Commentary on: Metabolic and Structural Effects of Phosphatidylcholine and Deoxycholate Injections on Subcutaneous Fat: A Randomized, Controlled Trial

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The report from Reeds et al represents data from a US Food and Drug Administration (FDA)-approved protocol that examined both safety and efficacy of injecting a combination of phosphatidylcholine (PC) and deoxycholate (DC) into abdominal fat. Mesotherapy, the use of multiple injections of chemical agents, pharmaceutical agents, or other ingredients into subdermal adipose tissue, is designed to ultimately generate necrosis that will lead to contour changes. Mesotherapy treatments have a long history, but with a lack of regulatory oversight and rigorous clinical protocols, the clinical outcomes have been suspect until recently.1,2 The PC-DC protocol from Reeds et al was designed to specifically test the premise that injections of PC-DC may be safe and efficacious.

The article describes 7 women who received 4 treatment sessions spaced 8 weeks apart. Tissue biopsies were obtained at the control site and treated sites at 1 week after the first treatment and at the end of the study. A number of tissue inflammatory markers (interleukin-6, tumor necrosis factor–α, monocyte chemotactic protein–1) and adipocyte-related enzymatic biomarkers associated with adipose tissue metabolism (leptin, adiponectin) were measured. In general, at 1 week posttreatment, a number of biomarkers in treated sites were noted to have significantly different levels from the respective control sites; many returned to their normal levels at the end of the study. The Discussion section of the main article states that the enzymatic or protein biomarker results were associated with an implied favorable adipose tissue loss, for which there were no results shown.

It is this point that requires clarification within the context of this study. The major hypothesis to be tested was the potential fat volume decrease in the treated versus control sites. I was asked to review these data on behalf of the American Society for Aesthetic Plastic Surgery (ASAPS) and presented my interpretation of the results at the annual conference. Dr Young, a senior author on the current study, had promptly provided all the data requested for this report. This FDA-approved study involved 6 women who completed the entire protocol (although 20 subjects were initially approved). Each subject received a different dose of PC-DC according to the various surface sizes of the abdominal areas that were labeled and treated. It is important to note that there were no clinical safety issues, and only anticipated adverse events were noted. At the end of the 4 injection sessions for each subject, the following summary results were noted: There were no significant differences in body mass index, skin fold thickness, fat mass, fat-free mass, percentage of body fat, visceral fat tissue, subcutaneous fat area, or adipose volume, size, diameter, or lipid content. There was 1 subset of magnetic resonance imaging data—subcutaneous fat site thicknesses—that did change over time in the treated sites (vs no change in control sites over the treatment intervals). The mean decrease in anterior fat width was 4.1 mm, and a 2.3-mm decrease was observed in the side fat width. In summary, the null hypothesis was met; there was no clinically distinguishable fat volume change in the patients who underwent hundreds of injections over a long period compared with controls.

The study was challenging on many different levels. Initially, FDA approval was acquired for PC-DC injections with an approved clinical protocol. However, many of the treatment parameters (dosing levels, surface area to be treated, timing of doses, number of doses, subject selection, adipose target site selection, etc) were not well documented in terms of safety, which is the first criterion for the FDA. A more conservative treatment protocol was ultimately approved. The methodology and techniques used in this study were impressive to document adipose volume changes and adipose-related metabolic consequences.
at 1 week for safety indications and at the end of the study for both safety and efficacy outcome measures. The scientific rigor presented in the protocol by Reeds and his coauthors met the criteria of ASAPS and its research arm, the Aesthetic Surgery Education and Research Foundation (ASERF), for examining the safety and possible efficacy of mesotherapy using PC-DC solutions.

Under these experimental conditions, the injection of PC-DC did not produce anticipated aesthetic results. This narrative does not imply that under different circumstances, PC-DC will not work. In fact, Kythera Biopharmaceuticals, Inc (Calabasas, California) has produced a first-in-class injectable drug that has undergone 4 successful clinical studies: 2 randomized, double-blind, placebo-controlled, Phase 2 studies using the injectable drug in the reduction of submental fat and 2 Phase 1 pharmacokinetic and histology studies. The company reports that the injectable is safe and shows efficacy in reducing localized fat deposits. The advancement of clinically translatable therapies carries risks and requires the fully informed consent of participating patients, but clinicians and patients ultimately benefit from the culmination of many studies in achieving evidence-based research milestones.

Disclosures

The author declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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