



Marren Campbell & Mackie

NATURAL KILLER CELLS

Recurrent miscarriage:

- Recurrent miscarriage is defined as ≥ 3 consecutive pregnancy losses that have occurred < 20 -weeks gestation
- Recurrent miscarriage affects approximately 1% of couples
- A cause can be found in approximately 50%

Natural Killer cells:

- Our immune system is designed to protect us from foreign cells (e.g. infection)
- Natural Killer cells (NK cells) are only one of many different types of cells that have a role in our immune system
- NK cells engulf and destroy cells that are considered foreign

Pregnancy and the immune system:

- A pregnancy presents the human body with a unique challenge
 - o On the one hand, it is the job of the uterus to support and nurture a pregnancy
 - o However, on the other hand, a pregnancy is actually made up of foreign cells
- Whilst it is biologically plausible that abnormal numbers of uterine NK cells could be responsible for recurrent miscarriage, studies that have been done have the following flaws:
 - o Individual studies include small numbers of patients making it difficult to form firm conclusions
 - o Studies performed have shown conflicting results
 - o Most of the studies performed have had no 'control' group as a comparison

Detection of NK cells:

- NK cells can be detected via an endometrial biopsy or a blood test
- There is much debate about the relevance of NK cells in the blood and their association to what is happening in the uterus
 - o Therefore, when I test NK cells, I tend to perform an endometrial biopsy
 - o The biopsy is performed day 10 of your cycle
 - o The biopsy involves passing a fine catheter through your cervix and into your uterus; the catheter is withdrawn removing with it a fine slice of endometrial tissue
 - o The results are generally available in 2-weeks time

Management:

- Unfortunately, just as there is inadequate evidence supporting a definite role of NK cells as a cause of recurrent miscarriage, conclusive evidence supporting proposed treatment options is also lacking
 - o A common treatment protocol involves a combination of Prednisone tablets and Clexane injections for those patients with a history of recurrent miscarriage and an endometrial biopsy demonstrating elevated concentrations of NK cells

Prednisone:

- Prednisone is an oral steroid
 - o Steroids act as immune system suppressors (i.e. they reduce the concentration of inflammatory cells)

- The regimen used is as follows:
 - o Prednisone 25mg orally daily to commence prior to embryo transfer
 - o This dose is to continue until your next period (if the cycle is unsuccessful) OR until 10-weeks gestation
 - At this point, it is essential that Prednisone is NOT ceased abruptly
 - Prednisone needs to be weaned
 - I suggest reducing the Prednisone dose by 5mg every 5-days
 - o Should the pregnancy end in miscarriage, Prednisone also needs to be weaned
 - Should you require a D&C (surgical procedure for miscarriage), you should inform the Anaesthetist that you are taking Prednisone

- Prednisone does have some risks:
 - o All steroids result in impaired glucose tolerance
 - This is usually only an issue in those patients with a background of or who are susceptible to Diabetes Mellitus
 - Prior to commencing Prednisone, you should have a Glucose Tolerance Test to ensure that this is not the case
 - In the event that you have impaired glucose tolerance, you will be reviewed by an endocrinologist prior to commencing Prednisone
 - o Long-term steroid use predisposes to osteoporosis (weakened bones)
 - It is unlikely that the duration of steroid use will have any significant detrimental effect
 - However, I recommend that you take Caltrate (600mg) with Vitamin D (400IU) one tablet twice daily to minimise this risk

- Prednisone is a Category A drug = drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed
 - However, it is known that Prednisone results in a small increase in the risk of cleft lip/palate
 - The background rate of cleft lip/palate is approximately 1:1000 pregnancies
 - Prednisone is thought to increase this risk to 2:1000
 - As the risk is small, Prednisone still has a Category A rating
 - In order to reduce this risk, I suggest that you take Folic Acid 5mg orally daily
 - The normal dose for women attempting pregnancy is only 0.5mg

Clexane:

- Clexane is an injectable anticoagulant
 - Clexane is also thought to have effects on the immune system
- The regimen is as followed:
 - Clexane 40mg subcutaneously daily to commence on the day of embryo transfer
 - This dose is to continue until your next period (if the cycle is unsuccessful) OR until 10-weeks gestation
 - At this point, Clexane can be ceased without weaning
- Clexane is usually well tolerated
 - At this dose, complications other than irritation at the injection site are rare

Dr Anthony Marren
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