Modern Management of Ectopic Pregnancy

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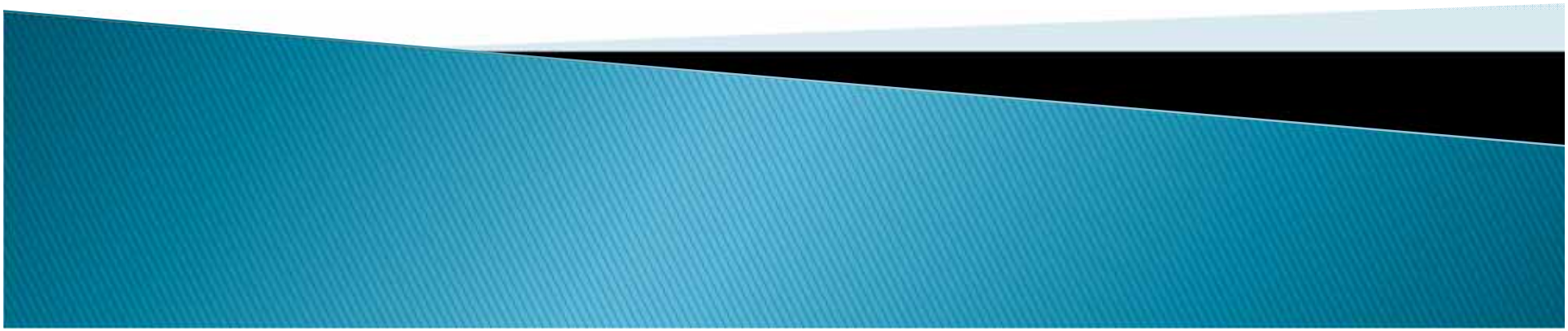

Introduction

- Implantation of fertilized ovum outside of uterine cavity
- Common cause of morbidity and mortality
- Diagnosis can be difficult
- A condition specific to humans
- Medical, Surgical and expectant

Incidence

- Previously estimated at 0.5%
- Significant increase in the last 30 years
  - Awareness of condition
  - Increase in incidence of PID
  - Smoking
  - Better diagnostic tools / EPU
  - Use of ART
- In developed world 1-2% risk (cf twin pregnancy)
- Higher in developing countries

Morbidity and Mortality

- Leading cause of death in the first trimester (UK 0.35/1000)
- Up to 10% die in developing countries amongst admissions.
- Pain - haemorrhage - surgery
- Long term: infertility

Risk Factors

- Often none
- Any condition resulting in damage / dysfunction of fallopian tubes
  - Surgery: Sterilization, ROS, Other pelvic surgery (CS, Ovarian Cystectomy, Appendicectomy, Bowel surgery)
  - PID strong association with Chlamydia Trachomatis (30 – 50%)
  - Endometriosis
  - Smoking (35%) : Dose effect relationship/ Past exposure

Risk Factors ctd

- ART
  - 1st IVF pregnancy (Lancet 76 : Steptoe & Edwards)
  - 2 – 5% risk

  Higher if existent tubal disease
- Contraceptive failure: POP IUCD
  - Absolute risk probably less – unchanged
- Previous ectopic

Risk Factors ctd

- Previous miscarriage : Spont. or induced
- Unexplained infertility
- Age>35 : More likely exposed to risk factors
  - Chromosomal anomalies in trophoblasts
  - Altered tubal motility

Aetiology

- Difficult to study mechanisms

- Embryo arrest in tube
- Tubal microenvironment
- Altered tubal smooth muscle contractility
- Impaired ciliary activity
- Wrong timing of pro-implantation signals

Sites of Implantation

- 98 % tubal
- 72% Ampullary
- 12% Isthmus
- 12% Fimbria
- 2% Intramyometrial
- Others rare : Ovary, Cervix , Broadligament, Abdominal, Liver, spleen and C-Section scar
- Doppler studies may help
- Multidose Medical treatment preferred

Clinical Presentation: Typical

- Pain
- Bleeding
- Experienced by 33% early pregnancies
- +ve urine pregnancy test
- Unilateral pain – Abdominal tenderness 75%
- Cervical motion tenderness 2/3 cases
- Bimanual examination: 50% cases palpable mass May exacerbate bleeding

Clinical Presentation: Typical ctd

- Acute abdomen
- Shock
  - Tachycardia
  - Pallor
  - Syncope
- Shoulder tip pain
- All late signs and clearly depends at which stage diagnosis made

Clinical Presentation : Atypical

- 10% : No symptoms
- 1/3 No signs
- Diarrhoea
- Dizziness
- Vomiting
- Maternal Deaths Enquiry : Misdiagnosis
  - 2006 – 2008 in 4 / 6 deaths
- All medical attendants should have high degree of suspicion/ awareness in women of reproductive age

Diagnosis

- 50% not diagnosed at initial presentation
- Combination
  - Hx and examination
  - Hormonal assay Urine and Serum
  - US Scan : PA TVS
  - Key element : Exclude an IUP
  - Pregnancy of unknown location (PUL)
    - 10 – 20% eventually diagnosed as ectopic

Diagnosis TVS ctd II

- TVS : Can identify IUP or ectopic
- IUP
  - Beware of pseudosac
  - Almost 100% accurate by 5 ½ wks
  - Presence of YS or FP within Gest. sac
  - Cardiac activity by 6 weeks
- Ectopic
  - Free fluid POD (cf normal pregnancy)
  - Adnexal mass
  - Side of CL
  - 90 % cases in a prospective study 6600 cases

Diagnosis: TVS ctd III

- False +ve :
  - Endometrioma
  - CL
  - Paratubal cyst

- False -ve
  - -Obscured by bowel
  - -Distorsion of uterine anatomy

Diagnosis: Use of B-HCG

- 1985 : Discriminatory level of B HCG
  - level at which IUP should be seen
  - Initially 6500 iu/ml for an abdominal scan
  - Nowadays 1000 – 1500 iu/ml by most units
- HCG Changes over time
  - -Minimal expected rise of 50 – 65% over 2 days
  - -Does not confirm viability
  - -Suboptimal rise indicative of pregnancy failure

Diagnosis : Use of B HCG

- Rapid fall over 48 hours
  - 20 – 35%
  - Indicative of a failing IUP
  - May indicate resolving ectopic

- With ectopics

  No specific patterns : May rise or fall

  70 % increase slower than viable IUP or decrease slower than sp. Miscarriage

Diagnosis : Serum Progesterone

- Useful if > 50 ng/ml as indicative of a viable IUP
- Cannot differentiate between ectopic and failing IUP
- Very low levels (< 5ng/ml) may allow conservative management with PUL

Diagnosis: Endometrial Bx

- As an OP procedure
- Cases of PUL
- Static HCG
- Chorionic villi
- If negative laparoscopy, may perform “D & C”
  - Have to ascertain non viability
  - Consent obtained prior to surgery

Diagnosis: Laparoscopy

- Considered as gold standard
- Other investigations inconclusive
- Fatalities described where delay / reluctance
- Negative laparoscopy : 5% subsequently diagnosed as an ectopic
- Other strategies exhausted

Repeat US Scan, Serial HCG, Ebx & Emperical medical treatment

- ? Acceptable negative diagnostic laparoscopy rate

Management

- Surgical
  - laparoscopy
  - laparotomy
- Medical

- Expectant

Surgery

- Laparoscopy preferable
  - Stable patient
  - Operating time less
  - Blood loss reduced
  - Less analgesic requirement
  - Reduced in-patient stay
  - Surgeon's experience
- Laparotomy: Unstable patients
- ABH : Last 17 patients : 7 laparoscopic, 8 laparotomy & 2 converted

Surgery: Salpingostomy

- Dissecting ectopic out of tube
- Incision along antimesenteric surface of tube
- Aim to conserve fertility on affected side
- Recommended if contralateral side diseased
- Risk of persistent trophoblastic disease
  - Up to 10%
  - Persistent serum B HCG levels

Surgery : Salpingostomy ctd

- Risk factors for persistent trophoblasts
  - Large ectopic > 2cm
  - Active tubal bleeding
  - Rising HCG prior to surgery
  - Initial HCG >3000 iu/ml
- Need follow up until HCG not detectable

Costs but still less than ART

Surgery : Salpingectomy

- Reproductive outcomes: probably not affected
- Advised if contralateral tube healthy
- Less risk of immediate post-operative tubal bleeding
- No follow up of HCG levels
- Histology
  - Confirmation
  - Molar change
- Surgical method of choice

Medical Treatment

- Methotrexate usually single dose
- Successful for small stable ectopics in 90% cases
- Folic Acid antagonist
- Arrests mitosis in rapidly dividing cells
- Various regimens
  - Most common is single dose at 50mg/m^2
  - $\sqrt{}$ ht (cm) x wt (kg)/ 3600

Medical Treatment ctd

- Multidose regimen (HCG 3000 – 5000)
  - Days 1, 3 , 5 and 7 (maximum of 4 doses)
  - Leucovorine rescue 0.1mg /kg on days 2,4,6 and 8
  - 5% higher success rate
- HCG levels measured 4 – 7 days later
- Single dose may require repeat if HCG falls by < 15% after 4 days
- Surgery mostly if HCG falls too slowly/ rupture

Patient Suitability

- Prefers medical treatment
- Willing to attend follow-up
- No alcohol for 1 week
- Not breastfeeding or agrees to discontinue
- Stable with minimal abdominal pain
- No active peptic ulcer disease
- Normal FBC and normal renal and hepatic function
- Serum B HCG < 3000

Patient Suitability ctd

- Ultrasound scan
  - No FH activity or yolk sac
  - Minimal free fluid POD
  - Unlikely to be early intrauterine failure
- Concurrent medication
  - Nsaid , penicillins, sulphonamides, trimethoprim tetracyclines, diuretics, phenytoin, antimalarials, cyclosporin, retinoids, folic acid, probenecid, hypoglycaemics, live vaccines, nephrotoxic and hepatotoxic drugs

Medical treatment ctd

- Baseline FBC U&E Cr LFT at start
- Well tolerated treatment generally
- Expect some abdominal discomfort 1 – 3 days after initiating treatment
- Significant hepatic or renal toxicity rare
- Alopecia extremely rare
- Faster recovery than surgery

Direct Injection of Methotrexate

- Under US Scan control
- During laparoscopy
- Less side effects
- Higher therapeutic level
- Risk of rupture during procedure
- No significant advantages in most patients

Expectant Management

- Spontaneous resolution
- Tubal abortion or regression of trophoblasts
- Overlap with PUL
- Asymptomatic
- Low HCG < 1000
- Rapidly falling HCG (20% or more over 48 hours)
- Need clear instructions to patients & follow-up

Fertility prognosis

- 15% risk of recurrence after 1 EP (5 – 20%)
- Doubles if 2 previous ectopics (1 in 3)
- May occur in tubal remnant after partial salpingectomy (spontaneous or ART)
- ? Total salpingectomy rather than partial
- Early scan advised in future pregnancy

Future

- High false positives
- Suspected much more commonly than occurs in units with a high awareness
- Other biomarkers under study
- Locally need to increase awareness
- More aggressive screening and treatment of STD esp chlamydia