RESEARCH
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Is Nutrient Content and Other Label Information for Prescription Prenatal Supplements Different from Nonprescription Products?

Leila G. Saldanha, PhD, RD, FAND; Johanna T. Dwyer, DSc, RD; Karen W. Andrews; LaVerne L. Brown, PhD; Rebecca B. Costello, PhD; Abby G. Ershow, ScD, RD; Pavel A. Gusev, PhD; Constance J. Hardy, MS, RD; Pamela R. Pehrsson, PhD

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ABSTRACT

Background Prenatal supplements are often recommended to pregnant women to help meet their nutrient needs. Many products are available, making it difficult to choose a suitable supplement because little is known about their labeling and contents to evaluate their appropriateness.

Objective To determine differences between prescription and nonprescription prenatal supplements available in the United States regarding declared nutrient and nonnutrient ingredients and the presence of dosing and safety-related information.

Design Using two publicly available databases with information about prenatal supplement products, information from prescription and nonprescription product labels were extracted and evaluated. For the 82 prescription and 132 nonprescription products, declared label amounts of seven vitamins and minerals, docosahexaenoic acid (DHA), the presence of other nonnutrient components, and the presence of key safety and informational elements as identified in two Department of Health and Human Services Office of Inspector General (OIG)'s 2003 reports were compiled and compared.

Results Compared with nonprescription products, prescription products contained significantly fewer vitamins (9±0.2 vs 11±0.3; $P \leq 0.05$) and minerals (4±0.1 vs 8±0.3; $P \leq 0.05$). Declared amounts of folic acid were higher in prescription products, whereas vitamin A, vitamin D, iodine, and calcium were higher in the nonprescription products. Amounts of iron, zinc, and DHA were similar. Virtually all products contained levels of one or more nutrients that exceeded the Recommended Dietary Allowances for pregnant and/or lactating women. Product type also influenced ingredients added. Fewer prescription products contained botanical ingredients (6% prescription vs 33% nonprescription) and probiotics (2% prescription vs 8% nonprescription). Only prescription products contained the stool softener docusate sodium.

Conclusions Our analysis of prenatal supplements indicates that prescription and nonprescription supplements differ in terms of declared composition and nutrient strength, but have labels that are similarly sparse regarding aspects of use such as dosing information.
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NATIONAL SURVEYS IN THE UNITED STATES REPORT that pregnant women are at risk of dietary deficiency in several key nutrients such as calcium, iron, folate, and vitamin D.[1,2] For example, per data reviewed in the 2015-2020 Dietary Guidelines for Americans, dietary intakes from food sources alone among pregnant women were 24% below the Estimated Average Requirement for calcium, 26% for vitamin A, 29% for folate, 30% for vitamin C, 90% for vitamin D, 94% for vitamin E, and 96% for iron.[2,3] Based on these types of data, guidance from government and professional organizations often suggest the use of a prenatal vitamin supplement to help meet nutrient needs during pregnancy.[1,2,4,5]

The prevalence of prenatal supplement use among pregnant women in the United States is high, with estimates ranging from 78% to 92%.[6-8] Prenatal supplements are products formulated to meet the nutrition needs of women who are pregnant or planning to become pregnant; however,

there is little information in the scientific literature on what these products contain. In the United States, prenatal supplements can be obtained with and without a prescription through a variety of channels, including online on the Internet, over the counter in supermarkets, in pharmacies, and from community health departments.

A prescription is required for reimbursement by private and public health insurance programs, and therefore providers often make prenatal supplements available by prescription. As the name suggests, nonprescription prenatal supplements are products available without a prescription, such as those sold over the counter. In the United States, virtually all nonprescription prenatal supplements are marketed and labeled as dietary supplements. A dietary supplement is a product that contains dietary ingredients, such as vitamins, minerals, herbs or other botanicals, amino acids, fatty acids, metabolites, and extracts, and is regulated as a food by the US Food and Drug Administration (FDA).[9]

Because there is no mandatory registration for either prescription or nonprescription prenatal supplements, no complete listing of these products is available. However, two publicly accessible databases contain information on their labeling and content. These databases are available through the National Library of Medicine (NLM) web portal. The Dietary Supplement Label Database (DSLD; https://dsld.nlm.nih.gov/dsld/, National Institutes of Health) catalogs virtually all information printed on dietary supplement product labels marketed in the United States, and consumed by participants in recent National Health and Nutrition Examination Surveys. The DSLD reflects only what is printed on labels. Information captured include the name and form of active and inactive ingredients, amount(s) of active ingredient(s) and percent of daily value of nutrients, and information about the manufacturer/distributor of products, label claims, warning statements, along with a photograph of the entire label. It currently contains information from more than 65,000 product labels out of an estimated 92,800 labels. The DSLD is updated periodically, and ~1,000 new labels are added to the database each month. DailyMed (https://dailymed.nlm.nih.gov/dailymed/index.cfm, National Institutes of Health), the official provider of label information for drugs marketed in the United States, contains drug labeling information submitted to the FDA by the pharmaceutical industry. It includes package inserts, strengthened warnings undergoing FDA review, or minor editorial changes and other information about drugs. The labels are reformatted by the NLM to make them easier to read. DailyMed currently contains more than 87,000 drug listings submitted to the FDA, including information on prescribed supplements.

Our objective was to determine whether and how prescription and nonprescription prenatal supplements differed in their labeling and contents, with the intent to provide health care professionals with the information they could use in their practice.

MATERIALS AND METHODS

The search features in DailyMed and DSLD were used to identify and include all types and forms of prescription (n=82) and nonprescription (n=132) prenatal supplements listed in these databases as of September 2015. The LanguaL intended target group code (P0253) for pregnant and lactating women under the advance search feature was used to identify all prenatal supplements coded as "on market" in the DSLD, and the search term *prenat* to identify prescription prenatal products in DailyMed. Duplicate entries in the DSLD were deleted. Data extracted from labels and manually entered in Excel 2016 (Microsoft) included the labeling format, the number of vitamins and minerals used in formulating the products, the amounts of three vitamins (vitamin A, vitamin D, and folate), four minerals (iodine, calcium, iron, and zinc), and docosahexaenoic acid (DHA) identified as shortfall nutrients and of special public health interest during pregnancy, and the presence of other substances (botanicals, probiotics, and the stool softener docusate sodium) of interest to practitioners. For this study, nutrients are defined as dietary ingredients with Daily Values (DVs) established by the FDA for labeling purposes. The FDA has established DVs for only 28 vitamins and minerals.[10] Institutional review board approval was not required because the data in this study are publicly available and do not involve research on human subjects. This study was deemed exempt under federal regulation 45 CFR 46.101(b).

All labels were also coded for the presence of key safety and information label content elements identified in the 2003 Office of the Inspector General (OIG) of the US Department of Health and Human Services reports.[11,12] A coding instruction sheet was created to ensure uniform scoring of labels. All data were entered by one individual and random samples of labels were sent to five other coders to verify the accuracy of the coding. Safety information coded included interactions, contraindications, possible side effects, and adverse reactions. An example of informational label content coded was minimum duration of time for which a supplement should be taken to see results.

Declared labeled values were compared with the "old" (established in 1990) and "new" (revised May 27, 2016) DVs established by the FDA for vitamin A, vitamin D, folate, iodine, calcium, iron, and zinc for pregnant and lactating women.[10,13] Comparisons of product contents were also made with the current Recommended Dietary Allowances (RDAs) and the Tolerable Upper Intake Levels (ULs) established by the Food and Nutrition Board (FNB) of the National Academies of Sciences, Engineering, and Medicine.[3] The FDA has substantially revised the DVs used to report amounts of nutrients on food and dietary supplement labels. For example, the DV for pregnant and lactating women have been substantially lowered for vitamin A and folate and substantially increased for iron, vitamin D, and iodine. Table 1 summarizes these recommendations.

Information from prescription and nonprescription prenatal supplement product labels compiled in Excel 2016 were analyzed using Stata version 14.2.[14] Pearson's χ^2 tests were conducted to test differences in the presence of nonnutrient components, and a two-sample *t* test and one-way analysis of variance was used to determine whether there were between-group differences in the number and declared nutrient amounts. Differences with a probability value <0.05 were considered statistically significant.

RESULTS

Virtually all (94%) of the prenatal supplements in our study were multivitamin and mineral products containing three or