Evaluating the role of insulin index in inducing nutritional ketosis for elderly health: A narrative review

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ABSTRACT

Introduction: The Insulin Index (II) measures how the body's insulin responds to various macronutrients over time-carbohydrates, proteins, and fats providing a wider view than the traditional glycaemic index (GI), which only shows how carbohydrates affect blood sugar. Chronic hyperinsulinemia has been linked to dyslipidaemia, non-alcoholic fatty liver disease, diabetes, heart disease, and other conditions related to aging. By inducing ketosis, insulin release is tapered down, leading to adipolysis. Nutritional ketosis by fasting or carbohydrates restriction is known to exert anti-ageing effects on the body. While the connections between the II and ketosis are not fully explored in clinical medicine, this review aims to highlight the current research update, the gaps and point out areas for future study. We hypothesize that food that secrete low insulin would induce ketosis. **Materials and Methods:** A literature search was carried out using PubMed, Cochrane and ResearchGate, Appropriate wordings for the search strategies were applied for II, ketogenic diets, and/or nutritional ketosis. The focus was on studies involving people aged 60 and older. Eligible study designs were randomized controlled trials, cohort studies, cross-sectional studies, systematic reviews and other reviews. **Results:** No existing studies that have evaluated usage of insulin index to induce ketosis. The usual state of nutritional ketosis is marked by a high glucose ketone index (GKI) and a moderate level of ketones in the serum. In diabetic, insulin and glucose responses often diverge. Meals with low II values were linked to a smaller insulin incremental area under the curve (iAUC), feeling of satiety and less hunger. High II values were associated with metabolic syndrome, insulin resistance, and type 2 diabetes. It was also a stronger predictor of post-meal insulin than counting carbohydrates. In older adults, nutritional ketosis has shown promise in enhancing cognitive and neurodegenerative health like Alzheimer's or Parkinson's. It also improves glycaemic control, lowers inflammation, improves liver and renal profiles, and prevents sarcopenia. Ketone bodies benefit heart failure patients by improving cardiac energy and reducing inflammation. In Malaysia, cancer is one of the major causes of premature mortality among elderly in Malaysia (16.6%), ketogenic diets may support cancer treatments by slowing tumour growth and improving the effectiveness and tolerability of chemotherapy. The anti-ageing or longevity effects of ketone bodies are attributed to the activation of AMP-activated protein kinase (AMPK) and sirtuins (SIRTs), along with the inhibition of the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and NOD-like receptor family pyrin domain containing 3 (NLRP3) inflammasome pathways, which collectively support antioxidant and anti-inflammatory effects. The role of the insulin/insulin-like growth factor 1 (IGF-1) signalling pathway during caloric restriction remains debated. Ketones also boost autophagy, mitohormesis, and telomere lengthening, improving lifespan and slowing aging. **Conclusion:** The nutritional ketosis seems to be useful dietary strategies for healthy aging. Current findings show no evidence of II inducing ketosis as we hypothesized. Hence, research on II inducing ketosis in general is warranted. These could help in sustaining ketosis related interventions, being an alternative therapy to fasting and ketogenic diets and to improve metabolic outcomes, cognitive function, and quality of life.

Keywords: Insulin index, nutritional ketosis, ketogenic diet, metabolism, cognitive function