

METHOTREXATE FOR ECTOPIC PREGNANCY

This LOP is developed to guide clinical practice at the Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this LOP.

1. AIM

- To outline the medical management of ectopic pregnancy

2. PATIENT

- Women with confirmed ectopic pregnancy who wish to receive medical management with single dose methotrexate.

3. STAFF

- Medical, midwifery and nursing staff

4. EQUIPMENT

- Methotrexate pre-filled syringe
- Cytotoxic disposal bin
- Cytotoxic spill kit

5. CLINICAL PRACTICE

- Ensure patient meets all selection criteria for methotrexate treatment:
 - Close proximity to Royal Hospital for Women
 - Patient compliance with regular follow ups
 - Less than 8 weeks gestation / amenorrhoea
 - Unruptured ectopic – less than 4cm in diameter
 - Haemodynamically stable
 - Normal liver function tests
 - Empty uterus
 - Beta HCG (β hCG) less than 5,000 units/L
 - No pelvic pain or tenderness
 - Patient agrees to avoid pregnancy for 3 months after treatment
 - Patient is suitable for single dose treatment methotrexate.

The multi-dose treatment will not be further considered in this protocol and liaison between clinical medical and nursing teams is required if multi-dose treatment is considered following the failure of single dose treatment. The decision for multi or single dose treatment will be made by the medical practitioner in consultation with the woman.

- Ensure an accredited clinician co-ordinates the treatment. Accredited clinicians are:
 - Jason Abbott
 - Michael Costello
- Obtain written consent from patient.
- Give patient written information (Appendix 1)
- Arrange treatment via the gynae-oncology CNC (page #44068, phone #26229 or mobile #0417944297). **All chemotherapy must be administered by staff trained in the handling, administration and disposal of cytotoxic drugs. Refer to Workcover NSW Cytotoxic Drugs and Related Waste Guide 2008 and Cancer Institute NSW (eviQ) Safe handling and waste management of hazardous drugs. 2014.**
- Admit patient as a day stay only if medically indicated, usually treated as an outpatient.
- Obtain baseline β hCG, FBC, U&Es, LFTs and commence treatment if blood values are within normal range and β hCG is less than 5,000 units/L
- Measure patients weight and height and calculate BSA using the formula below:

CLINICAL POLICIES, PROCEDURES & GUIDELINES

Approved by Quality & Patient Care Committee
16/2/17

METHOTREXATE FOR ECTOPIC PREGNANCY cont'd

$$\sqrt{\frac{\text{height (cm)} \times \text{weight (kg)}}{3600}}$$

(ie. Commence the calculation inside the brackets & then calculate the square root to reach the BSA)

E.g. A women 165cm & 60kg = $165 \times 60 = 9900 \div 3600 = 2.75$
square root of 2.75 = 1.65
which gives a BSA of 1.65m²
Note: BSA is capped at 2m²

- Calculate the dose of methotrexate (50mg/m²) and prescribe on the NIMC as a stat intramuscular injection (Note: BSA is capped at 2m² therefore the maximum dose is 100mg.)
Intramuscular methotrexate administration is the predominant and preferred route for treatment of tubal pregnancy although it can also be given by direct local injection into the ectopic pregnancy sac transvaginally ultrasound guided or laparoscopically (this must be administered by appropriately trained medical staff and is not covered in this LOP).
- Consult with the gynae-onc CNC then take NIMC to pharmacy. Pharmacist will clinically review order and dispense pre-filled syringes of methotrexate 100mg. If access is required after hours, the after hours nurse manager will be required to contact the on call pharmacist to be called in to clinically review the order and dispense. If administration is to occur in another area such as the radiology department all staff involved in the administration and handling must be compliant with safe handling of cytotoxic medication guidelines and know how to manage a cytotoxic spill.
- Administer methotrexate as an intramuscular injection in the buttock or lateral thigh. The empty syringe or needle should be placed in a purple cytotoxic sharps container as per cytotoxic handling guidelines.
- Provide patient with the methotrexate patient information leaflet along with contact numbers should they be required.
- Refer patient to Early Pregnancy Assessment Service clinic on:
 - Day 4 after treatment for repeat quantitative β hCG
 - Day 7 after treatment for quantitative β hCG, FBC, U&Es, LFTs
- Continue quantitative β hCG estimations weekly until the level falls to biological zero.
- Advise the woman to:
 - Refrain from intercourse until ectopic pregnancy has resolved
 - Commence oral contraceptives or barrier contraception at the conclusion of treatment and to continue contraception for 3 months.
 - Report any abnormal symptoms to the accredited clinician
 - Avoid taking herbal or vitamin supplements containing folate, including folic acid.
 - Avoid sun exposure to limit risk of methotrexate dermatitis
- Refer patient for gynaecological follow up approximately four weeks after cessation of the course of treatment assuming that the β hCG levels continue to fall. Earlier consultation to be arranged if β hCG levels plateau or commence to rise.

If the β hCG does not fall by > 15% between days 4 and 7, repeat in 3 days and if fall is not >20% of baseline, consider retreatment with methotrexate or surgical management.

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METHOTREXATE FOR ECTOPIC PREGNANCY cont'd

6. DOCUMENTATION

- Integrated Clinical Notes
- Medication Chart

7. EDUCATIONAL NOTES

Methotrexate is a folic acid antagonist (anti-metabolite) which prevents the growth of rapidly dividing cells including trophoblasts and fetal cells by interfering with DNA synthesis. The dose of methotrexate used to treat ectopic pregnancy is relatively low, safe and well tolerated.

Side effects:

Adverse reactions to methotrexate are usually mild and self-limited. Approximately 30 % of patients in the single dose protocol will have side effects. The most common are stomatitis and conjunctivitis. Rare side effects include gastritis, enteritis, dermatitis, pneumonitis, alopecia, elevated liver enzymes, and bone marrow suppression. All of these side effects resolve as methotrexate exposure wanes.

8. RELATED POLICIES / PROCEDURES / CLINICAL PRACTICE LOP

- Methotrexate- oral dosing and administration

9. RISK RATING

- Low- review in 5 years

10. NATIONAL STANDARD

- Medication safety

11. REFERENCES

1. Workcover NSW. 2008. Cytotoxic Drugs and Related Waste Guide 2008. New South Wales Government.
2. Bhattacharya S, McLernon DJ, Lee AJ, Bhattacharya S. Reproductive outcomes following ectopic pregnancy: register-based retrospective cohort study. PLoS Medicine. 2012;9(6):e1001243-e.
3. Royal College of Obstetricians and Gynaecologists. Ectopic pregnancy and miscarriage: Diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage. NICE Clinical Guidelines. 2012:1-287.
4. Stika C. Methotrexate: The Pharmacology Behind Medical Treatment for Ectopic Pregnancy. Clinical Obstetrics & Gynecology. 2012;55(2):433-9.

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MANAGEMENT OF ECTOPIC PREGNANCY WITH METHOTREXATE

ECTOPIC PREGNANCY occurs when the fertilised egg implants outside the uterus (womb) usually in the fallopian tube. In some cases it can lead to rupture of the tube causing pain and bleeding and is occasionally life threatening. Treatment may involve surgery or the use of a drug called methotrexate as an option for management.

METHOTREXATE is a cytotoxic (chemotherapy) drug that works by stopping the growth of rapidly dividing cells (that may be found in developing placental and embryonic tissue). As with all drugs there are some potential side effects but in most cases in this situation they are minor.

Methotrexate can only be used in certain cases and your doctor will explain this to you. There is no clear scientific research to suggest that the use of methotrexate offers an improved outcome to your fertility compared to surgery, however, there is a good chance that you will avoid surgery. There are disadvantages to taking methotrexate to be considered as well – it can take weeks to complete the treatment, you will require monitoring of blood hormone levels and the drug itself is not without side effects. You will be required to have several follow up visits and blood tests. You may require a second injection or may require surgery if the treatment is not successful. You are also advised to wait at least 3 months before trying to become pregnant again.

Treatment with Methotrexate

Once your doctor has discussed this option with you, you will need to sign a consent form for the treatment. Your dose of methotrexate will be individually calculated using your height and weight. You also are required to have a blood test prior to treatment. This will check your kidney liver and blood systems. There may be a delay of a few hours prior to your receiving the treatment.

Methotrexate is administered as a single injection into the buttocks; a trained member of staff in the oncology unit gives it. Providing there are no problems you should be able to go home shortly after receiving the injection.

For 7 days after your treatment you should either flush the toilet twice after using it (a portion of the drug is excreted in urine) with the lid shut

Follow up

You will be monitored in the EPAS (early pregnancy assessment clinic) with blood tests and review on days 4 and 7 post treatment.

The blood tests are to monitor your pregnancy hormone levels (this is called a BHCG test), kidneys, liver and blood system. If all is going well, monitoring of the BHCG will continue weekly until it reaches zero.

Side effects of treatment

- Abdominal cramping – usually occurs within 2 – 3 days of having your treatment. This should be relieved with paracetamol. As this is also a sign of a ruptured ectopic you will need to report this to the hospital if the pain doesn't settle with paracetamol or worsens. Also report if you feel faint or dizzy. You may want to avoid foods that cause bloating or wind such as beans, cabbage and broccoli as they may make the pain worse
- Vaginal bleeding or spotting (again if this is excessive you need to report this)
- Nausea, vomiting or indigestion
- Skin sensitivity to sunlight (you will need to wear sunscreen preferably factor 30 when out in the sun)

Rare side effects

- Mouth and throat ulcers (if you develop a sore mouth, use a non-alcohol based mouthwash for relief. Sodium bicarbonate 1 tsp dissolved in a glass of water is an ideal mouth rinse)
- Bone marrow suppression (lowering of your blood counts can make you more susceptible to infections and feel tired)
- Hair thinning
- Inflammation of the lung (pain when you breathe in and out)

If you experience any of these symptoms you should contact the hospital on 93826111

Things to avoid

- Folic acid (this is found in many multivitamins especially those designed for pregnancy)
- Avoid hot baths, hot showers and saunas whilst you are bleeding heavily as you may feel faint
- Use pads rather than tampons to reduce the risks of infection
- Use paracetamol rather than non-steroidal anti-inflammatory drugs (such as nurofen, brufen) as they can affect the level of methotrexate in your body.
- Smoking
- Alcohol
- Sexual intercourse (until you have had your follow up visit)
- If breast feeding it is advised that you express and discard for four days following injection (Further information available via the Infant Risk Centre website www.infantrisk.com)

CONTACT NUMBERS

EARLY PREGNANCY CLINIC 93826701
Monday – Friday 7.30am till 11.30am
Nikki Collins 93826111 and page 46520

JENNIE DUGGAN ONCOLOGY CNC
MON – FRI; 0830 – 1700 93826229 / 0417944297
Office hours 93826111 and page 44068

ROYAL HOSPITAL FOR WOMEN SWITCHBOARD 93826111
(Ask to speak to the registrar on call)

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