British Sjögren's Syndrome Association

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Urological and gynaecological disease in Sjögren's Syndrome

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Patients with Sjögren's Syndrome often complain of urinary tract and gynaecological problems. This article attempts to explain the commoner conditions and discuss their management.

Urinary Tract symptoms and Urinary Tract Infection (UTI)

Symptoms of urinary dysfunction such as urinary frequency and discomfort are fairly common in normal women. They are however increased in patients with Sjögren's Syndrome. A study by Haarala & colleagues (2000) found mild urinary symptoms in 61% of patients with Sjögren's compared with 27% of women without. Severe symptoms were seen in 14% and 7% respectively. Overall 27% of Sjögren's patients report urinary frequency and 36% complain of suprapubic pain. Infection should be excluded in the first instance, and if present treated appropriately with an appropriate antibiotic. A few patients with recurrent urinary tract infection benefit from taking regular, low dose antibiotic therapy.

In general good hydration levels should be maintained and some patients report benefit from drinking cranberry juice which has the effect of alkalinising the urine. A similar effect can be achieved using potassium citrate mixture – available via pharmacies in various commercial preparations e.g. cymalon, cystopurin.

The frequency of urinary tract infection (UTI) in patients with Sjögren's Syndrome is not accurately known but in general is probably higher than expected within the normal population. Certainly in patients with Rheumatoid Arthritis the frequency of recurrent UTI is increased if the patient also has Sjögren's from 6% in those with Rheumatoid alone to 30% in those with co-existent Sjögren's (Tischler et al 1992).

Vaginal Candidiasis (Thrush)

Vaginal Candidiasis (Thrush) is caused by overgrowth of the fungus candida albicans. This fungus is found in small amounts on the mucous membranes of the mouth and genital area of normal people but in the right conditions can multiply and cause problems. This is frequently seen in the dry conditions found in Sjögren's patients and can prove resistant to treatment. One study found evidence of candida in 80% of patients with Sjögren's (Rhodus et al). Simple creams and pessaries may be beneficial in some e.g. Clotrimazole (available over the counter or on prescription), although oral fluconazole may be needed in more resisitant cases. It is important to maintain moisture levels and treat partners too if you are sexually active.

Interstitial Cystitis

Interstitial cystitis is a chronic inflammatory bladder disease of uncertain cause. 90% of sufferers are female. It causes chronic inflammation of the bladder wall but in the absence of proven infection. No single treatment is universally effective and management includes good hydration and the use of anti-histamines. Some women find cimetidine helpful and both steroids and cyclosporine have been used. Some urologists treat it with bladder instillations. Two are available – Dimethyl suphoxide (Rimson-50) and Sodium hyaluronate, but both require expert supervision. There is no good data on the prevalence of interstitial cystitis in Sjögren's Syndrome although anecdotal reports suggest it is common. In one small study of 10 patients with interstitial cystitis 2 were found to have Sjögren's and 6 of the others had sicca symptoms (van der Merwe et al). In a more recent follow-up study the same authors suggest that Sjögren's is present in 23% of all patients with interstitial cystitis.

Renal involvement

Renal disease impacting on the quality of the life or kidney function is rare but mild abnormalities of kidney function can be detected in about 50% of patients with Sjögren's Syndrome. A study of patients with Sjögren's Syndrome in Finland revealed that mild proteinuria (the presence of more than 1.5 g of protein in the urine over a 24 hour period) was common (44%) but almost always asymptomatic. In the same study Renal Tubular acidosis was found in 33%. This is a condition where the tubules of the kidney are affected in such a way that they are unable to maintain the normal acid:alkali balance of their urine. In the majority of people it is asymptomatic but it can predispose towards kidney stones. Treatment when required is with bicarbonate to restore the urine pH. There is also a trend for those with renal involvement to have higher blood pressure than those without (Pertovaara et al 1999).

Vaginal dryness and dyspareunia

Vaginal dryness affects 76% of women with Sjögren's compared to 5% of those without (Lehrer et al 1994) and dyspareunia (pain on intercourse) is a problem in 40%. Microscopic examination of the vaginal lining tissue shows evidence of inflammation (Skopouli et al 1994). Treatment of vaginal dryness includes the use of lubricating gels to aid intercourse (e.g. KY jelly) and longer acting vaginal moisturisers to improve moisture levels within the vagina (e.g. Replens or Sylk, both available over the counter from pharmacies). Recurrent Candida infection (thrush) is common and can affect the mouth or vagina. Anything that improves moisture levels will help. Interestingly rates of oral candida infection fall in patients who start pilocarpine (Rhodus et al) and as some patients on pilocarpine report improved vaginal moisture levels it is possible it has a beneficial effect on vaginal candida too.

Continued next page

Sjögren's Syndrome and pregnancy

It seems likely that fertility (i.e. the ability to conceive) is normal in patients with Sjögren's Syndrome but that there is an increased risk of miscarriage. The actual risk is difficult to quantify because miscarriage is a common event in any case - estimates suggest that overall 12-15% of early pregnancies in healthy women end in miscarriage. Miscarriage rates increase with increasing age at conception so that miscarriage rates are over 20% in women over 40 years of age. Recurrent miscarriage (defined as three or more miscarriages) is much rarer and affects about 1% of women. Studies have shown an increased frequency of recurrent miscarriage in women with autoimmune disease. A study from Greece (Mavragani et al) found an increased risk of recurrent miscarriage in women who were positive for either anti-Ro and/or La autoantibodies. These autoantibodies are found in up to 60% of women with Sjögren's Syndrome.

Sjögren's Syndrome and infertility

Infertility rates are similar to those in the normal population at about 10%.

Ro and La antibodies and their effect on the child

The Ro and La autoantibodies associated with Sjögren's Syndrome are small enough to cross the placenta and enter the unborn baby's circulation. In the majority of pregnancies this does not cause any harm but in about 5% of cases problems occur. Two main problems are seen in the newborn. Firstly the rash of neonatal lupus is seen in about 5% of cases. It usually appears at about 6 weeks of age and lasts about 17 weeks before fading spontaneously. In most cases the rash clears completely but a few children are left with areas of depigmentation or telangiectasia (red spots). Of the mothers of these children one third of them are asymptomatic and the majority of the remainder have been diagnosed as suffering from either SS or SLE (Neiman et al).

Secondly the child can be born with congenital heart block (CHB). This is rare, occurring in less than 2% of pregnancies in women with anti Ro or La antibodies (Brucato et al) and may be detected during pregnancy by ultrasound scanning from about 16 weeks of pregnancy. It is slightly commoner in female children and if the mother has had a previous child with CHB then the risk of a subsequent pregnancy being affected goes up to 12%. Studies of children with CHB and their mothers show that up to half of the mothers were asymptomatic at the time of the birth although many of these went on to develop autoimmune disease later. Most had (or developed) either SS or SLE. 70% of affected children survive but nearly all require pacemakers in the first few months of life (Waltuck et al). In general women with anti-Ro or La antibodies should be offered foetal cardiology scans at about 18 and 32 weeks of pregnancy. These are similar to, but more detailed than, the normal ultrasound scans done during pregnancy. If CHB is detected then delivery should be in a centre with paediatric cardiology support available.

Other, very rare, complications include hepatitis (liver inflammation) and cytopenias (low blood counts) affecting the newborn. Only a handful of cases have been reported in the literature and in the majority of cases the child has improved spontaneously (Evans & Gaskin).

Antiphosphospholipid antibodies

Antiphophospholipid (APL) antibodies are found in a small number of patients with Sjögren's Syndrome, 38% of those with SLE and 19% of people with a first degree relative (i.e. a parent or sibling) suffering from SLE. The main clinical features seen in patients with these antibodies are recurrent thromboses (clots), low platelets and recurrent miscarriage. In pregnancy the presence of APL antibodies is also associated with other problems including an increased risk of stillbirth, poor growth in the unborn child and premature birth plus the development of pre-eclampsia (high blood pressure and other problems) in the mother. Many of these complications can be avoided or minimised by the use of 'blood thinning' agents during pregnancy. This often involves a combination of low dose aspirin, heparin and warfarin.

The effects of pregnancy on autoimmune disease

Studies have shown that there is a tendency for rheumatoid arthritis (RA) to improve and for systemic lupus erythematosus (SLE) to worsen during pregnancy. In women with pre-existing RA about 75% will see an improvement in their disease during pregnancy but there is an increased risk of relapse after the birth of the child. In women with pre-existing SLE there is an increased risk of relapse during pregnancy but in 60% of cases the relapse is mild. There are no documented data on the course of women with primary Sjögren's during pregnancy. Anecdotal reports suggest that most pregnancies progress normally with no detrimental effects upon the mother.

Medication and pregnancy

Ideally drug treatment should be minimised both before and during pregnancy to avoid any risks to the child. However it is important to bear in mind the health of the mother, as a 'disease flare' may endanger the health of the child more than the risk of continuing treatment.

Prednisolone in moderate dosage will not cross the placenta and is considered safe throughout pregnancy. Non steroidal anti inflammatories (NSAID) are problematic in later pregnancy although some of them can be used with caution in the early stages. In particular the newer NSAIDs i.e. the COX II inhibitors have been shown to be potentially harmful and should be avoided.

In general hydroxychloroquine is considered to be safe in pregnancy and current advice is that it should be continued. There have been several studies looking at its use in women with SLE throughout pregnancy (Levy et al, Costedoat-Chalumeau et al). They have shown that discontinuing hydroxychloroquine is more likely to lead to a disease flare in the mother and to be associated with the development of pre-eclampsia (a rare complication of pregnancy where the mother develops high blood pressure and other problems). No toxicity was seen in the infants of mothers taking hydroxychloroquine and these results were confirmed by following up the children to 3 years of age. Azathioprine has been shown to be safe at doses below 2mg/kg/day. Cyclosporin has also been shown to be safe.

Continued next page

Pilocarpine (salagen) has not been studied in human pregnancy but in animal studies using 10 times the human dose there was an increased risk of stillbirth and low birth weight babies (Briggs et al) & current advice therefore is that it should be avoided if possible.

Drugs commonly used in rheumatic diseases which are known to be harmful in pregnancy include methotrexate, cyclophosphamide, mycophenolate mofityl and leflunomide. These drugs should all be discontinued well in advance of conception. It is important to remember that certain drugs prescribed for other conditions can also be problematic in pregnancies and if in doubt it is always best to seek medical advice before conception.

Conclusions

- Urinary Tract infections are more common in women with Sjögren's Syndrome compared to those without.
- Dyspareunia & vaginal candidiasis (thrush) are common problems
- Interstitial cystitis is seen in patients with Sjögren's and may require specialist treatment
- Fertility is probably normal in patients with Sjögren's Syndrome.
- The majority of pregnancies in women with Sjögren's Syndrome are uncomplicated.
- It is safe to continue treatment with hydroxychloroquine throughout pregnancy.
- Women with anti-Ro and/or anti-La antibodies have a 5% risk of having a child with neonatal lupus rash and a less than 2% risk of having a child with congenital heart block.
- Women with anti-phospholipid antibodies have an increased risk of recurrent miscarriage which can be reduced by treatment with low dose aspirin +/- heparin.

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Glossary

Antiphophospholipid (APL) antibodies - proteins that can be detected in the blood that can lead to an increased risk of clotting and miscarriage
Dyspareunia - pain on intercourse
Dysuria - pain on passing urine
Interstitial cystitis - inflammation of the lining of the bladder of unknown cause
Pre-eclampsia - a rare complication of pregnancy where the mother develops high blood pressure and other problems.
Suprapubic - the area above the pubic bone
UTI - urinary tract infection