Empirical treatment of endometriosis

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Overview

• Rationale for empirical treatment
• Recommended empirical treatment options in the guideline
• Treatment options of uncertain place in empirical treatment
• Conclusions

• Empirical : based on observation and experience rather than theory or pure logic
  Compact Oxford English Dictionary

• Empirical treatment : Medical treatment that is given on the basis of the doctor's observations and experience.
Confirmed disease

- History
- Examination
- Imaging
- Laparoscopy
- Histology

Disadvantages of laparoscopy

- (Usually) Requires general anaesthesia
- Morbidity
- Mortality
- Cost

Why empirical treatment

- Is the diagnostic test too invasive/expensive?
- Is it essential/beneficial to know the diagnosis?
- Would diagnosis change the management?
Empirical treatment

- Simple
- Safe
- Few side effects
- Effective
- Cheap

Patient selection

- History
  - Dysmenorrhea
  - Dyspareunia
  - Other pain
- Examination: No obvious signs of endometriosis
- Investigations: Normal ultrasound, ?MRI

ESHRE Guideline, 2005
Options

• Counselling
• Analgesics
• Hormonal contraceptives
• Progestogens
• Danazol/Gestrinone
• GnRHa
• Complementary treatment

Analgesics

• Paracetamol
• Codeine
• Nonsteroid antiinflammatory drugs (NSAIDs)

Paracetamol

Supporting documentation 2007

• Paracetamol 500 mg qds vs placebo
  – Not effective
• Paracetamol 1 g qds vs placebo
  – Effective
• Paracetamol 1 g tds vs Ibuprofen/Naproxen
  – No difference
Codeine

- No RCTs

NSAIDs

Marjoribanks et al 2010

- NSAIDs vs placebo 56 trials
- NSAIDs vs NSAIDs 14 trials
- NSAIDs vs Paracetamol 3 trials

- Outcome measures
  - Primary
    - Pain relief
    - Adverse effects
  - Secondary
    - Requirement for additional medication
    - Interference with daily activities
    - Absence from work/school

NSAIDs

Marjoribanks et al 2010

- COX-1 NSAIDs
  - Aspirin: 160 mg/day
  - Naproxen: 500 mg 4-hourly
  - Diclofenac: 75-500 mg 4-hourly
  - Metaxalone: 200-400 mg daily in divided doses
  - Diclofenac: 200-400 mg twice daily
  - Fenoprofen: 100-250 mg twice daily
  - Ibuprofen: 600 mg 3-4 times daily
  - Indomethacin: 75 mg daily
  - Ketoprofen: 25-50 mg every 4-6 hours
  - Lysteda Clobenprop: 100 mg 4-hourly
  - Mefenamic acid: 500 mg 4-hourly
  - Naproxen sodium: 200-275 mg 4-hourly
  - Tolfenamic acid: 200 mg twice daily

- COX-2 NSAIDs
  - Diclofenac: 100 mg daily
  - Meclofenamate sodium: 250 mg daily
NSAIDs
Marjoribanks et al 2010

• Pooled data: NSAIDs vs placebo
  – NSAIDs more effective in pain relief
  – NSAIDs cause more side effects (GI and neurological)
  – NSAIDs group less likely to require additional medication
  – NSAIDs group less interference with daily activities
  – NSAIDs group less absenteeism

NSAIDs
Marjoribanks et al 2010

• NSAIDs vs NSAIDs
  – Diclofenac more effective than Meloxicam
  – Fenoprofen more effective than Aspirin
  – Naproxen more effective than Ketoprofen and Ibuprofen
  – Indomethacin more effective than Aspirin
  – No differences
    • Ibuprofen vs Nimesulide/Prinixicam/ Lysine clonixinate
    • Melonamic acid vs Meloxicam/Tolferamic acid
    • Naproxen vs Diclofenac/Etoricoxib/Piroxicam/Flurbiprofen
  – No differences in side effect profiles/secondary outcome measures

NSAIDs
Marjoribanks et al 2010

• NSAIDs vs Paracetamol
  – NSAIDs more effective than Paracetamol
  – No difference in side effect profile
  – No data on secondary outcome measures
Hormonal contraceptives

- Combined oral contraceptive pill (COC)
- Progestogen only (mini) pill
- Depo Provera
- Mirena IUS

COC

Supporting documentation 2007

- Long term safety
- Ability to use indefinitely
- Tricyclical or continuous use to avoid periods

COCs

Wong et al 2009

- Studies included 10
  - COC vs placebo 6 trials
  - COC with different progestogens 2 trials
  - COC with different doses of Oestrogen 2 trials
Pain improvement

Additional analgesia required
Absence from work or school

Progestogen only contraceptives
Mirena IUS/Depo Provera/POP

- Mirena effective in confirmed diagnosis
- Long term safety
- No RCTs in primary dysmenorrhoea
- Likely to be an acceptable option
Second line treatment options

- Progestogens
- GnRHa
- Danazol/Gestrinone

- Side effects
- Safety
- Cost

Second Line Hormones

Conclusions of Consensus Statement

- CPP frequently occurs secondary to nongynaecologic conditions
- For women in whom endometriosis is suspected, laparoscopic confirmation is unnecessary
- Trial of medical therapy including danazol, GnRHa and progestins is justified
Initial assessment

- Treatment modalities shown to be effective
  - Vitamin B1

- Treatment modalities which may be helpful
  - Behavioural interventions
  - Magnesium
  - Fish oil
  - High frequency TENS
  - Topical heat
  - Tki-shakuyaku-san
  - Chinese herbal medicine

- Treatment modalities of unknown benefit
  - Vitamin B12
  - Acupuncture

- Treatment modality of no benefit
  - Vitamin E
  - Spinal manipulation
Counselling

- When
  - Before
  - During
  - After diagnosis/treatment
- Who
  - Physician
  - Professional counsellor/psychologist
- Principles
  - Balanced view of diagnostics, treatment options, their efficacy, side effects and risk of recurrence

Conclusions

- Empirical treatment for pain acceptable
- Empirical options include analgesics and COCs
- Place of progestogens, danazol, gestrinone, GnRHa debatable
- There is a need for RCTs comparing the place of empirical treatment against laparoscopy