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Psoriasis in Pregnancy: A Review of Most Important Literature Data

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SUMMARY In women with psoriasis, the course of the disease during conception, pregnancy and delivery generally does not differ from other individuals involved. In psoriasis patients, pre-pregnancy period offers time to learn about the hereditary nature of the disease, the effect of hormonal changes and acceptable treatments during pregnancy. In the majority of patients, psoriasis improved during pregnancy and worsened six weeks after delivery. Women should tell their dermatologist early if they plan to become pregnant and the treatment during pregnancy should be considered carefully. This article provides a short review of the most important literature data on therapeutic options for psoriasis in pregnancy.

KEY WORDS: psoriasis, pregnancy, pre-pregnancy period, safe therapeutic options

INTRODUCTION

Psoriasis is a common inflammatory skin disease characterized by infiltration of inflammatory cells into the epidermis and altered keratinocyte differentiation (1). Psoriasis affects about 25 million people in North America and Europe, and is probably the most prevalent immune-mediated skin disease in adults (2). The incidence is similar for the two sexes, although women generally develop the disease earlier than men. Because the majority of psoriasis patients present before the age of 40, many female patients may become pregnant. Information regarding the heritability of psoriasis can be used on providing advice to patients that inquire about the potential risk to their children (3). If one parent is affected by psoriasis, the risk to offspring is 14%-15%. If both parents have psoriasis, the risk to offspring is 41%-75%. If neither parent has psoriasis but a child is affected, the risk to subsequent offspring is 6%-20% (4,5).

THE EFFECTS OF PREGNANCY ON PSORIASIS

It is generally accepted that pregnancy has favorable effects on psoriasis (6). In a retrospective study by Raychaudhuri *et al*., data on the clinical

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course of psoriasis during pregnancy were collected from Psoriasis Life History Questionnaires. Information relevant for the clinical course of psoriasis during pregnancy was evaluated in respect to improvement/worsening, number of pregnancies, severity of disease, and some other clinical parameters. Results showed that psoriasis improved during pregnancy in the majority of patients. Data available from 91 pregnancies revealed that psoriasis improved in 51 (56%), worsened in 24 (26.4%), and remained unchanged in 16 (17.6%) patients. Also, the appearance of new psoriasis lesions was quite frequent in the early postpartum period (7). In a study by Murase *et al*., the psoriatic body surface area was assessed 5 times over a year in pregnant patients with psoriasis and non-pregnant, menstruating patients with psoriasis as a control group. During pregnancy, 55% of patients reported improvement, 21% reported no change, and 23% reported worsening. Postpartum, 9% of patients reported improvement, 26% reported no change, and 65% reported worsening (8). Boyd *et al*. suggest the improvement of psoriasis in pregnancy to be associated with high concentrations of progesterone, which down-regulates T cell proliferative response (9). In contrast, Murase *et al*. found high levels of estrogen to correlate with improvement in psoriasis, whereas progesterone levels did not correlate with psoriatic change (8).

Pre-pregnancy period

Most doctors recommend that women suffering from psoriasis and considering pregnancy visit dermatologist to talk about everything that is connected with psoriasis and pregnancy. Pre-pregnancy is a perfect time to talk about genetic risk factors and treatments that will be safe during pregnancy and breastfeeding.

Psoriasis does not affect fertility or rates of miscarriage, birth defects, or premature delivery (10). Most of the information available on the use of medication during pregnancy is derived from case reports or retrospective collections of pregnancy outcomes in clinical series (11).

One reason why there is so little information regarding the use of medications during pregnancy is because there is selective bias against studies in pregnant women for ethical reasons (11). Most information on the effects of fetal exposure comes from inadvertent exposures by women who did not know they were pregnant at the time they were taking the medication (11).

TOPICAL TREATMENTS

Topical treatments are first line treatments for psoriasis. The potential absorption of topical medications through the skin must be considered. Emollients, anthralin (dithranol) and topical steroids are considered safe in pregnancy (10).

Anthralin

Anthralin is among the oldest topical treatments for psoriasis and it has been used safely for decades in pregnant women. No animal or human studies have examined the potential birth defects associated with the use of anthralin (10,11). Particular attention has been paid to the anthralin potential renal toxicity, but no evidence of systemic absorption or toxicity has been associated with topical anthralin treatment (12,13).

Corticosteroids

Topical corticosteroids are the most commonly used therapy for localized psoriatic plaques generally and also in pregnancy. It is believed that the usual treatment of pregnant women with topical corticosteroids is associated with little, if any, teratogenic risk (11). This belief is supported by several studies of corticosteroid use during pregnancy (14-16). If topical steroids are required, the amount should be limited. The degree of systemic absorption depends on many factors such as dose, use of occlusion, amount of surface area treated, number of applications, and duration of treatment (11). The more potent corticosteroids have been found to be absorbed in sufficient amounts to cause systemic effects such as adrenal suppression (6,11).

Lam *et al*. suggest a conservative approach to warn pregnant women not to use large amounts of topical corticosteroids over extensive parts of the body because of the possibility of having a newborn with low birth weight (11).

Salicylic acid

After topical application of salicylic acid or its derivatives, between 9% and 25% of salicylic acid has been reported to be systemically absorbed (17,18). This small systemic absorption and the lack of adverse reports suggest a low teratogenic potential of topical salicylic acid. Pregnant women should be warned against applying preparations containing topical salicylic acid over large areas of their bodies for prolonged periods of time (11). They should also be advised that combining topical salicylic acid with other medications and the use of occlusive dressing can potentially increase

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the systemic toxicity and teratogenic risk of topical salicylic acid (11).

Calcipotriene

Approximately 6% of calcipotriene, a synthetic vitamin D3 derivative, is absorbed systemically when the ointment is applied onto psoriatic plaques (3). There are no publications regarding topical use of calcipotriene in pregnant women (3). The use of topical calcipotriene during pregnancy at recommended doses is unlikely to be associated with a high risk of teratogenicity (11).

Tacrolimus

Tacrolimus, a macrolide immunosuppressant, has not yet been approved for the treatment of psoriasis, although some studies have shown favorable results in facial and intertriginous psoriasis (19,20). Systemic absorption of tacrolimus after topical application is very low and is not associated with systemic effects (21). There are no literature reports on women using tacrolimus topically during pregnancy (11).

Topical retinoids (tazarotene)

Topical tazarotene is approved for the treatment of psoriasis but it is recommended that tazarotene should be stopped immediately if the woman becomes pregnant while using it (22). Large doses of tazarotene caused fetal abnormalities in some animal studies, but no teratogenic effects occurred in human clinical studies (11,23).

It is generally advised not to use tazarotene in pre-pregnancy period and during pregnancy (3).

UVB phototherapy

UVB phototherapy UVB is considered to be a safe and effective form of treatment for psoriasis in pregnancy and there are no contraindications for its use (3,11,25). Treatment with UVB can be initiated in pregnant patients whose psoriasis has become more widespread and cannot be managed by topical treatments alone (3). During UVB phototherapy sunscreens should be applied on the face or the face should be covered to prevent melasma.

SYSTEMIC TREATMENTS

PUVA

PUVA (photochemotherapy) is contraindicated in pregnancy because both components in PUVA treatment, the oral medication psoralen and the UVA light, are potentially mutagenic (24). Photoactivation of psoralens has been found to be mutagenic and induce sister chromatid exchanges *in vitro* (11,25). This also applies to bath PUVA, where the entire body is immersed in a tub of water that contains psoralen. It should be noted that no adverse fetal outcomes have been reported for women that became pregnant while being treated with PUVA (10,26,27).

Topical PUVA for patients with localized psoriasis of the palm and sole showed no adverse systemic effects and undetectable blood levels of 8-methoxypsoralen; however, it cannot be recommended because of the mutagenic potential of PUVA (10,24,26).

Systemic retinoids

Retinoids are vitamin A derivatives and the retinoids etretinate and isotretinoin are on the list of known human teratogens; so, they should be avoided in pregnancy (3). The relative risk of fetal malformation in pregnancies exposed to an oral retinoid in early pregnancy is 25.6 times that in the general population (11,28). With fetal exposure to oral retinoids, there is a characteristic pattern of malformation involving craniofacial, cardiac, thymic and central nervous system structures (11).

It has been suggested that women of childbearing potential that require oral retinoid therapy for the treatment of psoriasis should consider isotretinoin rather than acitretin (3). Although both are potent teratogens, pregnancy can be safely initiated one month after discontinuation of isotretinoin therapy *versus* three years in case of acitretin (3,29). Isotretinoin is typically used in the treatment of severe acne, but it has been shown to flatten plaques and reduce desquamation in cases of psoriasis, particularly in combination with PUVA (30,31).

Teratogenic effect of all retinoids should be carefully considered before being prescribed to any woman of childbearing potential (10).

Cyclosporine

Most of the reports of prenatal effects of cyclosporine come from its use in patients undergoing transplantation (11,32). No recurrent pattern of congenital anomalies has been described among children born to women that were treated with cyclosporine during pregnancy, although low birth weight and premature birth were traced to cyclosporine use (11,33,34). There are no specific contraception guidelines when taking cyclosporine (24).

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In general, cyclosporine should only be used during pregnancy under careful clinical judgment if the potential benefit outweighs the potential risk (35). Cyclosporine is not known to affect male fertility (36).

Methotrexate

Methotrexate (MTX) is contraindicated in pregnancy because it is associated with spontaneous miscarriage, cleft palate and skeletal abnormalities (10). An effective method of contraception should be used in women receiving methotrexate (22). Both men and women should discontinue methotrexate for at least 12 weeks before trying to conceive (22,37). Methotrexate may lower sperm count temporarily but it then returns to normal (37). Methotrexate poses little or no risk to pregnancies that occur after it has been discontinued (38). It does not harm male or female long-term potential of conceiving a healthy child (38).

Biologics

Limited data are available on the use of biologics in pregnancy. Manufacturers of etanrecept and infliximab, which are licensed for use in severe psoriasis, advise avoidance in pregnancy (10).

CONCLUSION

An appropriate general approach to women of childbearing age who have psoriasis involves open communication between the clinician and the patient (3). Treatment of a pregnant woman with psoriasis should take into consideration therapeutic benefit to her and her fetus, and the availability of safe and effective alternatives (11). Hardly any controlled trials on the treatment of psoriasis in pregnancy, evaluating the effect and safety of different drugs, can be found in the literature. The most important therapeutic approach is to keep psoriasis under control during pregnancy.

References

1. Liu Y, Krueger JG, Bowcock AM. Psoriasis: genetic associations and immune system changes. Genes and Immunity 2007:8;1-12.
2. Lowes AM, Bowcock AM, Krueger JG. Pathogenesis and therapy of psoriasis. Nature online publication /V6/: 445 (22 February 2007) doi:10.138/nature 05663
3. Tauscher AE, Fleischer AB Jr, Phelps KC, Feldman SR. Psoriasis and pregnancy. J Cutan Med Surg 2002;6:561-70.
4. Swanbeck G, Inerot A, Martinsson T. A population genetic study of psoriasis. Br J Dermatol 1994;131:32-9.
5. Barker J. Genetic aspects of psoriasis. Clin Exp Dermatol 2001;26:321-5.
6. Dunna SF, Finlay AY. Psoriasis: improvement during and worsening after pregnancy. Br J Dermatol 1989;120:584.
7. Raychaudhuri SP, Navare T, Gross J, Raychaudhuri SK. Clinical course of psoriasis during pregnancy. Int J Dermatol 2003;42:518-20.
8. Murase JE, Chan KK, Garite TJ, Cooper DM, Weinstein MD. Hormonal effect on psoriasis in pregnancy and post partum. Arch Dermatol 2005;141:601-6.
9. Boyd AS, Morris LF, Phillips CM. Psoriasis and pregnancy: hormone and immune system interaction. Int J Dermatol 1996;35:169.
10. Weatherhead S, Robson SC, Reynolds N. Management of psoriasis in pregnancy. BMJ 2007;334:1218-20.
11. Lam J, Polifka JE, Dohil AM. Safety of dermatologic drugs used in pregnant patients with psoriasis and other inflammatory skin diseases. J Am Acad Dermatol 2008;59:295-315.
12. Gay MW, Moore WJ, Morgan JM. Anthralin toxicity. Arch Dermatol 1972;105:213-5.
13. Neill SM, Bugrein A, Coulson IH. Toxicologic study of anthralin in an aqueous cream formulation. Cutis 1984;34:563-6.
14. Moward CM, Margolis DJ, Halpern AC. Hormonal influences on women with psoriasis. Cutis 1998;61:257-60.
15. Czeizel AE, Rockenbauer M. Population-based case-control study of teratogenic potential of corticosteroids. Teratology 1997;56:335-40.
16. Mygind H, Thulstrup AM, Pedersen L, Larsen H. Risk of intrauterine growth retardation, malformations and other birth outcomes in children after topical use of corticosteroid in pregnancy. Acta Obstet Gynecol Scand 2002;81:234-9.
17. Morra P, Bartle WR, Walker SE, Lee SN, Bowles SK, Reeves RA. Serum concentrations of salicylic acid following topically applied salicylate derivatives. Ann Pharmacother 1996;30:935-40.
18. Schwarb FP, Gabard B, Rufli T, Surber C. Percutaneous absorption of salicylic acid in man

after topical administration of three different formulations. Dermatology 1999;198:44-51.

19. de Prost Y. New topical immunological treatments for psorasis. J Eur Acad Dermatol Venereol 2006;20(Suppl):80-2.
20. Martin Ezquerra G, Sanchez Regana M, Herrera Acosta E, Umbert Millet P. Topical tacrolimus for the treatment of psoriasis on the face, genitalia, intertriginous areas and corporal plaques. J Drug Dermatol 2006;5:334-6.
21. Soter NA, Fleischer AB, Webster GF. Tacrolimus ointment for the treatment of atopic dermatitis in adult patients: part II, Safety. J Am Acad Dermatol 2001;44:S39-S46.
22. Koo YM. Current consensus and update on psoriasis therapy: a perspective from the United States. J Dermatol 1999;26:723-33.
23. Menter A. Pharmacokinetics and safety of tazarotene. J Am Acad Dermatol 2000;43(Suppl): S31-5.
24. Spuls PI, Bossuyt PM, van Everdingen JJ. The development of practice guidelines for the treatment of severe plaque-form psoriasis. Arch Dermatol 1998;134:1591-6.
25. Bridges BA. An estimate of genetic risk from 8-methoxypsoralen photochemotherapy. Hum Genet 1979;49:91-6.
26. Gunnarskog JG, Kallen AJ, Lindelof BG. Psoralen photochemotherapy (PUVA) and pregnancy. Arch Dermatol 1993;129:320-3.
27. Stern RS, Lange R. Outcomes of pregnancies among women and partners of men with a history of exposure to methoxsalen photochemotherapy (PUVA) for the treatment of psoriasis. Arch Dermatol 1991;127:347-50.
28. Lammer EJ, Chen DT, Hoar RM, Agnish ND, Benke PJ, Braun JT. Retinoic acid embryopathy. N Engl J Med 1985;313:837-41.
29. Perlman SE, Enny Leach E, Dominiguez L. “Be smart, be safe, be sure”: the revised pregnancy prevention program for women on isotretinoin. J Reprod Med 2001;46(2 Suppl):179-85.
30. Anstey A, Hawk JLM. Isotretinoin-PUVA in women with psoriasis. Br J Dermatol 1997;136:792-806.
31. Hönigsmann H, Wolff K. Isotretinoin-PUVA for psoriasis. Lancet 1983;1:236.
32. Bar Oz B, Hackman R, Einarson T, Koren G. Pregnancy outcome after cyclosporine therapy during pregnancy: a meta-analysis. Transplantation 2001;71:1051-5.
33. Toma H, Tanabe K, Tokumoto T, Kobayashi C, Yagisawa T. Pregnancy in women receiving renal dialysis or transplantation in Japan: a nationwide survey. Nephrol Dial Transplant 1999;14:1511-6.
34. Armenti VT, Moritz MJ, Davison JM. Drug safety issues in pregnancy following transplantation and immunosuppression: effects and outcomes. Drug Saf 1998;19:219-32.
35. Berth-Jones J, Voorhees JJ. Consensus conference on cyclosporin A microemulsion for psoriasis, June 1996. Br J Dermatol 1996;135:775-7.
36. Wright S, Glover M, Baker H. Psoriasis, cyclosporine and pregnancy. Arch Dermatol 1991;27:426.
37. Morris LF, Harrod MJ, Menter MA. Methotrexate and reproduction in men: case report and recommendations. J Am Acad Dermatol 1993;29:913-6.
38. Perry WH. Methotrexate and teratogenesis. Arch Dermatol 1983;119:874.