnitine, Coenzyme Q10, and acetyl-L are supposed to be useful for aging brain and distressing condition from neurodegenerative diseases.^{4,6} Since mitochondria is one of the pivotal energy-producing organelles that abundantly reside in cells, therefore its bio(patho) physiological roles on many diseases is also well recognized. The extensive evidence from pre-clinical biomedical studies on the importance of "mitochondrial nutrients" such as LA should be followed up by a well designed clinical study. Case report on the use of LA for a certain disease, published in this MJI issue, should be a good start to develop the clinical evidence of LA.

The most distressing situation in diabetic care, despite of intensive glucose control through life style changes and pharmacotherapy, is diabetic foot. As it is reported

in the review written in this MJI issue by Kirana et al, there are 60.000 amputations performed every year in Germany. The main factors of these amputations are diabetic foot (DF) or arteriosclerosis. It is well known that diabetes mellitus has a long term effect on vascular system that leads to many disabilities.⁷⁻⁹ Amputation of lower limb is still used for patients with untreatable diabetic foot, but stem cell therapy gives a new hope to the patients.

The pathophysiology of diabetic foot is strongly related with the dysfunction of endothelial system where oxidative stress plays an important role. Angiogenesis, an endogen bioengineering of vascular system is dependent on the function of endothelium. Remodeling of the extra cellular matrix (ECM), tubular formation and expansion of the surrounding vascular tissue are key elements of angiogenesis. Clinical studies in stem cells in many areas have been emerged tremendously. Some of these studies showed significant results.^{10,11} The authors of the review explain the background theories, modes and approaches of stem cell therapy with regards to diabetic foot.

REFERENCES

1. Biewenga GP, Haenen GR, Bast A. The pharmacology of the antioxidant lipoic acid. *Gen Pharmacol.* 1997 Sep;29(3):315-31.
2. Sun M, Qian F, Shen W, Tian C, Hao J, Sun L, et al. Mitochondrial nutrients stimulate performance and mitochondrial biogenesis in exhaustively exercised rats. *Scand J Med Sci Sports.* 2011 Apr 21.
3. Koga H, Hagiwara S, Kusaka J, Goto K, Uchino T, Shingu C, et al. New α -lipoic acid derivative, DHL-HisZn, ameliorates renal ischemia-reperfusion injury in rats. *J Surg Res.* 2011 Feb 3. [Epub ahead of print].
4. Liu J, Killilea DW, Ames BN. Age-associated mitochondrial oxidative decay: improvement of carnitine acetyltransferase substrate-binding affinity and activity in brain by feeding old rats acetyl-L- carnitine and/or R- α -lipoic acid. *Proc Natl Acad Sci U S A.* 2002;99(4):1876-81.
5. Liu J. The effects and mechanisms of mitochondrial nutrient alpha-lipoic acid on improving age-associated mitochondrial and cognitive dysfunction: an overview. *Neurochem Res.* 2008;33(1):194-203.
6. Ziegler D, Ametov A, Barinov A, Dyck PJ, Gurieva I, Low PA, et al. Oral treatment with alpha-lipoic acid improves symptomatic diabetic polyneuropathy: the SYDNEY 2 trial. *Diabetes Care* 2006; 19;11: 2365-70.
7. Boulton AJ. The pathogenesis of diabetic foot problems: an overview. *DiabetMed* 1996; 13 (Suppl1): S12-6.
8. Maty SC, Fried LP, Volpato S, Williamson J, Brancati FL, Blaum CS. Patterns of disability related to diabetes mellitus in older women. *J Gerontol A Biol Sci Med Sci.* 2004; 59(2):148-53.
9. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates and projections. *Diabetes Care* 1998; 21:1414-31.

10. Kirana S, Stratmann B, Lammers D, Negrean M, Stirban A, Minartz P, et al. Wound therapy with autologous bone marrow stem cells in diabetic patients with ischaemia-induced tissue ulcers affecting the lower limbs. *Int J Clin Pract.* 2007; 61(4): 690-2.
11. Lu D, Chen B, Liang Z, Deng W, Jiang Y, Li S, et al. Comparison of bone marrow mesenchymal stem cells with bone marrow-derived mononuclear cells for treatment of diabetic critical limb ischemia and foot ulcer: A double-

blind, randomized, controlled trial. *Diabet Res Clin Pract.* 2011; 92,1: 26-36.

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