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Letter to Editor: Potential Use of Meldonium as Supportive Treatment in Lifestyle Diseases: Addressing Knowledge Gaps and the Need for Further Research

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Dear Editor,

Meldonium is more widely recognized in the sports world than in medicine. It is a structural analog of gamma-butyrobetaine, which undergoes enzymatic hydroxylation to be converted into carnitine. Meldonium inhibits the activity of gamma-butyrobetaine hydroxylase, resulting in reduced carnitine levels and decreased carnitine transport across cellular membranes in the liver and kidneys. By lowering carnitine levels, this drug reduces fatty acid β-oxidation while increasing glucose utilization [1]. This shift towards glycolysis is particularly significant in situations of reduced oxygen availability or increased oxygen consumption, as carbohydrate oxidation generates ATP more efficiently under low-oxygen conditions. Due to its properties, meldonium has been banned by the World Anti-Doping Agency as a metabolism modulator. However, these same properties confer cardioprotective effects. In situations of decreased oxygen supply, such as a heart attack or ischemia, the heart muscle can manage oxygen deprivation more effectively. In animal studies, meldonium has been shown to reduce infarct size and improve cardiac recovery after ischemia [1,2].

Moreover, positive effects have been observed in experimental animal models of right ventricular (RV) and left ventricular (LV) dysfunction. Meldonium has been shown to attenuate the development of RV hypertrophy and prevent decreased left ventricular ejection fraction (LVEF) [3]. Human studies have also demonstrated the normalization of autonomic balance, as evidenced by changes in heart rate variability in post-infarction patients with type 2 diabetes mellitus treated with both meldonium and taurine [4]. Although meldonium is registered in Poland for supportive treatment in mild chronic heart failure, its effects extend beyond cardiology. In addition to its cardiovascular effects, meldonium has shown beneficial metabolic effects, such as dose-dependent reductions in blood glucose levels. It also prevented diabetes-related endothelial dysfunction and the loss of pain sensitivity in an experimental model of type 2 diabetes in rats [5].

Furthermore, recent animal model studies indicate that meldonium rapidly mitigates neuronal pathological damage, cerebral blood flow alterations, and mitochondrial injury, along with its subsequent oxidative stress response, thereby enhancing survival rates in mice brains and primary hippocampal neurons. This demonstrates the remarkable pharmacological efficacy of meldonium in treating acute high-altitude brain injury [6]. If these observations are confirmed in humans, it could open up potential applications for meldonium in preventing acute mountain sickness.

Given its beneficial metabolic and cardioprotective properties, meldonium may serve as an adjunct in the pharmacotherapy of major lifestyle diseases, particularly in the evolving treatments for heart failure, type 2 diabetes, and ischemic heart disease. Considering that many patients suffer from these conditions concurrently, meldonium therapy holds particular promise in such cases. However, while the results from animal model studies are encouraging, human clinical trials are necessary to fully integrate meldonium into medical practice. Moreover, such studies could provide valuable insights into the safety profile of the drug, including its potential side effects, drug interactions, limitations of use, and conditions under which dose adjustments may be required. Although several studies in the Russian language have evaluated the efficacy of meldonium, these studies included small patient groups, and most were published around a decade ago when treatment algorithms and the therapeutic arsenal for managing heart failure and diabetes differed significantly. Despite the promising results from laboratory research and small randomized trials, a significant knowledge gap remains regarding the actual benefits of meldonium use.

To draw definitive conclusions, large double-blind randomized clinical trials are necessary to provide a more conclusive answer on the appropriateness of meldonium use. Should these trials yield positive results, meldonium could potentially support the treatment of heart failure and type 2 diabetes, thereby finding its place in the dynamically evolving treatment protocols for these diseases.

Author's contribution

Conceptualization, Oskar Szymański and Magdalena Grzesiak, methodology, Oskar Szymański; check, Magdalena Grzesiak; investigation, Oskar Szymański; data curation, Oskar Szymański; writing - rough preparation, Oskar Szymański; writing - review and editing,

Magdalena Grzesiak

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Conflict of Interest Statement

The authors declare that they have no conflicts of interest to disclose related to this study.

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