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A ketogenic diet reduces mechanical allodynia and improves epidermal innervation in diabetic mice

Aim: To evaluate whether a ketogenic (very-low-carbohydrate) diet improves sensation, reduces pain, and restores cutaneous nerve fiber density in type 1 diabetic mice.
Methods: C57Bl/6 mice were rendered type 1 diabetic through a single intraperitoneal streptozotocin injection (180 mg/kg) and then assigned to either an early dietary intervention or a dietary rescue paradigm. Mice on the early intervention paradigm received a ketogenic diet 3 weeks after STZ injection for a total length of 12 weeks. Mice in the rescue paradigm received a ketogenic diet for 4 weeks, 9 weeks after diabetes induction and neuropathy development, for a study duration of 13 weeks. Metabolic phenotyping as well as sensory behavioral testing were performed biweekly after diabetes induction and at sacrifice.
Results: At study termination, both dietary paradigms increased body weight, reduced glycemic status, and increased circulating ketone body levels in type 1 diabetic mice. These metabolic improvements were accompanied by restored mechanical and thermal sensitivity as well as normalized cutaneous innervation. Importantly, authors showed that a ketogenic diet induced nerve fiber regeneration in type 1 diabetic mice displaying neuropathy symptoms.
Conclusions: These findings highlight that a ketogenic diet improves metabolic parameters, reduces pain, and restores small fiber innervation in type 1 diabetic mice. These results further suggest that a ketogenic diet may be a promising non-pharmacological approach for alleviating painful diabetic neuropathy risk in type 1 diabetes.

Comments. This study examines the effect of a ketogenic diet on the metabolic phenotype as well as sensory neuropathy using the streptozotocin-induced type 1 diabetic mouse, which models the human disease. In addition to the beneficial effects of the ketogenic diet on metabolic health, the authors found that this diet prevents or reverses mechanical and thermal nociception in type 1 diabetes. They also showed that this diet restores nerve fiber density, which is usually reduced following neuropathy progression. These neuroprotective effects may be mediated by elevated ketone bodies, potentially through detoxification of methylglyoxal, an avenue warranting further investigation.

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Reference. Enders J, Swanson MT, Ryals J, Wright DE. A ketogenic diet reduces mechanical allodynia and improves epidermal innervation in diabetic mice. Pain. 2022 Apr 1;163(4):682-689.
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