Lupus Nephritis and Pregnancy: Concerns and Management

Liz Lightstone, PhD, FRCP,[*,†] and Michelle A. Hladunewich, MD, FRCP[‡]

Summary: Pregnancy associated with lupus, especially lupus nephritis, is often fraught with concern for both the mother and fetus. Thus, it is paramount that care begins preconception so that proper planning in terms of optimizing the medical regimen, discontinuation of fetotoxic agents, and treatment of active disease can occur. It is well known that active nephritis at the time of conception is associated with poor outcomes. Even with quiescent disease, recent data indicate that being lupus anticoagulant–positive, nonwhite or Hispanic, and using antihypertensive medications were all predictors of worse pregnancy outcomes. Further, prior lupus nephritis also predicts higher rates of preeclampsia and HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome. Differentiating lupus nephritis from preeclampsia often presents as a conundrum, but lupus nephritis can be confirmed by the presence of decreasing complement levels and increasing double-stranded DNA (dsDNA) antibody levels in addition to new onset hypertension and proteinuria. We hope that the more mechanistic approach of measuring angiogenic markers, which are diagnostic for preeclampsia, will be the standard of care in the future. Women with lupus and prior lupus nephritis can have successful pregnancies, but outcomes are dependent on "the art of planning" as well as close communication between the obstetrician, the nephrologist, and the rheumatologist.

Semin Nephrol 37:347-353 © 2017 Elsevier Inc. All rights reserved.

Keywords: Lupus nephritis, preeclampsia, pregnancy

Women with lupus, especially lupus nephritis, might be at increased risk for obstetric and fetal problems in pregnancy, as well as problems related to their disease. The key to successful outcomes is joint planning before pregnancy with a nephrologist well-versed in high-risk pregnancies to assess and minimize the risks. The woman needs to know about optimal timing and medication management and be aware of the potential pitfalls (Table 1). Of course, many women with lupus present for the first time during pregnancy, and the key to optimizing their outcomes is making the diagnosis quickly and initiating appropriate treatment along with immaculate fetal and maternal multidisciplinary care in an appropriate tertiary setting where available.

[*]*Imperial Lupus Centre, Department of Medicine, Imperial College London, London, UK.*

[†]*Section of Renal Medicine and Vascular Inflammation, Department of Medicine, Imperial College London, London, UK.*

[‡]*Divisions of Nephrology and Obstetric Medicine, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada.*

Financial disclosure and conflicts of interest: none.

Address reprint requests to Liz Lightstone, PhD, FRCP, Imperial Lupus Centre, and Section of Renal Medicine and Vascular Inflammation, Imperial College London, Hammersmith Campus, Du Cane Rd, London W12 0NN UK. E-mail: l.lightstone@imperial.ac.uk

0270-9295/ - see front matter

© 2017 Elsevier Inc. All rights reserved.

http://dx.doi.org/10.1016/j.semnephrol.2017.05.006

PREPREGNANCY PLANNING

Women with lupus face increased risks to themselves and to their fetus during pregnancy and should be offered prepregnancy planning. Because several of the drugs used to treat lupus and lupus nephritis are teratogenic, it is critical to explore a woman's wish to become pregnant very early on in management.

Fertility

The first issue to consider is her fertility. Lupus does not impair fertility, but use of cyclophosphamide might do so,[1] as well as advancing kidney impairment. Note how long the woman has been trying to conceive, how much cyclophosphamide she has had, and the degree of renal dysfunction. Regular periods do not confirm fertility, but clearly, amenorrhea should put the physician on guard. Importantly, many women with lupus have been advised to avoid pregnancy during active disease, and they might have been using long-acting forms of contraception and have no notion whether they have regular periods or not. Depending on the woman's age, and considering that lupus is a relapsing-remitting disease, women with lupus who have difficulty conceiving should be referred to an infertility expert sooner rather than later.

Timing

The next element to focus on is timing. A woman should be advised her lupus needs to be inactive for at least 6 months before attempting to conceive. This is

Table 1. Issues for Women to Discuss at Prepregnancy Planning and Once Pregnant

Topic	Prepregnancy	Once Pregnant
Fertility and contraception	• Refer early for fertility advice if concerned	• Advise contraception postpartum
Disease activity	• Ensure quiescent nephritis, biopsy if necessary and treat to complete remission before conception	• Monitor for disease flares, proteinuria, hypertension, impaired function, complement and dsDNA antibody levels
Pharmacological management	• Review all medication; advise what to stop, what to continue, what to add • Stop renin-angiotensin blockers and biopsy if proteinuria rises to >1 g/day • Ensure on safe immunosuppressants; stop MMF, cyclophosphamide, methotrexate at least 90 days prepregnancy; optimize maintenance therapy; steroids, azathioprine, tacrolimus, cyclosporine A all fine to continue • All women should be on hydroxychloroquine • Folic acid preconception	• Ensure renin-angiotensin blockers stopped as soon as pregnant if not already stopped • Ensure on safe immunosuppressants; if flares, increase steroids or consider pulse methylprednisolone, azathioprine, add tacrolimus or cyclosporine • Hypertension, control BP with pregnancy safe medications • Add aspirin by 12 weeks to reduce risk of preeclampsia • Low molecular weight heparin if heavy proteinuria; LAC-positive with prior thromboses
Identify women at high risk for adverse pregnancy outcomes[2]	• Lupus anticoagulant positive • Hispanic or nonwhite • On antihypertensive agents (ensure BP well-controlled) • Prior lupus nephritis • Platelet count <100 x 10^9 cells/L • *Physicians global assessment score >1	• As for nonpregnant
Preeclampsia	• Discuss ~8% of women with nephritis develop; risk increases if any of the above high-risk factors present	• Treat as high risk and monitor for onset of preeclampsia • Regular fetal growth scans • Not yet routine, sFlt1 levels and ratio of sFlt1 to PlGF might prove helpful
Delivery	• Advise if high risk that likely to deliver at <37/40 weeks and, if very early, there might be increased risk for operative delivery	• Timing based on evaluation of maternal and fetal well-being • Nephritis flare not an indication to deliver per se

Abbreviations: BP, Blood pressure; LAC, lupus anticoagulant; MMF, mycophenolate mofetil; PlGF, placental growth factor; sFlt1, soluble fms-like tyrosine kinase-1.
*PROMISSE Study[2]

particularly true if she has active lupus nephritis. In reality, this advice should be given when first meeting a patient with a flare of their disease that requires an increase in treatment. My standard phrase at that point is, "You will have your baby, but not yet." For women with lupus nephritis, it is safest to talk in terms of at least a year, considering the average time to remission is around 9 months, and they then might need to change their maintenance therapy to a baby-friendly drug to prove they can tolerate the new medication and remain stable. Of course the advice will be tempered according to the age of the woman, her degree of kidney impairment, and the severity of her disease, but the rule of thumb is that her disease should be quiescent for 6 months before conception.[3,4] There are good data to show that commencing a pregnancy with active disease is associated with remarkably worse maternal and fetal outcomes.[3]

Pharmacologic Management

Pharmacologic management is a crucial part of planning for pregnancy in a woman with lupus. It is not only important to advise on the medications they should not stop and the medications they should start in advance or soon after conception, but it is also important to advise on medications they must avoid when trying to conceive. The aim is to maintain them in remission. Just prior to or after conception is not the time to wean women off maintenance medications, such as low-dose prednisolone and azathioprine. If they are on low-dose aspirin, they should remain on it, and if not, they should plan to start it once pregnant to reduce the risk for preeclampsia. Hydroxychloroquine reduces the incidence of flares, infections, and thrombosis, and is associated with better long-term renal survival.[5,6] It also appears to reduce the risk for

Download English Version:

https://daneshyari.com/en/article/5691616

Download Persian Version:

https://daneshyari.com/article/5691616

Daneshyari.com