

Metformin Preserves Peripheral Nerve Damage with Comparable Effects to Alpha Lipoic Acid in Streptozotocin/High-Fat Diet Induced Diabetic Rats (*Diabetes Metab J* 2020;44:842-53)

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Using a streptozotocin/high-fat diet-induced diabetic rat model, Kim et al. [1] showed metformin to have a comparable effect on protection against diabetic neuropathy to that of alpha lipoic acid (ALA). Metformin and ALA showed similar effects on preservation of sensory threshold and intraepidermal nerve fiber density of peripheral nerves [1].

The mechanism of the preventive role of metformin on peripheral neuropathy has been reported to be reduced expression of inflammatory mediators (interleukin-1 β , inducible nitric oxide synthase, and nitric oxide) [2], and the anti-oxidative effect occurs via the adenosine monophosphate-activated protein kinase pathway [3]. Unfortunately, there was no measurement of pro-inflammatory and inflammatory markers to explain the neuroprotective effect of metformin. In addition, as Kim et al. [1] mentioned, the glucose-lowering effect of metformin might have the benefit of neuroprotection in diabetic animals. If there had been another anti-diabetic medication arm in the study, the effect of metformin on glucose control could have been separated from the benefit of neuroprotection by metformin independent of its glucose-lowering effect. The same group previously reported a neuroprotective benefit of pioglitazone compared to ALA in diabetic polyneuropathy [4].

Interestingly, metformin has been reported to be protective for paclitaxel (PAC)-induced neuropathic pain in a non-dia-

betic rat model [5], which might be evidence of the neuroprotective benefit of metformin independent of its glucose-lowering effect. In contrast, ALA had different effects between diabetic polyneuropathy and PAC-induced neuropathy; its protective effect was significant only in diabetic neuropathy [6].

Mechanistic study to investigate the effect of metformin on non-diabetic neuropathy such as PAC-induced neuropathy compared to other anti-diabetic agents or anti-neuropathic medications might provide insight on the neuroprotective benefit of metformin independent of its glucose-lowering effect.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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