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Psoriasis during pregnancy. A literature review

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Abstract

Psoriasis is a chronic, recurrent inflammatory disorder characterized by the occurrence of well demarcated, erythematous papules and plaques covered by thick, silvery-white scales, generally affecting the elbows, knees, sacral area and scalp. It is a common disorder affecting women during their reproductive years. There is evidence that psoriasis might affect the course of pregnancy and that pregnancy can influence the course of psoriasis. The aim of this paper is to look over the most recent data regarding the impact of psoriasis on pregnancy and vice versa reviewing the current evidence for the safety of topical and systemic treatments for psoriasis during pregnancy.
Keywords: *psoriasis, pregnancy, estrogens, treatment, biologic agents*

Introduction

Psoriasis is a chronic, recurrent inflammatory disorder characterized by the occurrence of well demarcated, erythematous papules and plaques covered by thick, silvery-white scales, most often affecting the elbows, knees, sacral area and scalp. It can, however, occur at any site. It has a worldwide occurrence and affects 1-2% of the population. Males and women are equally affected. It can occur at any age but it usually appears between the ages of 15 and 30 years. Therefore, psoriasis affects many women during their reproductive years[1-6].

The effect of pregnancy on psoriasis

Psoriasis is a common disorder affecting women during their reproductive years. As a result, several authors studied the effect of pregnancy on psoriasis. Boyd and contributors evaluated 90 women with psoriasis by questionnaire to assess the changes in psoriasis during pregnancy. About 63.3% of patients noticed an improvement in their disease while 13.4% noticed an exacerbation. The authors also described that 87.7% of patients had a postpartum flare within four months of delivery[7].

Raychaudhuri and contributors also aimed to describe the course of psoriasis during pregnancy[8]. The scientists analyzed the data from 736 patients with psoriasis. The database included 333 females, 79 (23.7%) of whom had been pregnant. The authors report that in 56% of women psoriasis improved during pregnancy, in 26.4% it worsened and in 17.6% it remained unchanged. The authors also noticed that 62% of patients presented new lesions within 6-8 weeks of delivery and that patients who experienced an improvement at the first pregnancy also experienced improvement at the second pregnancy while patients who experienced flares at the first pregnancy had a similar response at the following pregnancies[8].

Murase and contributors performed a prospective study in which they aimed to investigate how psoriasis fluctuates in pregnancy on one hand and the level of hormones in pregnancy on the other hand[9]. The authors evaluated 47 pregnant patients with psoriasis and 27 non-pregnant patients with psoriasis and observed that 55% of patients had an improvement of the disease, 21% had no change and in 23% the disease worsened. They also reported that post-partum, 65% had a worsening of the disease. The authors also measured the levels of hormones in the studied patients and concluded that high levels of estrogen are associated with an improvement in psoriasis and progesterone levels do not correlate with the course of the disease[9].

Apart from the above-mentioned authors, other scientists support the general idea that psoriasis improves during pregnancy and exacerbates postpartum. This fact might be explained by the complex interactions between the endocrine and the immune system[10].

During pregnancy the immune system must be altered in order for the fetus to survive. Several inflammatory disorders, psoriasis included, often have a favorable course during this period. Hormones seem to have an important role in modulating the immune response and promoting a state of immune tolerance.

Estrogens and progesterone are both found in very high levels in pregnant women. Estrogens stimulate B-cell mediated immunity and suppress T-cell mediated immunity. The role of estrogens in improving the course of psoriasis during pregnancy is supported by the observation that estrogen concentrations increase during pregnancy and decrease postpartum. The evolution of the disease, with remissions during pregnancy and flare-ups after parturition, parallels the concentrations of estrogens. It has been shown that there is a significant inverse correlation between estradiol and psoriasis area severity index. This also supports the modulatory role of estrogens in psoriasis[8,9,11,12].

The role of progesterone on the course of psoriasis during pregnancy is not as well established as the role of estrogens. Progesterone down-regulates T-cell proliferative response and is a key factor in immunosuppression. Murase et al. concluded in their study that the levels

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of progesterone do not correlate with the course of the disease[9]. However, other authors showed that progesterone levels increased more than estrogen levels during pregnancy and that the change in estrogen-progesterone ratio produces altered immunity which might determine the improvement of psoriasis[9,11].

Pustular psoriasis of pregnancy, also known as impetigo herpetiformis, is a rare disorder of unknown etiology which occurs during pregnancy and usually disappears postpartum. It clinically presents as generalized plaques with peripheral pustules located in the intertriginous areas. It typically occurs during the third trimester in females with no predisposing skin conditions. Some cases however have been described in women with personal and family history of psoriasis. In rare cases patients presented no regression after delivery. In predisposed women, impetigo herpetiformis reappears during every pregnancy and it usually worsens and occurs at an earlier gestational age with each pregnancy. Usually, it is associated with an increased risk of stillbirth and fetal abnormalities[13-15].

It is known that psoriasis is significantly associated with the human leukocyte antigens (HLA) Al, B13, B17, B37, B39, Cw*0602, Cw11, and DR7 but psoriasis is unique because of its association with certain HLA-C loci. The HLA-Cw*0602 positive psoriatic women are more likely to experience an improvement in the disease during pregnancy while in HLA-Cw*0602 negative patients the disease is more likely to remain unchanged or worsen. Therefore, the course of psoriasis during pregnancy might be genetically determined[16,17].

The effect of psoriasis on pregnancy

Pregnancy outcome in patients with psoriasis is also an important issue since psoriasis is an inflammatory disease characterized by dysregulation of T-cell response and high levels of cytokines like interleukin (IL)-6, tumor necrosis factor (TNF)-α, interferon-γ and C-reactive protein. These cytokines might determine maternal endothelium dysfunction and lead to complications.

Ben-David and contributors evaluated pregnancy outcome in 145 deliveries in women with psoriasis and concluded that recurrent abortions, chronic hypertension and cesarean delivery are significantly associated with psoriasis[18].

Cohen-Barak et al.[19] performed a study on 68 deliveries in 35 women with moderate to severe psoriasis and 237 deliveries in 236 women without psoriasis and concluded that psoriasis patients are more likely to have spontaneous and induced abortions, hypertensive disease, premature rupture of membranes and newborns with higher birth weight than normal and macrosomia[19].

The same results however were not found by other authors. Lima and contributors evaluated the outcomes of 162 pregnancies in 122 females with psoriasis and 501 pregnancies in 290 patients without psoriasis and found that psoriasis is associated with a higher risk of preterm birth and lower birth weight but not with a risk of cesarean delivery, preeclampsia or eclampsia and spontaneous abortion[20].

A nationwide population-based study performed by Yang et al. in Taiwan which included 1463 women with psoriasis who had had children and 11 704 mothers without psoriasis showed that mothers with severe psoriasis had a higher risk of having infants with low birth weight than mothers without psoriasis. The authors however noticed no difference between patients with mild psoriasis and those without psoriasis. The scientists also reported that patients with severe psoriasis who received systemic treatment during pregnancy did not have a higher risk of low birth weight than non-psoriasis patients and showed that low birth weight is a result of psoriasis itself[21].

Psoriasis comorbidities are also important and should be taken into account when evaluating pregnancy outcome in those patients. Psoriasis is associated with diabetes mellitus, cardiovascular disease and metabolic syndrome. Some authors also showed that psoriatic patients are more likely to be obese, have hypertension and psychiatric disorders which negatively impact the course and outcome of pregnancy[6]. Bandoli et al. performed a study in which they aimed to establish if psoriasis patients have more modifiable risk factors for adverse pregnancy outcomes than patients without psoriasis. The authors included 178 pregnant women with psoriasis and 158 controls and concluded that psoriatic patients were more likely to be obese, depressed, smoking, without taking preconceptional supplements. Maternal obesity was associated with macrosomia, premature birth and low Apgar scores while smoking was associated with congenital anomalies such as oral clefts, spontaneous abortion and placental growth problems[22].

Harder et al. analyzed data on 87 692 pregnancies from the Danish National Patient Registry, 2553 pregnancies being from psoriatic women[23]. The authors showed that as compared to non-psoriatic patients, women with psoriasis were older, more often overweight and smoked more often. They did not identify however an increased risk of fetal death or prolonged time to pregnancy[23].

In conclusion, the data on pregnancy outcome in psoriasis is scarce and contradictory. However, it seems like there might be a link between psoriasis severity and pregnancy outcome[17].

The treatment of psoriasis during pregnancy

Data regarding the treatment of psoriasis during pregnancy is limited due to ethical concerns. Most data available is coming from case reports of women who continued treatment because they did not know they were pregnant. Most therapies available for the treatment of psoriasis are included in the pregnancy risk category B (i.e. animal studies showed no risks on the fetus and there are no adequate well controlled studies in pregnant women), pregnancy risk category C (i.e. animal studies showed some adverse effects on fetus, there are no adequate studies in pregnant women but the benefits may warrant the use of the drug)

and pregnancy risk category X (i.e. studies in animals and humans showed fetal abnormalities). The risks overweight the potential benefits.

Topical therapies are the first-line treatment for psoriasis during pregnancy. Emollients and moisturizers can be useful and they lack adverse effects. If those are not enough, mild and medium potency corticosteroids should be used. High potency corticosteroids should be avoided, unless absolutely necessary. They are classified as pregnancy risk category C. To avoid adverse effects corticosteroids should not be used over large areas or under occlusion. They are generally considered safe during pregnancy, the main adverse effect being low birth weight[24-26].

Data regarding the use of other topical agents routinely recommended in non-pregnant patients with psoriasis, such as coal tar, topical salicylic acid and calcipotriol is scarce and authors suggested to be avoided it. Coal tar was associated with spontaneous abortion, topical salicylic acid could cause salicylism and calcipotriol can determine vitamin D-induced toxicity[24,25].

Ultraviolet (UV)B phototherapy is the second-line treatment in pregnant patients with psoriasis and it should be considered first-line treatment in patients who require systemic therapy. Narrow band UVB and broad band UVB can both be used as light penetration is limited to the mother's skin. It should be utilized with caution in the first 28 days of pregnancy as it could cause neural tube defects if overheating happens during treatment[24-27].

Data regarding the use of systemic and topical psoralen plus ultraviolet A (PUVA) during pregnancy is limited. Oral psoralen is classified as pregnancy risk category C. It could cause low birth weight and fetal abnormalities and it is therefore contraindicated. Topical PUVA might be safe but there is no data available to support its use in pregnancy[24,27].

Systemic corticosteroids and cyclosporine are the third-line treatment in pregnant women with psoriasis. They both belong to the pregnancy risk category C. Systemic corticosteroids are not routinely recommended in psoriasis and should be reserved for severe cases like erythroderma or impetigo herpetiformis. They are generally considered safe but some cases of low birth weight and intrauterine growth retardation have been described. Cyclosporine A can be safely used in patients with severe psoriasis. It does not have mutagenic properties and it does not increase the risk of congenital malformations. Some cases of premature delivery and low birth weight have been reported. Breastfeeding should be avoided though because cyclosporine can determine immunosuppression of the neonate[24-26,28].

Methotrexate and Acitretin are classified as pregnancy risk category X and are therefore absolutely contraindicated in pregnancy. Methotrexate can have negative effects on central nervous system, craniofacial, limb and growth abnormalities as well as abortion. It should be discontinued at least 3 months before conception. Most malformations occur in the first 6-8 weeks after conception. Acitretin is teratogenic and causes abortion, central nervous system, cardiac, craniofacial and thymic malformations. The risk is higher when it is administered in the first trimester. Pregnancy should be avoided for up to two years after Acitretin cessation[24,25,28].

Biological treatments during pregnancy in psoriatic patients

Four biologic agents are currently approved for the treatment of psoriasis: Infliximab, Adalimumab, Etanercept (TNFα inhibitors), and Ustekinumab, an IL-12/23 inhibitor. All four biologic agents are classified as category B drugs for pregnancy[24,25,28].

Animal studies showed that TNFα has an essential role in embryonic and fetal development, its depletion leading to fetal death and structural defects. The human placenta permits little transfer of antibodies, including Adalimumab, a human antibody, and Infliximab, a chimeric antibody, during the first trimester. Studies showed that exposure to Adalimumab and Infliximab during pregnancy was associated with favorable outcomes and that the risk of malformations was similar to that encountered in the general population[24,25,28].

Etanercept is a fusion protein with less transplacental transport than Adalimumab and Infliximab. A case of VATER syndrome (vertebral anomalies, anal atresia, cardiac disorders, tracheoesophageal fistula, esophageal atresia, kidney malformation, and limb anomalies) was reported after Etanercept treatment during pregnancy. Most studies however showed that Etanercept is not associated with malformation and prematurity patterns[24,25,28].

Ustekinumab is a monoclonal antibody and its transplacental transport is small before the third trimester. The experience with this drug is so far limited. Some cases of miscarriages were however reported[24,25,28,29].

Since the data regarding the use of biologic treatments during pregnancy is still scarce, treatment cessation is recommended before conception, taking into consideration the half-life of each product. If administration is justified by the severity of the illness, the treatment may be continued during pregnancy as long as it is discontinued before the 30th week of gestation. Children whose mothers received the treatment in the late second and third trimester should not receive live vaccines before the age of 7 months[24,25,28].

Conclusions

Psoriasis is a common disorder affecting women during their reproductive years. The disease often improves during pregnancy, probably due to the high levels of hormones which have an important role in modulating the immune response and promoting a state of immune tolerance. The data on pregnancy outcome in psoriasis is scarce but there seems to be a link between psoriasis severity and pregnancy outcome. Several therapies are available for the treatment of psoriasis during pregnancy and further studies are however needed to prove their safety. ■

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