

Letters to the Editor

Effect of Soy Protein on Testosterone Levels

In Response: We appreciate the comments by the authors as they highlight important points for the relationship between soy and testosterone that may direct future studies. They have suggested that the 19% decrease in mean serum testosterone levels reported in our study (1) may have been largely due to the change in one subject (SP#2) and suggested that we reanalyze our data excluding this subject's values, as our data are not consistent with their unpublished meta-analysis. Although we cannot comment on an unpublished meta-analysis and its strengths or limitations, we remind the authors that in general it is not within good statistical principles to selectively delete any legitimate data. As stated in our article, testosterone and luteinizing hormone values were analyzed with the use of the Wilcoxon signed-rank test, which minimizes the influence of any particular subject on inference. The Wilcoxon signed-rank test is a nonparametric method, robust to outliers, and it does not delete any legitimate observation. Additionally, as stated in our article, we calculated percent change, not absolute change. Therefore, the highest initial value would not create the largest drop. In fact, the high denominator actually makes the percent change smaller for the same drop. Finally, the data we have been requested to delete do not represent the largest percent change. It was the 4th out of a total of 12 patients. Therefore, although we understand the author's question about an outcome that differs from their meta-analysis, we would like to point out that, as stated in our article, different soy preparations may behave differently in their selectivity for the estrogen receptor and small studies such as ours, and those with heterogeneous soy products included in a meta-analysis, require larger definitive studies to confirm activity.

We also agree that clarification of the correct values for baseline testosterone and luteinizing hormone levels reported in the article is important. Although the conclusion, the statistically significant reduction in testosterone of $19 \pm 22\%$ from baseline to day 28, and Figs. 1 and 2 (depicting data for each patient) are correct, the mean testosterone and luteinizing hormone at baseline should be clarified correctly in the text. The baseline values were calculated with the average of days -7 and 0, as this is a common practice to use more observations before treatment to decrease variation. The mean testosterone at baseline was 491 ± 240 ng/dL (range, 276-1,181 ng/dL). At day 14 of therapy (not at the start of therapy), the testosterone was 411 ± 175.82 ng/dL (range, 198-872 ng/dL). Similarly, the mean luteinizing

hormone at baseline was 4.79 ± 1.9 mIU/mL (range, 1.8-8.35 mIU/mL), whereas at day 14 (not at the start of therapy), the luteinizing hormone was 5.2 ± 2.36 mIU/mL (range, 2.5-11.1 mIU/mL).

Finally, as stated in our article, we chose a commonly used soy protein supplement that was widely available. We did not evaluate isoflavone content, as a correlation between the content and effects on testosterone has not been consistent (2-5). Instead, we assessed the effect of this product on estrogen receptor- α and estrogen receptor- β in an *in vitro* assay. Given that it is currently unclear which, if any, specific phytoestrogen could be responsible for activity *in vivo*, we also suggest that such assays be included in studies of soy in the future because of the power of this assay to detect the effect of many different estrogen compounds. Our studies also emphasize the need for efforts to standardize the variable soy preparations available, a problem with many dietary supplements, and estrogen receptor assays may contribute greatly. Given the common use of soy products in the general population, we encourage additional larger definitive studies with well-characterized products and hope that our data will help guide such future efforts.

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