COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS, SINGAPORE 2006

SUMMARY STATEMENT ON THE INVESTIGATION AND TREATMENT OF COUPLES WITH RECURRENT PREGNANCY LOSS

1. Summary

Recurrent miscarriage, defined as the loss of 3 or more pregnancies, is a condition that has many possible causes. Active research has yielded useful information with regard to the appropriateness of certain investigations and treatment modalities. Useful investigations include parental karyotyping, pelvic sonography and tests for antiphospholipid antibodies, bacterial vaginosis and inherited thrombophilic defects. Therapeutic strategies will depend on the underlying cause found. Supportive care has a beneficial effect on unexplained recurrent miscarriage.

2. Introduction

Recurrent miscarriage is a distressing problem that affects 1% of all women. Only a proportion of women presenting with recurrent miscarriage will have a persistent underlying cause. More than one contributory factor may underlie the losses. These recommendations hope to address these complex issues and to assist individual clinicians and hospital departments in producing local protocols for the management of recurrent miscarriage.

3. Detailed guidelines

3.1 Investigations

3.1.1 Genetic factors

RECOMMENDATION : All couples with a history of recurrent miscarriage should have peripheral blood karyotyping performed. Cytogenetic analysis of the products of conception may be of prognostic use.

EVIDENCE : (1, 2) In approximately 3 - 5% of couples with recurrent miscarriages, one of the partners carries a balanced structural chromosomal anomaly, most commonly balanced reciprocal or Robertsonian translocations. Future pregnancies have a 5 - 10% chance of an unbalanced translocation.

3.1.2 Anatomical factors

RECOMMENDATION : Routine hysterosalphingography as a screening test for uterine anomalies in recurrent miscarriage is questionable. A pelvic ultrasound with (or without) sonohysterography is as effective in assessing uterine anatomy.

EVIDENCE : (3) The exact contribution that congenital uterine anomalies make to recurrent pregnancy loss has not been clearly established. A recent retrospective study suggested that these women experience high rates of miscarriage and preterm delivery.

3.1.3 Endocrine factors

RECOMMENDATION : Routine screening for occult diabetes and thyroid disease with oral glucose tolerance and thyroid function tests in asymptomatic women presenting with recurrent miscarriage is uninformative. Routine screening for thyroid antibodies is not recommended.

EVIDENCE : (6, 7, 8, 9) Well-controlled diabetes mellitus is not a risk factor for recurrent miscarriage, nor is treated thyroid dysfunction. The presence of thyroid antibodies in euthyroid women does not affect future pregnancy outcome in recurrent miscarriage.

3.1.4 Infective agents

RECOMMENDATION : TORCH (toxoplasmosis, other [congenital syphilis and viruses], rubella, cytomegalovirus and herpes simplex virus) screening is unhelpful in the investigation of recurrent miscarriage.

EVIDENCE : (18, 19) Toxoplasmosis, rubella, cytomegalovirus, herpes and listeria infections do not fulfil the criteria for an infective agent to be implicated in aetiology of repeated pregnancy loss.

RECOMMENDATION : Screening for and treatment of bacterial vaginosis in early pregnancy among high risk women with a previous history of second-trimester miscarriage or spontaneous preterm labour may reduce the risk of recurrent loss and preterm birth. There is no benefit in screening and treating all pregnant women for bacterial vaginosis.

EVIDENCE : (20) The presence of bacterial vaginosis in the first trimester of pregnancy has been reported as a risk factor for second trimester miscarriage and preterm delivery.

3.1.5 Inherited thrombophilic defects

RECOMMENDATION : Routine screening for inherited thrombophilic defects may be offered in the investigation of recurrent miscarriage.

EVIDENCE : (21, 22, 23, 24) Activated protein C resistance (most commonly Factor V Leiden mutation), deficiencies of protein C/S and antithrombin III, hyperhomocysteinaemia and prothrombin gene mutation are established causes of systemic thrombosis. Retrospective studies have suggested an association between these conditions and fetal loss. Prospective data are scarce.

3.2 Treatments

3.2.1 Genetic factors

RECOMMENDATION : The finding of an abnormal parental karyotype should prompt referral to a clinical geneticist.

3.2.2 Cervical weakness

RECOMMENDATION : (4, 5) Cervical cerclage should only be considered in women who are likely to benefit due to the potential hazard of surgery and stimulating uterine contractions. Transabdominal cerclage has been advocated in selected women with previous failed transvaginal cerclage and/or a very short and scarred cervix.

3.2.3 Endocrine factors

RECOMMENDATION : Human chorionic gonadotrophin (hCG) or progresterone supplementation have not shown any significant benefit in improving pregnancy outcome in recurrent miscarriage.

RECOMMENDATION : Prepregnancy suppression of luteinising hormone (LH) levels among women with recurrent miscarriage who hypersecrete LH is not recommended.

EVIDENCE : (10, 11, 12) Several controlled trials did not show any significant improved pregnancy outcome with these measures.

3.2.3 Antiphospholipid syndrome

RECOMMENDATION : A combination therapy of aspirin plus heparin is recommended in women with a history of recurrent miscarriage and aPL. Currently, there is no place for steroid therapy.

EVIDENCE : (13, 14, 15) A randomised controlled trial showed that the live birth rate of women with recurrent miscarriage associated with aPL significantly improved when they are treated with low-dose aspirin in combination with low-dose heparin. There is not enough reliable evidence to show that steroids improved the outcome in these women.

3.2.4 Alloimmune factors

RECOMMENDATION : Immunotherapy, including paternal cell immunisation, thrid-party donor leucocytes, trophoblast membranes and intravenous immunoglobulin (IVIG), for the treatment of unexplained recurrent miscarriage should not be practised.

EVIDENCE : (16, 17) Randomised controlled trials have shown that various forms of immunotherapy in unexplained recurrent miscarriage provided no significant beneficial effect over placebo.

3.2.5 Inherited thrombophilic defects

RECOMMENDATION : These couples should have thromboprophylaxis in view of the poor pregnancy outcome and maternal risks during pregnancy.

3.2.6 Unexplained recurrent miscarriage

RECOMMENDATION : Women with unexplained recurrent miscarriage have an excellent prognosis for future pregnancy outcome without pharmacological intervention if offered supportive care alone in the setting of a dedicated early pregnancy assessment unit.

EVIDENCE : (25, 26, 27)

Data from several non-randomised studies have suggested that attendance at a dedicated early pregnancy clinic has a beneficial effect, although the mechanism is unclear.

This consensus statement is produced on behalf of the College of Obstetricians and Gynaecologists, Singapore by:

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Valid until 2008
unless otherwise indicated

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