Does Thermal Therapy Benefit Patients With Chronic Heart Failure?

To the Editor: The recent symposium by Ramani et al[1] is a concisely written overview of the current management of chronic heart failure, surely to be of value to both the specialist and generalist. Absent from this review, however, is any mention of "Waon" or thermal therapy, likely in part because Waon therapy is not well known or appropriately used by most clinicians in the United States.

First described by Tei et al[2] in 1995, the methodology of thermal therapy and its benefits for patients with chronic heart failure (CHF) have been detailed extensively in the literature.[3-6] These studies demonstrate improved New York Heart Association classification, decreased heart size, improved cardiac function, lowered incidence of arrhythmias, reduced brain natriuretic peptide and norepinephrine levels, and improvement in endothelial function. Furthermore, although not germane to this article, additional benefits have been described for thermal therapy in several other diseases, including Sjögren syndrome, peripheral vascular disease, pulmonary hypertension, and fibromyalgia.

It is interesting to speculate about reasons for the failure to use this therapeutic modality in this country, including absence of any financial incentives, but clearly a deficiency in knowledge of Waon therapy plays an important role. A brief discussion of thermal therapy in CHF would have been appropriate in this symposium in *Mayo Clinic Proceedings*, especially because Tei's original research into this modality was done while he was an international fellow at Mayo Clinic.

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1. Ramani GV, Uber PA, Mehra MR. Chronic heart failure: contemporary diagnosis and management. *Mayo Clin Proc*. 2010;85(2):180-195.
2. Tei C, Horikiri Y, Park JC, et al. Acute hemodynamic improvement by thermal vasodilation in congestive heart failure. *Circulation*. 1995;91(10):2582-2590.
3. Kihara T, Biro S, Ikeda Y, et al. Effects of repeated sauna treatment on ventricular arrhythmias in patients with chronic heart failure. *Circ J*. 2004; 68(12):1146-1151.
4. Cider A, Sveälv BG, Täng MS, Schaufelberger M, Andersson B. Immersion in warm water induces improvement in cardiac function in patients with chronic heart failure. *Eur J Heart Fail*. 2006;8(3):308-313.
5. Cider A, Schaufelberger M, Sunnerhagen KS, Andersson B. Hydrotherapy—a new approach to improve function in the older patient with chronic heart failure. *Eur J Heart Fail*. 2003;5(4):527-535.
6. Kihara T, Biro S, Imamura M, et al. Repeated sauna treatment improves vascular endothelial and cardiac function in patients with chronic heart failure. *J Am Coll Cardiol*. 2002;39(5):754-759.

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In reply: Dr Hanlon raises an interesting and thought-provoking point regarding the beneficial effects of Waon therapy (soothing warm therapy) in patients with CHF. This therapy, which uses repeated 15-minute treatments in a 60°C infrared sauna, has been reported in small studies to improve left ventricular systolic function and favorably affect natriuretic peptide levels.[1] Several behavioral and nontraditional approaches have been studied in CHF, including conscious breath control with extended expiration and reduced respiratory rate,[2,3] enhanced external counterpulsation,[4] and warm water immersion.[5] However, these therapies have not gained widespread acceptance, not because of third-party reimbursements but rather because the history of therapeutic trials in CHF has taught us several important lessons. First, the benchmark of therapeutic efficacy must be assessed by multicenter studies because single-center studies often provide findings that cannot be replicated by other groups and are debunked in larger well-controlled investigations. Second, the placebo effect and clinical trial inclusion ("Hawthorne" effect) can have a significant positive influence on study findings—simply via more frequent physician visits or patient-perceived benefits.[6] Finally, a satisfactory duration of follow-up is required to ensure safety and retention of benefit.[7] Consequently, although Waon therapy may show some promise as a therapy in patients with CHF, additional randomized, multicenter studies documenting safety and efficacy are needed before inclusion of this therapy in an evidence-based discussion of heart failure therapeutics.

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1. Miyata M, Kihara T, Kubozono T, et al. Beneficial effects of Waon therapy on patients with chronic heart failure: results of a prospective multicenter study. *J Cardiol*. 2009;53(2):214-218.
2. Bernardi L, Spadacini G, Bellwon J, et al. Effect of breathing rate on oxygen saturation and exercise performance in chronic heart failure. *Lancet*. 1998;351(9112):1308-1311.
3. Bernardi L, Porta C, Spicuzza L, et al. Slow breathing increase arterial baroreflex sensitivity in patients with chronic heart failure. *Circulation*. 2002;105(2):143-145.
4. Feldman AM, Silver MA, Francis GS, et al. Enhanced external counterpulsation improves exercise tolerance in patients with chronic heart failure. *J Am Coll Cardiol*. 2006;48(6):1198-1205.
5. Cider A, Schaufelberger M, Sunnerhagen KS, Andersson B. Hydrotherapy—a new approach to improve function in the older patient with chronic heart failure. *Eur J Heart Fail*. 2003;5(4):527-535.
6. Gottlieb SS, Pina IL. Enhanced external counterpulsation: what can we learn from the treatment of neurasthenia [editorial]? *J Am Coll Cardiol*. 2006;48(6):1206-1207.
7. Cohn JN, Goldstein SO, Greenberg BH, et al. A dose–dependent increase in mortality with vesanrinone among patients with severe heart failure. *N Engl J Med*. 1998;339(25):1810-1816.

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Editor's Note: Correction of Missing Page in the June 2010 Issue

In the June 2010 (volume 85, number 6) issue of *Mayo Clinic Proceedings*, a production error resulted in the redundant publication of page 518 and the omission of page 520 from the print (but not the electronic) version of the journal. To correct this error, page 694 of this July issue provides a reproduction of the missing page, formatted in a manner that will permit photocopying and substitution for the erroneously duplicated page. The journal's leadership regrets this error and apologizes to the authors and readers for any inconvenience the error has caused.

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during the DB phase included those from the 2-week dose taper during which the placebo group received 600 mg of gabapentin enacarbil.

A strength of the current study was the stringent definition of relapse, which provided a rigorous measure of maintenance of efficacy and not simply a reflection of transient worsening of RLS symptoms or of the natural course (eg, worsening) of this disorder.[32,33] Furthermore, the masked downward dose titration of gabapentin enacarbil for patients randomized to placebo after the SB phase likely reduced the chance of a transient RLS symptom rebound effect mimicking treatment relapse. This masked transition may explain the gradual increase in the number of placebo-treated patients experiencing relapse over time because they would have been unaware when they had switched from gabapentin enacarbil to placebo. A limitation of the study design is that it may have enriched the DB population for responders to active treatment by allowing only those meeting the SB response criteria to enter the DB phase. However, because all treatment responders were randomized at the end of the SB phase to continue to take gabapentin enacarbil or to receive placebo, this potential for "enrichment" was balanced across both treatment arms in the DB phase.

CONCLUSION

These findings provide clinical insight into the long-term management of RLS and the maintenance of efficacy and tolerability of gabapentin enacarbil in adults with moderate to severe primary RLS.

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REFERENCES

1. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisir J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology: a report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med*. 2003;4(2):101-119.

2. Allen RP, Walters AS, Montplaisir J, et al. Restless legs syndrome prevalence and impact: REST general population study. *Arch Intern Med*. 2005;165(11):1286-1292.

3. Hening W, Walters AS, Allen RP, Montplaisir J, Myers A, Ferini-Strambi L. Impact, diagnosis and treatment of restless legs syndrome (RLS) in a primary care population: the REST (RLS epidemiology, symptoms, and treatment) primary care study. *Sleep Med*. 2004;5(3):237-246.

4. Kushida CA, Allen RP, Atkinson MJ. Modeling the causal relationships between symptoms associated with restless legs syndrome and the patient-reported impact of RLS. *Sleep Med*. 2004;5(5):485-488.

5. Winkelman JW, Johnston L. Augmentation and tolerance with long-term pramipexole treatment of restless legs syndrome (RLS). *Sleep Med*. 2004;5(1):9-14.

6. Bogan RK, Fry JM, Schmidt MH, Carson SW, Ritchie SY. Ropinirole in the treatment of patients with restless legs syndrome: a US-based randomized, double-blind, placebo-controlled clinical trial. *Mayo Clin Proc*. 2006;81(1):17-27.

7. Driver-Dunckley ED, Noble BN, Hentz JG, et al. Gambling and increased sexual desire with dopaminergic medications in restless legs syndrome. *Clin Neuropharmacol*. 2007;30(5):249-255.

8. Ferini-Strambi L, Aarskog D, Partinen M, et al. Effect of pramipexole on RLS symptoms and sleep: a randomized, double-blind, placebo-controlled trial. *Sleep Med*. 2008;9(8):874-881.