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LUPUS WITH PREGNANCY : BEYOND THE BASICS

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Summary

Pregnancy in patients with systemic lupus erythematosus is associated with a high risk of maternal disease exacerbation and adverse fetal outcome. This review summarizes recent published findings on lupus pregnancy. Literature review: The literature has profound agreement on the fact that, for most women with inactive and stable systemic lupus erythematosus, pregnancy is safe for both mother and fetus. The main risk factors for adverse pregnancy course and outcome are active disease, nephritis with proteinuria, hypertension, and maternal serum antibodies to SS-A/Ro, SS-B/La, cardiolipin, 2-glycoprotein I, and lupus anticoagulant. Recent studies have broadened our understanding of the immunological mechanism underlying congenital heart block induced by anti-Ro/La antibodies. Pregnancy in patients with systemic lupus erythematosus is safe and manageable provided the disease is stable. Patients should be closely followed up before pregnancy for pregestational risk factors and should get extra attention during pregnancy. The disease can be safely managed in some cases of lupus flare during pregnancy

Key words

Systemic lupus erythematosus(SLE); pregnancy; complications; flare

Introduction

To be a mother is a heavenly blessing for every women. Pregnancy is a physiological process in which there are hormonal changes in the body like increased level of oestrogen and progesterone along with vascular and other changes in different organ system.

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease affecting various organ systems of the body and occurs frequently in women of childbearing age. SLE patients are as fertile as women in the general population, but their pregnancies in some cases may be associated with complications. Treatment with cyclophosphamide can however increase the risk of infertility.

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Women with this disease found to be at higher risk for various complications of pregnancy, and those with antiphospholipid antibodies may have an increased risk of miscarriage. It has been found that more the disease activities of SLE, more the chances of complications. In general, women with SLE and, in addition, hypertension, proteinuria, and azotemia have an extra increased risk for pregnancy complications[1]. Women pregnant and known to have anti-Ro (SSA) or anti-La antibodies (SSB) often have chances of developing cardiac abnormalities[2].

But the outcome for both mother and child is found to be best when systemic lupus erythematosus has been under good control for at least six months before pregnancy and when the kidney disease is in remission. Maternal health and fetal development should be monitored frequently during pregnancy in a patient of SLE. Where ever possible, delivery should be done in a well equipped center under the supervision of Internist, Rheumatologis and Obstericians along with specialist opinion for any complications. The SLE patient needs extra attention during postpartum period and proper counseling has to be given for breast feeding.

A clinician engaged in managing SLE patients with pregnancy should be aware of one or more of the following clinical features[2]: Prior history of poor obstetric outcomes, Renal involvement (creatinine >2.8 mg/dL), Cardiac involvement, Pulmonary hypertension (mean pressure >50 mmHg), Interstitial lung disease, Evidence of active lupus, High-dose glucocorticoid therapy, Antiphospholipid antibodies/syndrome, History of severe preeclampsia or HELLP syndrome, Stroke within the previous six months, Antibodies to Ro/La (predisposing to neonatal lupus) and Multiple gestation.

In this topic it will be reviewed and discussed about the major issues unique to pregnant patients with SLE and their children like exacerbation of the disease, pregnancy complications, Neonatal lupus and Breast feeding.

Materials and methods

Recent updates on SLE with pregnancy were reviewed using google scholar and pubmed as search engines. We searched electronic databases from 2005 to 2010 and reviewed papers published in different journals.

Literature review

Systemic lupus erythematosus has become more successfully treated over the past few decades, making a viable pregnancy outcome for most of the women. It is generally assumed that there is an increased risk of a flare of systemic lupus erythematosus during pregnancy but recent reports say 7 and 33 percent of women who have been in remission for at least six months have a flare during pregnancy; this rate is comparable to the number of women who have flares and are not pregnant[3,4].

In contrast, more than 60 percent of women with active systemic lupus erythematosus at the time of conception will have a flare during pregnancy. Increased risks of a disease flare have also been found in women who have undergone in vitro fertilization. Flares occurred during all three trimesters with approximately equal frequency and often in the immediate postpartum period.

It has been observed that there is progressively diminishing tendency of diseases flare in SLE in the recent years. The reduction in rates of SLE flares could be a result of reporting bias, better disease control, or a better understanding of how one defines a flare during pregnancy. According to some investigators it is believed that the rate of flares during pregnancy may be similar to the frequency of exacerbation while not pregnant, while other researchers proposed that pregnancy is a time of vulnerability to increased disease activity[5-9]. Flares presented most commonly as constitutional symptoms, renal disease, or involvement of the skin and joints[10].

What could be the complications of pregnancy in a SLE patient?

Women with SLE have an increased risk of complications of pregnancy. Probable complications may include high blood pressure, preeclampsia, preterm delivery, unplanned Cesarean section, excessive bleeding after delivery or blood clots in the leg or lung. Infants of women with systemic lupus erythematosus, may suffer from low birth weight, prematurity and early fetal loss.

Preeclampsia occurs in approximately 13 percent of women with SLE. It may occur even more frequently among women with kidney disease, antiphospholipid antibodies (aPL), diabetes mellitus, or prior episode of preeclampsia[11].

Fetal loss is defined as the death of a fetus at 10 or more weeks of pregnancy. In one center, approximately 17 percent of women with SLE had a fetal loss[12].

The risk of delivering before 37 weeks of pregnancy (pre term) and chances of having low birth weight infant are increased in women with more severe SLE, specially to those who require higher doses of glucocorticoids (eg, steroids) during pregnancy, on certain immunosuppressive medications such as azathioprine and cyclosporine and has kidney complications, high blood pressure, antiphospholipid antibodies and preeclampsia.

Neonatal lupus is an autoimmune disease which occurs in babies born to mothers with anti-Ro/SSA and/or anti-La/SSB antibodies. Signs of neonatal lupus include a red, raised rash on the scalp and around the eyes. The rash almost always resolves by six to eight months of age because the antibodies are cleared out of the infant's bloodstream; most (90 percent) of these infants do not develop lupus in later years. The most serious complication of neonatal lupus is complete heart block, which occurs in approximately 2 percent of newborns whose mothers have SSA (Ro) or SSB (La) antibodies.

Is there any care needed before pregnancy?

Women with SLE should express their will to have a child to a rheumatologist and obstetrician before trying to become pregnant. Nutritional supplement containing at least 400 mcg of folic acid should be given to all women. Folic acid can reduce the risk of a specific birth defect, called a neural tube defect and should be started before trying to conceive and continued until at least the end of the first trimester. Women should stop smoking and consuming alcohol or any recreational drugs before trying to become pregnant. Blood testing for rubella (German measles), varicella (chicken pox), HIV, hepatitis B, and inherited genes (eg, cystic fibrosis) may be recommended.

Women with lupus nephritis are encouraged to delay pregnancy until their disease is inactive for at least six months[13,14].

Often it is troublesome to distinguish between the common discomforts of pregnancy and the symptoms of lupus. Those are fatigue, swelling of the hands, feet, or ankles joint pain, especially in the low back, shortness of breath, numbness or pain in one or both hands (caused by carpal tunnel syndrome of pregnancy) and skin changes (eg, darkening of facial skin)

Management of SLE with pregnancy

Two issues related to therapy of women with lupus will be considered in pregnancy: monitoring of disease activity in both asymptomatic and symptomatic patients and treatment of active disease.

Women with SLE when becomes pregnant need regular monitoring of their disease at an interval of 2- 4 weeks or at least once in each trimester, even if it has been stable. SLE disease activity index (SLEDAI) will be measured in every visit and many women will need treatment of active disease. A complete physical examination, including measurement of blood pressure, and blood testing important to asses the disease flare, test to measure the current kidney function (glomerular filtration rate, urine protein/urine creatinine ratio) along with antiphospholipid and anti-Ro/SSA and anti-La/SSB antibodies test will be performed. Common investigations that will be done for assessment of disease flare are urine R/M/E, for hamaturia, proteinuria, complete blood count with ESR, serum uric acid, testing of complement levels (CH50 or C3 and C4), and testing for anti-dsDNA antibodies.

During the first 2 trimesters, a monthly platelet count or CBC is recommended

Aggravation of SLE in pregnancy may be confused with SLE-unrelated complications of pregnancy. For example, chloasma may appear like the malar rash of SLE, proteinuria from preeclampsia may appear like that of lupus nephritis, thrombocytopenia of the HELLP syndrome may appear like that of SLE, and pregnancy-related edema of joints can appear like arthritis of SLE[1].

Thrombocytopenia, elevated serum levels of liver enzymes and uric acid, and decreased urinary excretion of calcium are more prominent in patients with preeclampsia than in those with lupus nephritis.

Is renal biopsy is at all necessary in pregnancy?

In pregnant patients with renal disease, renal biopsy should be performed to differentiate preeclampsia from active lupus nephritis when differentiation on clinical grounds is not possible.

After 28 weeks of pregnancy, most patients will be followed every one or two weeks. At these visits, along with other tests assessment of fetal condition will be assessed by monitoring biophysical profile. A biophysical profile (BPP) score is calculated to assess the fetus' health. It consists of five components, nonstress testing and ultrasound measurement of four fetal parameters: fetal body movements, breathing movements, fetal tone (flexion and extension of an arm, leg, or the spine), and measurement of the amniotic fluid levels. Each component is scored individually, with two points given for a normal result and zero points given for an abnormal result. The maximum possible score is 10.

Doppler ultrasonography helps guiding decision making regarding timing of delivery and has been proven to reduce perinatal mortality.

Medications during pregnancy

During the first trimester, most of the drugs should be avoided. Medications that are needed to treat SLE may be divided into three categories: those that should be avoided during pregnancy, those that may have a small risk of harm to the fetus, and those that are probably safe.

Drugs having high risk of causing birth defects (Mycophenolate mofetil, Cyclophosphamide, Methotrexate) should be avoided. Men and women who take methotrexate should stop it at least three months before trying to conceive. This three-month period is necessary to completely eliminate methotrexate from the body.

Until more data are available, biologic medications like etanercept, infliximab and rituximab should be avoided in pregnancy.

NSAIDs, aspirin, prednisone, and azathioprine have a small risk of causing fetal harm; their use may be acceptable if necessary to control systemic lupus erythematosus during pregnancy. NSAIDs such as ibuprofen and naproxen cross the placenta and can potentially cause harm to the fetus, especially during the third trimester. NSAIDs are generally safe during the latter part of the first and during the second trimester but should be discontinued in the last trimester of pregnancy as in the third trimester it may cause premature closure of the ductus arteriosus and inhibition of labor. Acetaminophen (325mg – 4000mg) and low dose aspirin (160 mg) is a safe alternative.

If SLE flares during pregnancy, most experts recommend prednisolone at the lowest dose possible. Prednisolone crosses the placenta but appears in only small amounts in the infant's blood. Few studies showed Glucocorticoid (steroids) medications (including prednisone) may increase the risk that the infant will have a cleft lip and/or palate, premature rupture of membranes and growth retardation.

There are controversies about the safety of azathioprine (AZA) during pregnancy. Few studies suggest that this medication does not increase the risk of fetal anomalies and azathioprine will generally be limited to women with severe disease who have not responded to other treatments[15].

SLE patients can continue their antimalarial drugs during pregnancy as it may decrease the risk of flares, decrease the risk of miscarriage or birth defects at normal doses and help manage antiphospholipid syndrome and possibly decrease the risk of neonatal lupus.

SLE flare can be happened after delivery especially to those who have had active disease in early pregnancy and significant organ damage. NSAIDs but not aspirin can be used during breast feeding. Prednisone can be taken in low doses under 20 mg/day. Antimalarials, warfarin, and heparin appear to be safe while Azathioprine, cyclosporine, methotrexate, cyclophosphamide and chlorambucil should be avoided[16].

Conclusion

A rheumatologist, an obstetrician, and a nephrologist (if renal disease present or if it develops later) should work as a team to care for a pregnant patient with SLE. Preconception counseling must be stressed. Patients should be aware of the potential teratogenic effects of the drugs they are taking. When patients are taking teratogenic medications, use of contraception must be enforced. During pregnancy, disease flare should be treated adequately and patients must be informed of the potential adverse effects of the drugs on the fetus.

Disclosure

The author declared no competing interestes

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More informations: www.uptodate.com/patients

The following organizations also provide reliable health information.

National Library of Medicine, (www.nlm.nih.gov/ medlineplus/healthtopics.html)

National Institute of Arthritis and Musculoskeletal and Skin Disease, (www.niams.nih.gov)

American College of Rheumatology, (www. rheumatology .org)

Lupus Foundation of America, (www.lupus.org)