MK-677

Background

According to Sigalos & Pastuszak (2018), “Growth hormone (GH) increases lean body mass, reduces fat mass, increases exercise tolerance and maximum oxygen uptake, enhances muscle strength, and improves linear growth” (p. 1). [2] Murphy et al. (1998) describe MK-677 as an orally active nonpeptide mimic of Growth hormone-releasing peptides (GHRPs), agents synthesized to stimulate release of endogenous Growth hormone (GH). [3] MK-677 is receiving widespread attention as a potentially viable, safer, and effective alternative to exogenous GH treatment for an array of therapies in patients with growth hormone deficiency (GHD).

Research

In a MK-677 study conducted by Nass et al. (2008) titled *Effects of an Oral Ghrelin Mimetic on Body Composition and Clinical Outcomes in Healthy Older Adults*, researchers report positive findings from a two-year, double-blind, randomized, placebo-controlled, modified-crossover clinical trial involving the oral ghrelin mimetic. [1] Study participants (*n* = 65 healthy men & women; ages 60-81; 43 experimental; 22 placebo) were randomly assigned and received oral administration of 25 mg MK-677 or placebo once daily. [1] Primary measurements consisted of Growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels and clinical outcomes at one year suggest significant increases in both hormones. [1] These results offer a potentially promising future for clinical application of MK-677 in anti-aging therapies.

Sigalos & Pastuszak (2018) conduct a literature review to investigate the efficacy and safety of GH secretagogues (GHSs). [2] A GHS (e.g. MK-677) is synthetically designed to promote secretion of endogenous Growth hormone (GH) and possibly attenuate negative outcomes associated with exogenous GH treatment. The authors suggest MK-677 may be promising due to its small molecular structure, and, by extension, asserted ability to offer robust oral bioavailability and potency. [2] The authors conclude that GHSs appear to be well tolerated overall in available studies, however, such findings should be balanced with reports of certain negative side effects linked to use (e.g. blood glucose regulation) and lack of rigorous, long-term studies. [2]

In an earlier study, Murphy et al. (1998) examined if MK-677 can mitigate diet-induced protein catabolism. [3] The researchers employed a double-blind, randomized, placebo-controlled, two-period, cross-over design with healthy volunteers (*n* = 8; ages 24-39) on a calorically restricted diet for two 14-day periods. [3] The primary endpoint measure was nitrogen balance and results suggest the GH secretagogue can reverse diet-induced nitrogen damage. [3] Another investigation by Murphy et al. (1999) generated evidence to suggest once daily oral administration of MK-677 may support bone turnover in the elderly, perhaps enhancing quality of life for this population. [5] Practitioners could potentially leverage MK-677s ability to promote nitrogen retention and consequent interim anabolic activities in therapies designed for anti-aging, catabolic conditions resulting from acute or chronic disease, weight-loss, and exercise & surgery recovery. [3]

Lee et al. (2018) observed MK-677s ability to augment peak GH concentrations via oral administration in rats, however, sustained dosing did not promote somatic growth. [4] Findings parallel previous studies that cite anabolic effects of MK-677 (e.g. GH increase & nitrogen retention) in early administration phases coupled with an apparent desensitization to GHS in prolonged use. [3, 4]

Conclusion

Although more rigorous research is needed to better understand MK-677s potential role in stimulating anabolic effects, existing data suggests this GH secretagogue may be useful in a variety of clinical anti-aging applications. Provided its purported robust oral bioavailability and potency, MK-677 could be a suitable substitute to exogenous GH treatment for a variety of therapies in patients with growth hormone deficiency (GHD).

References

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[3] Murphy, M. G., et al. "MK-677, an Orally Active Growth Hormone Secretagogue, Reverses Diet-Induced Catabolism1." *The Journal of Clinical Endocrinology & Metabolism*, vol. 83, no. 2, 1998, pp. 320–325., doi:10.1210/jcem.83.2.4551.

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[5] Murphy, M. G., et al. "Oral Administration of the Growth Hormone Secretagogue MK-677 Increases Markers of Bone Turnover in Healthy and Functionally Impaired Elderly Adults." *Journal of Bone and Mineral Research*, vol. 14, no. 7, 1999, pp. 1182–1188., doi:10.1359/jbmr.1999.14.7.1182.