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The Applicability of L-type Calcium Channel Blockers for Reducing Cardiac Iron Deposition in Transfusion-Dependent Thalassemia Patients

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Dear Editor,

There are a considerable number of transfusion-dependent thalassemia (TDT) patients in Iran, and the costs for the treatment of these patients are overwhelming for the health system.[1] Iron deposition in the vital tissues of TDT patients seems to be an inevitable phenomenon, which has been reported to be correlated with age, the volume of blood transfusion, and serum ferritin levels.[2] Cardiac failure due to iron deposition is the main cause of mortality in TDT patients, and therapeutic interventions, particularly conventional iron chelation regimens, largely fail to prevent this unfortunate outcome.[3] This is mainly because iron chelators, despite promoting a fall in ferritin levels, are ineffective in reducing iron accumulation in the heart.[4] Besides, increasing the dose of iron chelators or the use of combinational therapy may not always be applicable due to associated complications and patients' lack of adherence.[5] Another problem with conventional iron chelators is that the efficacy of these agents is unsatisfactory in patients with high tissue iron loads[6] and depends on the duration of treatment.[7]

Instead of iron chelation therapy, targeted therapy using therapeutic agents that specifically modulate iron uptake by cardiomyocytes seems to be a viable option to prevent cardiac iron overload.[8] It has been hypothesized that L-type calcium channels are the main routes for the entry of iron into cardiomyocytes. In this vein, recent clinical trials on TDT patients have noted that the combination of iron chelators with a blocker of these calcium channels (i.e., amlodipine) can be an effective strategy to decrease iron deposition in the heart.[8-11] However, amlodipine was unable to reduce hepatic iron, further suggesting that the main function of this drug can be attributed to its suppressive effects on the activity of these calcium channels.[9] In another study, the administration of L-carnitine for 6 months could significantly improve cardiac functional parameters in TDT patients,[12] and the ability of L-carnitine to regulate L-type calcium channels has been elucidated.[13] The administration of N-acetylcysteine for 6 months restored heart rate variability in thalassemia major patients.[14] This compound has also been reported to suppress the activity of L-type calcium channels in cardiomyocytes.[15] The potential role of these calcium channels in cardiac iron accumulation was also reported in another study, suggesting an inverse correlation between parathormone and cardiac iron overload.[16] This hormone has been noted to be involved in the regulation of L-type calcium channels in cardiomyocytes.[17]

These findings suggest that we should pay more attention to therapeutic agents other than available iron chelators for more effective removal of iron deposition from tissues, especially the heart. In this regard, a viable option may be the targeted suppression of L-type calcium channels as possibly the main route of iron entry to cardiomyocytes. In recent years, platforms for the targeted delivery of therapeutic agents to the heart have represented great leaps and breakthroughs. Examples of these platforms are nano-carriers which are successfully employed to carry drugs to the heart.[18,19] It seems that these technologies can be used in the near future to improve the delivery of therapeutic agents to the heart in TDT patients.

Authors' Contribution

Conceptualization: Ali Bazi, Iraj Shahramian. Roohollah Mirzaee Khalilabadi.
Supervision: Roohollah Mirzaee Khalilabadi.
Writing – original draft: Ali Bazi.
Writing – review & editing: Ali Bazi.

Competing Interests

There is no conflict of interests.

Ethical Approval

Not applicable.

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