

12. Behçet's - Pregnancy

Introduction

Behçet's is commonly diagnosed during the child bearing years, at a time when you may be thinking about starting a family. It is therefore important to understand what potential problems you may experience and what treatments are considered safe to use before, during and after pregnancy. Although Behçet's is not thought to affect fertility in women, in men with disease affecting the testes, sperm quality may be reduced.

Behçet's in pregnancy is not usually associated with any harmful effects on the mother or her baby. In most women Behçet's seems to improve during pregnancy, however it may not always follow a similar course in successive pregnancies, and there is no clear way of predicting whether the disease will get better or worse in a particular pregnancy.

Planning a pregnancy

If you are thinking about starting a family, it is important to discuss this with your specialists. Some of your treatments may need to be altered. It is important for all women planning a pregnancy to start taking folic acid (which can be bought in any pharmacy) for 3 months prior to conception to reduce the risk of spina bifida. It is also important to ensure that you are immune to rubella, which can be checked with a blood test from your GP.

What effect will Pregnancy have on my Behçet's?

During pregnancy the various changes in your hormone and immune systems, designed to protect and nurture your growing baby, may also directly affect the clinical course of your Behçet's. In the majority of women who fall pregnant (up to 2/3rd) at a time when their Behçet's is active, pregnancy appears to improve the disease, with remission often continuing after birth. There are, however, those less fortunate (1/3rd) in whom their disease gets worse during pregnancy, giving rise to painful ulceration of the mouth and genitals. This can have implications with regard to vaginal delivery and the need for effective pain relief. Other areas

of the body which may become inflamed (during pregnancy) include the large joints and the eyes, with ongoing symptoms persisting after delivery.

Occasionally due to the needs of either the mother or baby, delivery via Caesarean section is necessary. Following delivery some women with Behçet's Syndrome may experience an exaggerated inflammatory reaction around the site of an episiotomy or Caesarean section wound, a phenomenon referred to as pathergy. This is a result of overactive white blood cells and can mimic the signs of infection, which *must* be excluded prior to starting treatment with steroid cream. Wound healing appears not to be altered.

What effect will my Behçet's have on a Pregnancy?

Behçet's appears to have little or no detrimental effect on pregnancy; however, there is some evidence to suggest that the rate of miscarriage may be increased. In addition, gestational diabetes (diabetes developing during and resolving after pregnancy) may be more common, however this may be related to steroid and other treatments used. Caesarean section rates may also be higher due to the baby or mother getting tired and labour not progressing or because some clinicians may recommend Caesarean section in cases of severe genital ulceration.

During pregnancy, all women are more prone to blood clots. In Behçet's, where there is already a tendency for blood clots to develop in the veins and the arteries due to inflammation of the blood vessels, this risk is increased further (and may be related to an increased risk of miscarriage). The most commonly affected veins are in the legs resulting in deep vein thrombosis (DVT). Rarely, in Behçet's the veins within the liver (Budd Chiari syndrome) or brain (cerebral venous thrombosis) may be involved. The use of blood thinning agents, such as low molecular weight heparin is sometimes recommended in women who have had a previous thrombosis or in those with other risk factors for blood clots to help reduce this risk. Heparin is given by injections, which you can be taught to give yourself once a day during pregnancy and for six weeks after your baby is born.

What about my baby?

In exceptional circumstances there have been isolated reports of babies of affected mothers suffering a transient form of Behçet's, which may last up to six to eight weeks following birth. This is thought to be the result of antibodies crossing the placenta, which give rise to ulceration of the mouth and genital areas of the baby, as well as changes to the skin. Although this is extremely rare, following prompt exclusion of other conditions, doctors may wish to prescribe steroids to promote rapid healing.

Is it safe to continue my treatment in pregnancy?

Many of the medications used in the treatment of Behçet's Syndrome are safe to use during pregnancy. These include, colchicine, prednisolone, ciclosporin, tacrolimus and azathioprine. Prednisolone, ciclosporin and tacrolimus increase the risk of developing gestational diabetes.

The intermittent use of pain killers such as paracetamol and ibuprofen are safe to use during pregnancy, however ibuprofen should be avoided from 32 weeks as after this point it may adversely affect the baby's circulation.

The past decade has seen a significant expansion in the use of newer anti (TNF) inflammatory agents - Infliximab, Adalimumab & Etanercept - to treat Behçet's Syndrome, with growing evidence to support their safe use during pregnancy; however, if treatment extends beyond 22 weeks' gestation, exposed infants should not receive live vaccines (BCG, rota virus) in the first 6 months after birth. All other routine vaccinations involve dead vaccines and are safe.

Although certolizumab may be continued throughout pregnancy (due to low placental transfer) there is currently insufficient evidence to support its effective use in Behçet's. Other anti (IL) inflammatory agents currently being tested for use in the treatment of Behçet's include Tocilizumab and Anakinra. At present their effects on pregnancy remain unknown and although unintentional early exposure is thought unlikely to be harmful, on-going treatment is currently not advised.

Unsafe treatments

Thalidomide was originally developed as a treatment for morning sickness in pregnancy but it was withdrawn following its use in the late 1950s and early 1960s when it was realized that it caused a specific congenital abnormality leading to short or absent limbs. It is an effective treatment of oral and genital ulceration in Behçet's Syndrome but should *never* be used in pregnancy or in the absence of effective contraception. Mycophenolate mofetil may cause fetal malformations and should ideally be discontinued prior to pregnancy. It may sometimes be replaced with azathioprine. Disease modifying drugs such as low dose methotrexate, and cytotoxic drugs such as chlorambucil and cyclophosphamide used in Behçet's to treat inflammation of the brain and eye should also be avoided when planning a pregnancy as they too may cause fetal abnormalities. These drugs should be discontinued at least three months prior to conception and alternative medications commenced if necessary.

Breast feeding

During breast feeding the risk of taking medication that may suppress your baby's immune system must be balanced against the many benefits that breast milk confers, and the risk of your disease relapsing if medication is not taken.

Prednisolone and azathioprine are safe to use during breast feeding and with only low concentrations of ciclosporine and tacrolimus transferred to the breast milk these medications are also considered safe. Similarly, colchicine, which is secreted into breast milk, has had no adverse side effects associated with its use in mothers who are breast feeding. The transfer of infliximab, adalimumab, etanercept and certolizumab to breast milk is low / zero and continuation of these medications is considered compatible with breast feeding.

Medications for the treatment of Behçet's Syndrome in men

Sperm production is not thought to be affected by treatment with steroids, azathioprine & colchicine, with limited but reassuring evidence to support the safe use of ciclosporin, tacrolimus, infliximab, adalimumab & etanercept. Although methotrexate has been shown to cause fall in the sperm count, this appears to be reversible on stopping the treatment, with no reports of an increased risk of birth defects while exposed to low-doses. Thalidomide may be found in sperm, and therefore the current advice is that it should be stopped at least a month prior to pregnancy with the use of effective barrier contraception during and for up to 4 weeks after its withdrawal.

Additional source material

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