Effect of nicotinamide on microglia activation in an experimental model of diabetic neuropathy

Master's Degree in Nutrition and Metabolism

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1. ABSTRACT:

INTRODUCTION: Diabetes mellitus is frequently linked to chronic neuroinflammation. Accumulating evidence suggest that activated microglia underlies diabetic neuropathy. Currently there are no specific treatments for diabetic neuropathy. Noteworthy, the content of NAD+ is frequently reduced in target tissues. NAD+ is a mandatory coenzyme for the action of several NAD+ consuming enzymes that are involved in the inflammatory response. Therefore, its replenishment was considered as a potential therapy to prevent neuroinflammation. In this context, nicotinamide (NAM), which is a precursor of NAD+, may have positive effects on diabetic neuroinflammation.

HYPOTHESIS: We tested the hypothesis that increased bioavailability of NAM will attenuate activation of microglia in diabetic brains.

OBJECTIVE: The main aim of this study was to investigate whether NAM can improve neuroinflammation in a mouse model of experimental diabetes mellitus type 1 (T1D).

MATERIALS AND METHODS: C57BL/6J male mice were made diabetic with streptozotocin. Diabetic mice (defined by hyperglycemia >16 mM) were randomly distributed in different experimental groups and challenged to different doses of NAM for 25 days. A control, non-diabetic group of mice was used as reference. Neuroinflammatory biomarkers were determined by real time qPCR or immunohistochemistry (IHC), as appropriate. Tissue content of NAD+ was determined using a commercial kit.

RESULTS: IHC analysis revealed that microglia was activated in T1D mice, as shown by the increased abundance of IBA-1 in diabetic brain sections. Noteworthy, the gene expression of Aif1, the gene encoding IBA-1, in diabetic brains did not differ from those non-diabetic. The brain content of NAD+ was not significantly reduced in diabetic compared with non-diabetic mice; however, the administration of NAM increased the NAD+ in brains of treated T1D mice. This was accompanied by a

significant downregulation of a key marker of activated microglia (IBA-1), though only in those mice that received the highest dose of NAM.

CONCLUSIONS: These findings suggest that NAM may be useful for treating neuroinflammation in diabetes.

KEY WORDS: Neuroinflammation, microglia, NAD+, type 1 diabetes mellitus, vitamin B3.