Sibutramine in the management of obesity

TO THE EDITOR:

While Dr Sheperd's review of obesity management ("Effective management of obesity," 2003; 52(1):34–42) is timely and appropriate, given the significant impact of this problem for both the individual and society, unfortunately his brief review of sibutramine therapy contains an inaccuracy. Although he correctly states that sibutramine is approved by the US Food and Drug Administration (FDA) for long-term obesity management, he is mistaken in his view that "long-term use of sibutramine cannot be recommended, and safety data are unavailable beyond 1 year of use."

Sibutramine (Meridia), used in combination with diet and lifestyle modification, has been demonstrated to promote weight loss and weight maintenance in obese subjects for up to 2 years,[1] and in fact is currently approved by the FDA for 2 years of therapy.[2]

There can be no doubt that obesity is a worldwide health problem. More than 60% of the adult population in the United States are overweight or obese, and the numbers are growing steadily.[3] It is estimated that nearly 300,000 deaths annually in the US may be attributed to obesity.[4] Given the enormous challenges faced by physicians and other health care professionals who treat obese patients, we need all the tools that are available to us, and therefore accurate information about safe and effective therapies for the treatment of obesity is essential.

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Immediate- vs extended-release metoprolol in heart failure

TO THE EDITOR:

The Clinical Inquiries article by Jon Neher and Sarah Safranek ("What is the most effective beta-blocker for heart failure?," *J Fam Pract* 2003; 52(5):396–398) was well-written, but one important point was missing: the distinction between immediate-release metoprolol (metoprolol tartrate [Lopressor]) and extended-release metoprolol (metoprolol succinate [Toprol XL]).

The important difference between these 2 medications—based upon the well-designed trials in the literature—cannot be understated. In the Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF),[1] extended-release metoprolol demonstrated a 34% relative risk in mortality, whereas in the Dilated Cardiomyopathy Trial,[2] the immediate-release metoprolol demonstrated no significant reduction in mortality compared with placebo.

Kukin and colleagues[3] compared the pharmacodynamic effectiveness and clinical effectiveness with regards to blood pressure reduction, and showed a similar hemodynamic effect with the 2 medications—although the titration

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schedule was somewhat different, making the titration of the extensed-release metoprolol easier and possibly more tolerable.

An article recently published by Kukin[4] addressed the differences in beta-blockers for the treatment of congestive heart failure. Kukin correctly distinguishes between the 2 forms of metoprolol currently available in the US.

Since carvedilol and bisoprolol are both produced in only 1 form, the distinction between the tartrate and the succinate forms of metoprolol are exceedingly important. In the table in the article, each medication is listed, but again, it is not made clear to the reader that it is the succinate form of metoprolol used in the MERIT-HF study.

I hope that this letter makes it to the readers of your magazine for clarification. Confusion between different forms of similar medications can present a significant problem.

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DR NEHER RESPONDS:

I would like to thank Dr Huneycutt for emphasizing that extended-release and immediate-release metoprolol differ chemically and should not be considered equivalent. It was extended-release metoprolol (containing a succinate salt) that was used in MERIT-HF,[1] so the recommendation to use metoprolol in heart failure applies only to the extended release formulation. I regret that the original article was not clearer about the formulation, and I hope these letters help prevent possible misinterpretation by readers.

What do we know about immediate-release metoprolol (which contains a tartrate salt)? It has not been studied as comprehensively as its sister compound, and study size has proven to be very important in answering this clinical question. The article cited by Dr Huneycutt—where no effect on mortality was seen—had 383 participants.[2] However, CIBIS-I, which had 641 participants, failed to document a significant reduction in mortality with bisoprolol,[5] while CIBIS-II, with 2647 participants, found a strong beneficial effect from the drug.[6]

So the final word on immediate-release metoprolol may not have been written. Still, the data we currently have does not support its use to prolong life in heart failure.

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