Women's Experiences With Isotretinoin Risk Reduction Counseling

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Importance Isotretinoin, an effective anti-acne therapy, is a known teratogen that is strictly regulated through the iPLEDGE program. However, since this program has not significantly reduced rates of pregnancies exposed to isotretinoin, new strategies for reducing rates of isotretinoin-exposed pregnancies are needed.

Objective To explore women's experiences with counseling about isotretinoin risk reduction.

Design, Setting, and Participants Structured interviews were conducted between January and September 2012. Two independent coders performed content analysis using a grounded theory approach. The study participants were 16 women who had used isotretinoin to treat severe skin disease and who were recruited from a single urban community via flyers displayed on college campuses, at dermatology clinics, and at student health facilities.

Main Outcomes and Measures Perceptions of isotretinoin-associated risks and understanding of ways teratogenic risks can be avoided.

Results Participants clearly understood that isotretinoin is teratogenic but had less understanding of contraceptive methods that effectively prevent pregnancy. Most described the counseling they received as anxiety provoking. Few were counseled about highly effective reversible contraceptives such as the subdermal implant or intrauterine contraception; most counseling focused on oral contraceptives. Women cited multiple influences on their contraceptive choices, including friends, family, physicians, the internet, and other media; however, some expressed concerns about the accuracy of these sources of information. For many, iPLEDGE was their first introduction to contraception. When presented with evidence-based information on the relative effectiveness of available contraceptives, participants expressed surprise that this was not part of the iPLEDGE materials.

Conclusions and Relevance Since few clinicians provide women information on highly effective (ie, intrauterine or subdermal) contraceptives, the iPLEDGE program increases anxiety about isotretinoin more than it helps women feel protected from the teratogenic risks of isotretinoin.
Severe acne can be debilitating, adversely affecting both physical and mental health. Isotretinoin continues to be the most effective anti-acne therapy, producing long-term remission or significant improvement for patients with treatment-refractory acne. As a result, isotretinoin significantly improves the quality of life for many persons affected by acne.

Because isotretinoin is known to induce birth defects if used during pregnancy, the US Food and Drug Administration (FDA) strictly regulates its distribution to female patients of childbearing potential. Initial risk reduction efforts included Roche's Pregnancy Prevention Program (PPP) and the FDA's System to Manage Accutane-Related Teratogenicity (SMART) program. The PPP required patients to sign a consent form, undergo pregnancy testing, and select 2 contraceptive methods prior to initiating isotretinoin therapy. The PPP was less successful than anticipated in reducing pregnancies affected by isotretinoin; thus, the SMART program was initiated in 2000. The SMART program added a mandatory sticker on dispensed isotretinoin bottles, formal patient registration in the program, and an optional pregnancy prevention education course sponsored by Hoffman-LaRoche. Prescribers were also required to provide written acknowledgment that they understood measures to minimize fetal exposure before they were given access to stickers and required forms.

Unfortunately, between 1984 and 2002, population-based estimates of the annual incidence of isotretinoin-exposed pregnancy ranged from 26.6 to 40.1 per 1000 woman-years of treatment. Persistent concerns about the relative ineffectiveness of these programs led to the creation of “iPLEDGE” in 2006, which requires women to review an educational booklet and complete monthly comprehension tests. In addition, women must pledge to use 2 forms of contraception and take monthly serum pregnancy tests 1 month before, during, and 1 month after isotretinoin treatment. Although the iPLEDGE requirements have unintentionally limited the use of isotretinoin by young women, 122 isotretinoin-affected pregnancies were still reported in the first year of this program, the majority due to contraceptive failure. When studied within a managed care setting, iPLEDGE did not significantly reduce rates of isotretinoin-exposed pregnancies compared with prior programs. Thus, we explored women's experiences with the iPLEDGE isotretinoin and pregnancy prevention counseling in an effort to guide future efforts to decrease rates of pregnancies exposed to isotretinoin.

Methods

This study was approved by the institutional review board of the University of Pittsburgh. All participants provided written informed consent.

Study Participants

We recruited women aged 14 to 45 years from Pittsburgh, Pennsylvania, using flyers posted on local college campuses, in dermatology clinics, and in student health facilities. Sixteen English-speaking women who had used isotretinoin to treat severe acne or, in 1 case, hidradenitis suppurativa were purposely selected to ensure inclusion of a range of age and race perspectives in this qualitative study.

Interview Procedures

Interviews were conducted from January to September 2012. Each interview lasted 1 to 2 hours. All but 2 interviews were conducted in person; these 2 were conducted by telephone. Participants received $20 compensation. Interviews were conducted using a structured interview guide (available on request) by a single interviewer.

The interviews explored women's experiences with isotretinoin, counseling about isotretinoin and pregnancy prevention, experiences with contraceptives, strategies to answer health-related questions, and the role of family, friends, and the media in women's contraceptive choices. Finally, women were asked for suggestions to improve the counseling given to other women considering treatment with isotretinoin. Women were asked to review and respond to a variety of contraceptive educational materials that were used as conversation prompts (available on request). All interviews were audio recorded and transcribed verbatim.

Participants completed a brief survey after the interview that assessed demographic information (eg, age, race, educational level, employment status, insurance coverage, and relationship status), pregnancy, and contraceptive history. In addition, after viewing the assorted educational materials, patients were asked to rank the effectiveness of available contraceptive methods.

Data Analysis

Transcripts were coded by 2 independent coders (C.A.W. and M.J.P.), who read them line by line to identify words, phrases, and passages related to women's pregnancy prevention counseling experiences when using isotretinoin. Coders also identified what women knew about different forms of contraception, especially the relative effectiveness of different contraceptive methods. Each unit of qualitative text was coded. The coders compared codes and developed a codebook. An iterative process or rereading and recoding transcripts refined the codebook. The senior author (E.B.S.) was available to adjudicate differences in the coding scheme. Final codes were thematically examined and provided insight into the study's research questions. Thematic saturation was reached by the 14th interview. Representative quotations were selected to illustrate central themes.

Results

Participants ranged in age from 17 to 34 years (mean age, 25 years). Most participants had used isotretinoin for at least 5 months within the past 5 years; however, 1 participant had been treated with isotretinoin in 2003 before iPLEDGE was instituted. During treatment with isotretinoin, 13 women used an oral contraceptive or contraceptive ring as their primary form of birth control; the other 3 women had been abestinent while...
taking isotretinoin. Additional participant characteristics are listed in Tables 1 and 2.

Sources of Information
A dermatologist was the sole source of teratogenic risk counseling for 7 participants; 5 were counseled by their dermatologist and a nurse and/or physician’s assistant, 3 by a nurse or physician assistant alone, and 1 was counseled by her pediatrician. Only 3 participants were given referrals to a family planning specialist for information on pregnancy prevention. All participants who enrolled in iPLEDGE (n = 15; 1 participant used isotretinoin prior to the introduction of the iPLEDGE program) remembered receiving printed iPLEDGE materials and completing online quizzes as part of the program. In addition, 5 women recalled watching an educational video.

Contraceptive Counseling
For many of the younger participants, iPLEDGE was their first introduction to contraception. As 1 participant put it, “I was kind of glad about [the opportunity to learn about contraception] because I was like ‘Oh cool. Now if I ever want to start having sex I don’t have to have an awkward conversation with my mom about starting birth control. I’m already on it.’”

other woman stated that beginning to take the birth control pill for iPLEDGE “made me more comfortable with birth control for the future.”

Some participants felt that pregnancy prevention counseling was absent or overly brief prior to initiating isotretinoin treatment. Circumstances varied: half of the participants had previously used contraception, while one-fourth had never been sexually active. A 17-year-old, non–sexually active woman stated that the only adverse effects of isotretinoin described to her were “side effects in terms of [skin] dryness,” without any discussion of contraception. Another who was already using the pill said “The two things they pushed were the pill and abstinence… they briefly discussed the other options, but it was not really a choice, it was like, this is what you should do.” Another woman also reported feeling that her contraceptive counseling was overly abbreviated, stating “no one ever explained anything to me, ever. They just said you are going to have to be on hormonal birth control.” However, most participants reported being presented with at least a few contraceptive options.

Some participants felt that clinicians did not provide additional counseling because they assumed the woman would continue using the contraceptive she had previously used. One woman described her experience as “I just kept doing whatever I had been doing”; another indicated she did not get any contraceptive counseling because she was “already on the pill.”

Overall, most participants felt that their contraceptive counseling was incomplete. As 1 participant stated, “looking back, I wish it had been longer because now that I know more about various types of birth control and the various side effects… I wish they would have told me some of those things.”

Influences on Contraceptive Choice
Most participants perceived personal autonomy when deciding to initiate isotretinoin therapy and use of contraceptive
methods. However, women reported influences on both of these decisions. Of sexually active participants, most reported speaking with their sexual partner about the risks of isotretinoin, with the exception of 2 who did not discuss the potential risk to a fetus with their partners. As one put it, “I think I felt like it was my issue.” Three-fourths of the women interviewed spoke with female family members about contraception, and all of the women mentioned discussions with friends. Women also consulted other resources for further information about birth control (Table 3), but many participants were concerned about the reliability of information from these sources.

Perceptions of Highly Effective Reversible Contraceptives

Of the 16 women interviewed, most (n = 13) had heard of intrauterine contraception (IUC). Half had heard of the subdermal contraceptive implant, but only 1 mentioned its superior effectiveness, and 1 mentioned she would have liked learning more about it while using isotretinoin. Although some participants had positive perceptions of these contraceptive options (Box), most acknowledged that they had limited familiarity with IUC or subdermal contraception, with statements like “I actually don’t know anyone who uses one.” One participant noted “I think I remember them being fairly effective.” Of those aware of IUC, most acknowledged that IUC was effective, but only 3 had ever seriously considered using IUC.

The interviews revealed many misconceptions about highly effective reversible contraceptives. For example one worried “I have just heard that sometimes it [the IUC] comes out during sex.” Another woman said, “they [IUCs] have a terrible reputation... word on the street is that it is like being an oyster and having that little sand bit in you.” Some women disliked the fact that these contraceptives are placed inside a woman’s body and had fears such as “having it dislodge or mis-carrying.” In general, participants were far less familiar with and had more negative reactions to the contraceptive implant than IUC. One woman said “anything being implanted in me sounds scary.” Another worried “what do I do if I want it pulled out?” Another, “I don’t think I would ever have anything implanted in me; it’s a little too much.”

Interestingly, after reviewing educational materials that provided current, evidence-based information about highly effective reversible contraceptives, such as the FDA’s contraception guide and a chart developed by the World Health Organization, many women changed their opinions about IUC and subdermal contraception. In the words of 1 woman, “Well, I might be more tempted to explore the arm implant and IUD since it’s the most effective. I mean I wouldn’t have thought of that before, until I saw your 99% on how it works.” Many participants expressed dismay that no one had ever told them about the differences in contraceptive effectiveness. One woman stated “I do remember, after having made that decision, thinking ‘Could I have gotten an IUD or something like that?’ I knew that those things existed but I didn’t really recognize that they were an option for me.” Another woman, when asked if she felt satisfied with the counseling she received, responded “[I thought] I did. But now I don’t.”

Anxiety-Producing Counseling

Former participants in the iPLEDGE program remembered monthly blood tests and online quizzes and mentioned that the booklet’s red and yellow cover looked like hazard warnings. As 1 woman put it, “it first made me feel a little scared. I mean I had no intentions of getting pregnant during the time I was taking it, but I just thought it was very dramatic, and I definitely realized how important it was.” Another said “I was a little bit concerned, because reading through the pamphlet is scary—it says it can kill your liver, it can kill children. And you have to be on birth control. So I was like ‘o…k…’” One woman summed up her experience saying “there was definitely anxiety, and when I look back on the experience I think that taking the pill and having to use condoms at the same time was kind of a lot to do daily, and have to think about. I think it

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Table 3. Sources of Contraceptive Information Consulted After Being Prescribed Isotretinoin

<table>
<thead>
<tr>
<th>Information Source Used</th>
<th>Participants, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friends</td>
<td>16</td>
</tr>
<tr>
<td>Family members</td>
<td>11</td>
</tr>
<tr>
<td>Internet resources</td>
<td>10</td>
</tr>
<tr>
<td>WebMD</td>
<td>4</td>
</tr>
<tr>
<td>Google</td>
<td>3</td>
</tr>
<tr>
<td>Government and/or nonprofit websites (ie, websites ending “.gov” or “.org”)</td>
<td>2</td>
</tr>
<tr>
<td>Forums</td>
<td>2</td>
</tr>
<tr>
<td>Manufacturers’ websites</td>
<td>1</td>
</tr>
<tr>
<td>Clinician</td>
<td></td>
</tr>
<tr>
<td>Obstetrician/gynecologist</td>
<td>9</td>
</tr>
<tr>
<td>Primary care provider</td>
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</tr>
<tr>
<td>Pharmacist</td>
<td>1</td>
</tr>
<tr>
<td>Dermatologist</td>
<td>2</td>
</tr>
<tr>
<td>Medical colleagues</td>
<td>2</td>
</tr>
<tr>
<td>Package insert</td>
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</tr>
</tbody>
</table>

* Nine participants mentioned consulting more than 1 source of information.

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Box. Participants’ Comments on Advantages of Intrauterine and Subdermal Contraception

**Intrauterine Contraceptive (IUD)**

After I had taken the Accutane, a couple of years, a year or so ago, I had a roommate that...ended up getting an IUD. I thought “Man, I wish that I had known about that.” But no one had really offered it to me. Takes out human error—it’s in there and you can’t mess that up.

I think everyone that I know of really liked [the IUD] and to be honest, if I had to go back, honestly hindsight is 20/20. But if I had to go back and know what my plan was, it probably would have been a pretty good option. Because I know paying for birth control every month is probably more expensive than getting that for 5 years.

**Subdermal Contraceptive**

You wouldn’t have to take it everyday. God! That works for three years?

Yeah! That is definitely a benefit.

Once it is in you wouldn’t have to remember to take anything.
really stressed me out. It was very stressful, more than I think it needed to be.”

**Information Overload**
A number of women seemed overwhelmed by the amount of pretreatment information presented to them and confused about what the iPLEDGE program actually entailed. As 1 woman said, “I mean I scanned through [the iPLEDGE material] but I didn’t really read it.” In the words of another, “I think I signed stuff that said if I were to get pregnant I’d have to get an abortion.” While this participant was relatively young when treated with isotretinoin, this misperception is distressing.

Overall, 11 of the participants reported feeling “satisfied” with the counseling they had received. However, 5 participants expressed unease with their counseling experiences. One stated “I assumed that everything we talked about was going to be in [the iPLEDGE pamphlet], and I didn’t ask any questions, I didn’t really read it, but probably what would have been nice if someone had sat with me and flipped to a page and was like ‘okay, this is what we are talking about’—maybe it would have stimulated some process in my mind to ask questions.”

Opinions varied concerning the time health care providers spent on counseling, and many had a number of suggestions to improve counseling, including using more visuals in educational materials, highlighting differences in contraceptive effectiveness, and mentioning adverse effects of isotretinoin other than teratogenesis.

**Discussion**
This qualitative study found that women who had participated in the iPLEDGE program clearly understood that isotretinoin adversely affects pregnancies; all participants recalled receiving strong warnings about the risk of birth defects, and many found these warnings anxiety provoking. Women received less information about how to effectively protect themselves from unintended pregnancy while using isotretinoin. Although most initially reported satisfaction with counseling, none were fully informed about the pros and cons of all contraceptive options, and many had misconceptions about highly effective reversible contraceptives. This is unfortunate because women need accurate information to make informed decisions and avoid the teratogenic risks of isotretinoin.

Outside of the United States, a range of pregnancy prevention programs have been designed to reduce pregnancy exposure to isotretinoin. The Pregnancy Prevention Programme in the European Union (EU) and Drug Risk Assessment in Pregnancy program in Germany are very similar to the iPLEDGE program, and in both the United States and Europe, exposed pregnancies continue to occur.12,13 Recently, a retrospective study in Germany found that most (70%) of exposed pregnancies in a 15-year period were due to lack of contraceptive use at the time of conception, while 30% resulted from contraceptive failure.13 Elsewhere in the EU, ongoing reports of isotretinoin-exposed pregnancies sparked a number of initiatives, yet in 1 recent study, 50% of responding physicians did not believe that women would be sufficiently protected even with the additional procedures recently implemented in the EU.13

The contraceptive choices of our study participants while taking isotretinoin were similar to those of most iPLEDGE participants (condoms and oral contraceptives).13 Unfortunately, with typical use, 15% of women become pregnant within their first year of using condoms, and 8% within the first year of use of oral contraceptives.14 Thus, it is not surprising that the majority (72%) of isotretinoin-affected pregnancies have been found to occur in women attempting to use condoms and oral contraceptives.13 In contrast, intrauterine contraceptives and subdermal implants are over 20 times as effective as oral contraceptives.14 Yet few participants in this study were aware of these differences in contraceptive effectiveness. Neither iPLEDGE nor treating clinicians provided educational materials that emphasized the increased effectiveness or encouraged participants to select one of these more highly effective irreversible contraceptives. In some cases, clinical inertia appeared to limit the contraceptive information clinicians provided to their patients.

Since this was a qualitative study, our findings should be interpreted in the context of several important limitations. First, we recruited participants from a single urban community, although our study population included women from a range of racial and ethnic backgrounds. In addition, social desirability bias may have prevented some participants from fully sharing their reproductive health experiences; for example, only 1 participant reported a history of undesired pregnancy. Nonetheless, these women’s insights should help shape efforts to refine counseling for women prescribed isotretinoin.

The iPLEDGE program appears to be successful in informing women that isotretinoin is teratogenic, but participants need more information about available contraceptive options, particularly those with the highest levels of effectiveness. Although some prescribers of isotretinoin may be unfamiliar with these dramatic differences in contraceptive effectiveness, their patients have a critical need for this information. Whether these patients would be best served by revision of the iPLEDGE education materials, updates for prescribing physicians, or referral to a local family planning specialist deserves further study.
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REFERENCES