Pain, endometriosis and quality of life

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Conflict of interest:

- Grünenthal GmbH
- Ferring GmbH
- Jena Pharm GmbH
- Bayer GmbH
- Das FORTBILDUNGSKOLLEG GmbH
Impact of the disease on the life of a woman

Mood
- Depression
- Anxiety
- Bladder and bowel dysfunction

Infertility

Organ damage

Pain

Menarche — Menopause

W. Schweppe, 2011
Impact of endometriosis on women’s lives

Table 2: Themes and categories that emerged from the data

<table>
<thead>
<tr>
<th>Themes</th>
<th>Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiences of living with endometriosis</td>
<td>1. Symptoms related to endometriosis</td>
</tr>
<tr>
<td></td>
<td>2. Delayed diagnosis</td>
</tr>
<tr>
<td></td>
<td>3. Treatment of endometriosis</td>
</tr>
<tr>
<td></td>
<td>4. Experience with health care providers</td>
</tr>
<tr>
<td></td>
<td>5. Lack of information</td>
</tr>
<tr>
<td>Impact of endometriosis on women’s lives</td>
<td>1. Physical impact</td>
</tr>
<tr>
<td></td>
<td>2. Psychological impact</td>
</tr>
<tr>
<td></td>
<td>3. Marital/sexual relationship impact</td>
</tr>
<tr>
<td></td>
<td>4. Social life impact</td>
</tr>
<tr>
<td></td>
<td>5. Impact on education</td>
</tr>
<tr>
<td></td>
<td>6. Impact on employment</td>
</tr>
<tr>
<td></td>
<td>7. Financial impact</td>
</tr>
<tr>
<td></td>
<td>8. Impact on life opportunities</td>
</tr>
<tr>
<td></td>
<td>9. Impact on lifestyle</td>
</tr>
</tbody>
</table>

Moradi et al., 2014
# Impact of endometriosis

## Table 3: Most highlighted impact of endometriosis for the different age groups

<table>
<thead>
<tr>
<th>Age group</th>
<th>Group1 (16–24 years)</th>
<th>Group2 (25–34 years)</th>
<th>Group3 (35 and above years)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Similarities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Differences</strong></td>
<td>Education</td>
<td>Life opportunities</td>
<td>Financial impact</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table II. Medians, 25th and 75th percentiles of the scores in the health-related quality of life 36-item short form (SF-36) questionnaire in healthy women (control) and those with endometriosis.

<table>
<thead>
<tr>
<th>SF-36 domains</th>
<th>Control (n = 82)</th>
<th>Endometriosis (n = 93)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>90</td>
<td>70*</td>
</tr>
<tr>
<td></td>
<td>85–91</td>
<td>55–84</td>
</tr>
<tr>
<td>Role-physical</td>
<td>100</td>
<td>50*</td>
</tr>
<tr>
<td></td>
<td>67–82</td>
<td>25–100</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>74</td>
<td>41*</td>
</tr>
<tr>
<td></td>
<td>67–77</td>
<td>26–62</td>
</tr>
<tr>
<td>General health</td>
<td>82</td>
<td>52*</td>
</tr>
<tr>
<td></td>
<td>75–82</td>
<td>32–72</td>
</tr>
<tr>
<td>Vitality</td>
<td>60</td>
<td>35*</td>
</tr>
<tr>
<td></td>
<td>55–63</td>
<td>25–52</td>
</tr>
<tr>
<td>Social functioning</td>
<td>75</td>
<td>50*</td>
</tr>
<tr>
<td></td>
<td>71–80</td>
<td>25–75</td>
</tr>
<tr>
<td>Role-emotional</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td></td>
<td>58–75</td>
<td>33–100</td>
</tr>
<tr>
<td>Mental health</td>
<td>72</td>
<td>40*</td>
</tr>
<tr>
<td></td>
<td>65–72</td>
<td>24–60</td>
</tr>
</tbody>
</table>

\( n \) is the number of subjects; *statistically significant difference versus control group (\( p < 0.0001 \); Mann–Whitney test).
Therapeutic options

- Surgery
- Infertility
- Hormonal and analgesic treatment
- Pain
How successful are the current treatments?

- No pain reduction
- Pain symptoms remaining at end of treatment
- Recurrence of pain symptoms after treatment cessation

Becker et al., 2017 F&S
Pain reduction

Becker et al., 2017 F&S
Patient satisfaction

Without/mild complaints after surgical and/or hormonal treatment

Side effects
Becoming pregnant

Complaints after surgical and/or hormonal treatment

Reduced QoL

ENDO BAY
gestrandet in der Endometriose...
Pain profile of patients with „treated“ endometriosis

89% of patients with treated endometriosis (surgery and with/without hormonal treatment) suffer from pain

<table>
<thead>
<tr>
<th>pain</th>
<th>all</th>
<th>with HT</th>
<th>without HT</th>
<th>significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>no pain</td>
<td>23</td>
<td>13 (56,5%)</td>
<td>10 (43,5%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>pain</td>
<td>216</td>
<td>108 (50%)</td>
<td>108 (50%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>cyclic pain*</td>
<td>154</td>
<td>64 (41,6%)</td>
<td>90 (58,4%)</td>
<td>p≤0,001</td>
</tr>
<tr>
<td>Acyclic pain *</td>
<td>119</td>
<td>66 (55,5%)</td>
<td>53 (44,5%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>other pain*</td>
<td>85</td>
<td>44 (51,8%)</td>
<td>41 (48,2%)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

* More than one answer possible

Brandes et al., JEPPUD 2017
Nociceptive pain

- 4 basic steps: Transduction, transmission, modulation and perception
  - **Transduction**: the conversion of the noxious stimulus into a biochemical neural signal
  - **Transmission**: conduction of the neural impulse to the central nervous system
  - **Modulation** within the central nervous system, which may either increase or decrease the intensity of the neural signal
  - Ascent to the cerebral cortex leads to **perception** of the neural signal as pain

- The nerves that function as nociceptors are primarily C and A delta fibers
- Nociceptive pain could be somatic or visceral

Stratton and Berkley, Hum Rep Upd 2010
Pathogenesis of EM-associated pain

- **Visceral pain**
  - viscus
  - hard to locate
  - dull, cramping, emission over several dermatomes
  - vegetative reaction such as vomiting/emesis
  - complex interaction between the organs, hard to differentiate

- **Somatic pain**
  - pelvic wall, muscle
  - easily located
  - sharp and pointy
Endometriotic lesions – an important factor in pain generation

- Proliferative disease with development of endometrium-like tissue
- Release of
  - Pain mediators
  - Inflammatory mediators
  - Growth factors
- Inflammation
  - Chemotaxis of immune cells (MC, MØ, DC)
  - Neurogenesis
  - Neuroimmunomodulation
  - Angiogenesis
  - Lymphangiogenesis
  - Smooth muscle metaplasia
  - Fibrosis
Neurogenic inflammation

NGF  NT-3  II1ß  PG  Ostrgen
SP  CGRP
Semas
Noradrenalin
NGF  NT-3  II1ß  PG  Ostrgen
SP  CGRP
Semas
MO

Scheerer, submitted
Chronic pelvic pain (CPP)
Pathway of central sensitisation (CS)

- Unexplained CPP
  - Central Generators
    - ↑ Facilitation
    - ↓ Inhibition
    - 1) ↑ Synaptic Excitation
    - 2) Wind Up
    - 3) Expanded Receptive fields
    - 4) Cross Talk
  - Peripheral Generators
    - Somatic Nociceptive Pain
    - Visceral Nociceptive Pain
- Central Sensitization
  - Somatic Hyperalgesia
  - Visceral Hyperalgesia

Review by D. Hoffman, 2015
Pathway of central sensitisation

A Periphery
- Uterus afferents
- Bowel afferents
- Bladder afferents

B CNS
- Dorsal Horn of spinal cord
- Sensory neurons/ nociceptors in peripheral tissues
- Neuropeptides: Substance P, Glutamate, GCRP
- Myofascial afferents (pelvic floor, abdominal wall)

C Periphery
- Visceral Hyperalgesia: Central cause of Visceral pain
- Somatic Hyperalgesia: Central cause of Somatic pain
- Peripheral Pain Generators:
  - Vulva/Vestibule
  - Muscles
  - Joints
  - Connective Tissue/Fascia

Peripheral Pain Generators
Brain
Central Sensitization

(PUS)
Altered brain morphology and chemistry

As-Sanie et al., 2012 and 2016;
Revers central hyperalgesia after surgical excision

We et al., Rep Sci, 2010
Chronic acyclical CPP with cyclical enhancement

1. Peripheral sensitisation
2.-5. Central sensitisation

• Mechanisms:
  – Neurogenic inflammation (Mechsner et al., 2016)
  – Spinal hyperalgesia (Möller et al., 2014)
  – Pelvic floor tenderness (Young et al, 2014, Raimodo et al., 2016)
  – Neuropathic pain due to affection of peripheral nerves (SIQUARA DE SOUSA et al., 2015)
Changes of the pelvic floor function in women with CPP

- **Tonus**
  - Palpation (Reissing 2005; Gentilcore-Saulnier 2010; Bo 2015; Loving 2014)
  - Dynamometer (Morin 2010; Davidsson 2014)
  - Ultrasound (Morin 2014)
  - Pressure Perimetrie (Naess 2015)

- **Power**
  - Palpation (Reissing 2005; Gentilcore-Saulnier 2010; Loving 2014; Bo 2015)
  - EMG (Reissing 2004; Glazer 1998)
  - Ultrasound (Morin 2014)
  - Dynamometer (Morin 2014)

- **Endurance**
  - EMG (Engman 2004; Reissing 2004; Glazer 1998; Bo 2015)
  - Dynamometer (Morin 2010)

- **Coordination/Contraction speed**
  - Dynamometer (Morin 2010)

- **Relaxation**
  - Palpation (Reissing 2005; Loving 2014; Chiarelli 2012)
  - EMG (Reissing 2005; Chiarelli 2012)
  - Ultrasound (Morin 2014; Chiarelli 2012)
  - Dynamometer (Morin 2010)
Multimodal treatment strategy for endometriosis

- Surgery
- Hormonal and analgesic treatment

- Infertility
- Pain

- CAM
- Multimodal pain treatment

modif. nach J. Bartley
Manual therapies and muscle relaxing exercises

- Pelvic floor relaxation exercises
- Yoga
- TENS/Biofeedback
- Osteopathy
- Acupuncture
Peripheral mechanisms
Release of pain mediators
Neurogenic inflammation
Activation of silent nociceptors
Infiltration/destruction/compression
Neuropathic pain

Central sensitisation
Hyperalgesia
Pelvic organ cross sensitisation
Changes in brain morphology

Psychological factors
Anxiety about pain (Ploghaus, 2001)
Depression (primary or reactive)
stress
Social isolation

Endocrine factors
Hypothalamic-pituitary-adrenal-axis (HPA-Axis)
low cortisol levels
Estrogen-influence
cyclical low $E_2$-levels with increased threshold
$E_2$ modulates nociceptors
$E_2$ stimulates pain by growth of the lesion

Myofascial pain
Pelvic floor tenderness
Conclusion – What should we do?

- Consequent surgical therapy
- Consequent postoperative hormonal treatment
- Consequent analgesic therapy
- Early information about chronic disease and its possible progression
- Professional pain management including pain coping strategies
- Avoidance of secondary “pain intensifying“ changes of the pelvic floor (tension) or malposition through relieving posture
- Early use of pelvic floor exercises and osteopathy with a manual resolve of muscle blockades
- When chronic pain syndrome is already apparent, it is hard to break the cycle
Thank you

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