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Letter to the Editor

Periodic Intensive Insulin Therapy Remains Experimental



Dear Dr. Watson:

We would like to express our concerns regarding the conclusions of Lakey et al,¹ which suggest therapeutic efficacy, superiority, and significant clinical benefits of periodic intensive insulin therapy (PIIT). These strong conclusions are based on weak observational studies lacking control groups and studies that are methodologically seriously flawed.^{2,3} More specifically, none of the observational studies included any control groups on either current therapies or placebo. Instead, 1 article³ was based on self-reported testimonials and questionnaires about neuropathy symptoms and comparisons to national hospitalization and emergency department statistics. Without proper clinical trials using direct comparators, the treatment remains unproven.

Lakey et al¹ conclude PIIT improves ulcer healing time by citing an observational study.² We would like to note that in selecting a "literature comparison," Elliott et al² may have erroneously quoted an article by Zimny et al,⁴ whose study found an average healing time for neuropathic ulcers and occlusive peripheral vascular disease ulcers, respectively, of 77 days and 133 days. Elliott et al² omit the 77 day average in their article where patients receiving PIIT had an 84-day average. The 77-day average may be a better comparator and would lead to different interpretation of PIIT. The omission is unexplained.

Finally, we believe the clinical research findings from a cited pilot study have been misrepresented by concluding that PIIT treatment produced reductions in nephropathy based on changes in serum creatinine level when the true measure of nephropathy is creatinine clearance, in which the study found no significant difference.⁵

PIIT is a business product of Trina Health, an entity in which several of the authors hold commercial interest. The authors cite 2 articles^{2,3} in support of their conclusions that were conducted by the Trina Health infusion business and were written by authors who hold commercial interest. This significant conflict of interest may lead to overstated conclusions. Moreover, the conclusions may be incorrectly interpreted by patients who believe PIIT treatment results are proven by strong clinical research and may be willing to pay for them out of pocket, and, even worse, forgo other treatments with proven effectiveness.

We believe the editors acted with good faith in accepting this article, but a better choice of words for the conclusion of this review article would have been "PIIT has a theoretical basis, but remains experimental and requires further clinical research with appropriate design, methodologies, and comparators to determine whether the therapy results in significant clinical benefits."

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