Empirical treatment of endometriosis

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ES has no conflict of interest to declare related to this talk

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

ESHRE Guideline, 2005

Empirical treatment of pain symptoms without a definitive diagnosis

GPP	Empirical treatment for pain symptoms presumed to be due to endometriosis without a definitive diagnosis includes counselling, adequate analgesia, antimitotic therapy, progestagens or the combined oral contraceptive (COC). It is unclear whether the COC should be taken conventionally, continuously or in a tricyclic regimen. A GnRH agonist may be taken but this class of drug is more expensive, and associated with more side-effects and concerns about bone density.

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**
  - **Aceclofenac 100 mg/day**
  - **Aspirin 650 mg 4 hourly**
  - **Dexketoprofen 12.5-25 mg 6 hourly**
  - **Diclofenac upto 200 mg daily in divided doses**
  - **Etodolac 200-300 mg twice daily**
  - **Fenoprofen 100-200 mg 4 hourly**
  - **Fentiazac 100 twice daily**
  - **Ibuprofen 400 mg 3, 4 or 6 times daily**
  - **Indomethacin 25 mg tablets or 100 mg supp 3 times**
  - **Ketoprofen 25-50 mg 6 hourly**
  - **Lysine Clonixinate 125 mg six hourly**
  - **Meclofenamate sodium 100 mg eight hourly**
  - **Mefenamic acid 250 mg eight hourly**
  - **Naproxen/Naproxen sodium 250-275 mg four to eight hourly**
  - **Niflumic acid 250 mg three times daily**
  - **Nimesulide 50-100 mg twice daily**
  - **Piroxicam 20-40 mg daily**
  - **Tolfenamic acid 200 mg eight hourly**
- **COX-2 NSAIDs**
  - **Etoricoxib 120 daily**
  - **Meloxicam 7.5-15 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/Prixicam/ Lysine clonixinate
    - Mefenamic acid vs Meloxicam/Tolfenamic 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

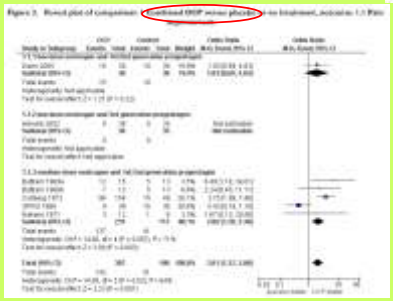
COCs

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

COCs

Wong et al 2009



Pain improvement

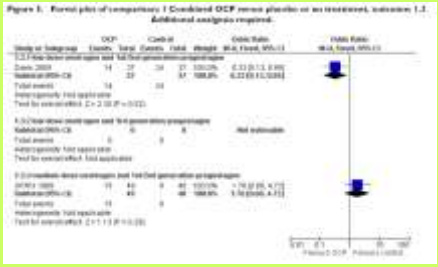
COCs

Wong et al 2009

Pain score

COCs

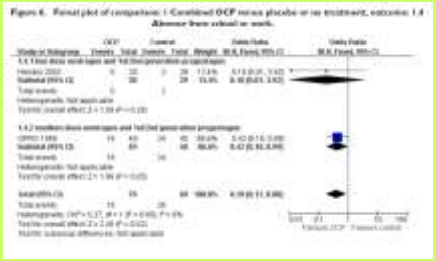
Wong et al 2009



Additional analgesia required

COCs

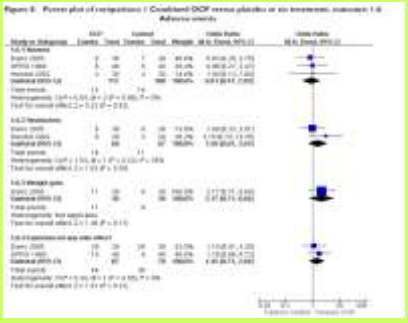
Wong et al 2009



Absence from work or school

COCs

Wong et al 2009



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

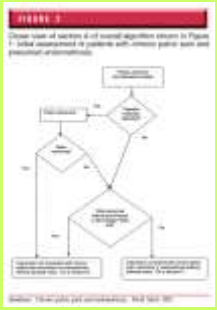

ENDOMETRIOSIS

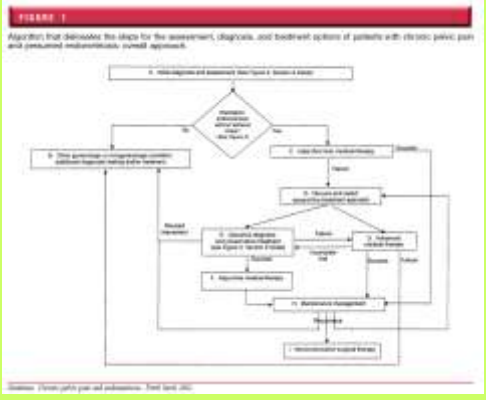
Consensus statement for the management of chronic pelvic pain and endometriosis: proceedings of an expert-panel consensus process

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





Complementary therapy

Proctor & Murphy 2009, Proctor et al 2009, Proctor et al 2010, Zhu et al 2010

- 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-shakiyaku-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