월경전 불쾌증후군의 새로운 가이드라인

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송 재 연

Guidelines

1. Management of Premenstrual syndrome
   - Royal College of Obstetrics & Gynecologists (RCOG)
   - BJOG. 2017 Feb;124(3):e73-e105.

2. Management of premenstrual syndrome.
   - The National Association for Premenstrual syndrome (NAPS)
   - J Fam Plann Reprod Health Care 2009;35:187-94

3. ISPMD consensus on the management of premenstrual disorders.
   - International Society for Premenstrual Disorders (ISPMD)
   - Arch Womens Ment Health. 2013 Aug;16(4):279-91.

4. Premenstrual syndrome
   - American Congress of Obstetricians and Gynecologists (ACOG)
   - ACOG Practice Bulletin No 15 : Obstet Gynecol. 2000 Apr;95(4):suppl 1-9
   - ACOG Q&A, 2015

5. Premenstrual syndrome (임상지침)
   - 대한산부인과내분비학회, 2016

Introduction and background epidemiology

(1) Definition

psychological symptoms

: depression, anxiety, irritability, confusion, crying spell, loss of confidence, mood swings, less alertness, poor concetration, changes in sexual desire, insomnia, increasing nap taking, withdraw from family and friends.

physical symptoms

: bloating, weight gain, swelling, mastalgia, food craving, lack of energy, aches and pains (headache, cramp, low back pain), fatigue, GI Sx, skin problem

symptoms cause significant impairment to the individual during the luteal phase of the menstrual cycle

ACOG (2000) : 전향적으로는 2번 이상, 신체적 증상, 정서 증상이 적어도 각각 1개씩

ICD-10 : 신체증상, 정서증상 구분 없이 적어도 한 가지 증상이 있을 때

(2-1) PMS Classification (ISPMD consensus)

Core premenstrual disorders (PMDs)

: severe enough to **affect daily functioning**
or interfere with work, school performance or interpersonal relationships,
symptoms of core PMDs are **nonspecific**,
recur in ovulatory cycles during the **luteal phase**
→ **abate as menstruation begins**
→ which is then followed by **a symptom-free week**.

Variant' PMDs

Premenstrual exacerbation of an underlying disorder (diabetes, depression, anxiety, epilepsy, asthma, migraine, IBS, chronic fatigue syndrome, allergy)

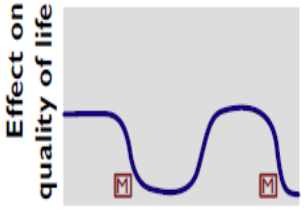
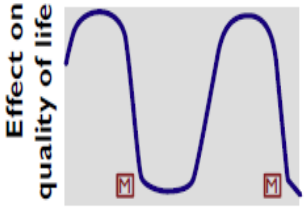
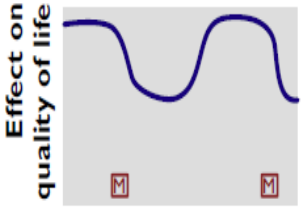
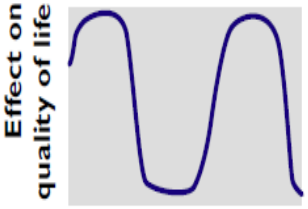
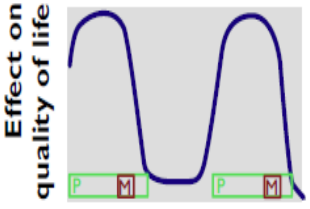
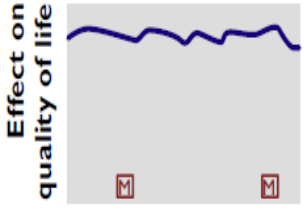
Non-ovulatory PMDs : presence of ovarian activity without ovulation.
follicular activity of the ovary can instigate symptoms.

Progestogen-induced PMDs : by exogenous progestogens in HRT, COCs
who may be particularly sensitive to progestogens.
not progestogen-only contraceptives - noncyclical

PMDs with absent menstruation: hysterectomy, endometrial ablation, LNG-IUS
+ functioning ovarian cycle

Patient presenting with premenstrual symptoms

Patient records menstrual symptoms and effect on daily life for two consecutive menstrual cycles

Symptoms cyclical and relieved by menstruation Symptom-free week No influence on quality of life Menstruation M No additonal factors	Symptoms cyclical and relieved by menstruation Symptom-free week Affects quality of life Menstruation M No additonal factors	Symptoms cyclical and relieved by menstruation No symptom-free week Affects quality of life Menstruation M Existing non-menstrual condition	Symptoms cyclical Symptom-free week Affects quality of life No menstruation No additional factors	Symptoms cyclical and relieved by menstruation Symptom-free week Affects quality of life Menstruation M Progestogen treatment P	Non-cyclical symptoms No symptom-free week Constant influence on quality of life Menstruation M No additional factors
					
Physiological (mild) premenstrual disorder	Core premenstrual disorder (premenstrual syndrome or premenstrual dysphoric disorder)	Premenstrual exacerbation	Premenstrual disorder with absent menstruation	Progestogen induced premenstrual disorder	Underlying psychological disorder, not premenstrual disorder
Counselling and reassurance required, no need for treatment	Consider all alternative approaches to treatment	Treatment should aim to treat underlying medical, physical. or psychiatric condition or suppress ovulation (or both)	Treat as core premenstrual disorder	Alternative progesterone treatment	Psychiatric referral

(2-2) PMDD (premenstrual dysphoric disorder)
by DSM – V (The Diagnostic and Statistical Manual of Mental Disorders)

진단 ⇒ 생리 전 주에 시작되어 생리 시작 며칠 내에 증상 소멸 (황체기)
직업, 학업, 일상생활, 사회관계 수행을 악화 (impair).
다른 질환 배제 (정신질환, 약물, 신체질환)
OCS 복용 안 할 때 진단
prospective daily ratings 통해 2 주기 이상 지속.
핵심증상 4개 (1~4) 중 1개 이상 포함하여 총 5개 이상.

1. 정서 불안정 (affective lability)
2. 성급함 (irritability), 분노(anger)
3. 우울증, 무희망 (depressed mood or hopeless)
4. 불안, 긴장감 (anxiety or tension)
5. 일생생활에 대한 흥미 부족 (decreased interest of usual activities)
6. 집중장애 (concentration difficulties)
7. 무기력 (marked lack of energy)
8. 식욕 이상 (overeating, food craving)
9. 수면 장애 (hypersomnia, insomnia)
10. 압도감 (feeling overwhelmed)
11. 다른 신체 증상

(3) Prevalence and Etiology

Prevalence

40% : PMS
24% : PMS by 6wk prospective symptom diary
5-8% : severe PMS, PMDD

Etiology

uncertain
ovarian hormone cycle 관련 - 사춘기 전, 임신 중, 폐경 후에는 증상 (-)

(1) some women are 'sensitive' to progesterone and progestogens
: serum estrogen or progesterone are the same
in those with or without PMS.

(2) neurotransmitters - serotonin, c-aminobutyric acid (GABA)
: serotonin receptors are responsive to E & P,
selective serotonin reuptake inhibitors (SSRIs) reduce PMS,
GABA levels are modulated by the metabolite of
progesterone, allopregnanolone,
in women with PMS the allopregnanolone levels appear
to be reduced

(4) Diagnosis

- When clinically reviewing women for PMS,
  symptoms should be recorded prospectively,
  over two cycles using a symptom diary,
  as retrospective recall of symptoms is unreliable.

  Daily Record of Severity of Problems (DRSP), - m/c, simple
  Premenstrual Symptoms Screening Tool (PSST),
  Symptom diary on NAPS website (www.pms.org.uk)

- A symptom diary should be completed by the patient
  prior to commencing treatment.

- Gonadotrophin-releasing hormone (GnRH) analogues may be used
  for 3 months for a definitive diagnosis
  if the completed symptom diary alone is inconclusive.

  a month for the agonist to generate a complete hormonal suppressive effect,
  2 months' worth of symptom diaries.

DAILY RECORD OF SEVERITY OF PROBLEMS

Please print and use as many sheets as you need for at least two FULL months of ratings.

Name or Initials _____

Month/Year _____

Each evening note the degree to which you experienced each of the problems listed below. Put an "x" in the box which corresponds to the severity: 1 - not at all, 2 - minimal, 3 - mild, 4 - moderate, 5 - severe, 6 - extreme.

Enter day (Monday-"M", Thursday-"R", etc) >																														
Note spotting by entering "S" >																														
Note menses by entering "M" >																														
Begin rating on correct calendar day >	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
1 Felt depressed, sad, "down" or "blue", or felt hopeless; or felt worthless or guilty	6 5 4 3 2 1																														
2 Felt anxious, tense, "keyed up" or "on edge"	6 5 4 3 2 1																														
3 Had mood swings (i.e. suddenly feeling sad or tearful) or was sensitive to rejection or feelings were easily hurt	6 5 4 3 2 1																														
4 Felt angry or irritable	6 5 4 3 2 1																														
5 Had less interest in usual activities (work, school, friends, hobbies)	6 5 4 3 2 1																														
6 Had difficulty concentrating	6 5 4 3 2 1																														
7 Felt lethargic, tired or fatigued; or had lack of energy	6 5 4 3 2 1																														
8 Had increased appetite or overate; or had cravings for specific foods	6 5 4 3 2 1																														
9 Slept more, took naps, found it hard to get up when intended; or had trouble getting to sleep or staying asleep	6 5 4 3 2 1																														
10 Felt overwhelmed or unable to cope; or felt out of control	6 5 4 3 2 1																														
11 Had breast tenderness, breast swelling, bloated sensation, weight gain, headache, joint or muscle pain, or other physical symptoms	6 5 4 3 2 1																														
At work, school, home or in daily routine, at least one of the problems noted above caused reduction of productivity or inefficiency	6 5 4 3 2 1																														
At least one of the problems noted above caused avoidance of or less participation in hobbies or social activities	6 5 4 3 2 1																														
At least one of the problems noted above interfered with relationships with others	6 5 4 3 2 1																														

The premenstrual symptoms screening tool (PSST)

(please mark an "X" in the appropriate box)

Do you experience some or any of the following premenstrual symptoms which *start before* your period and *stop* within a few days of bleeding?

Symptom	Not at all	Mild	Moderate	Severe
1. Anger/irritability				
2. Anxiety/tension				
3. Tearful/Increased sensitivity to rejection				
4. Depressed mood/hopelessness				
5. Decreased interest in work activities				
6. Decreased interest in home activities				
7. Decreased interest in social activities				
8. Difficulty concentrating				
9. Fatigue/lack of energy				
10. Overeating/food cravings				
11. Insomnia				
12. Hypersomnia (needing more sleep)				
13. Feeling overwhelmed or out of control				
14. Physical symptoms: breast tenderness, headaches, joint/muscle pain, bloating, weight gain				

Have your symptoms, as listed above, interfered with:

	Not at all	Mild	Moderate	Severe
A. Your work efficiency or productivity				
B. Your relationships with coworkers				
C. Your relationships with your family				
D. Your social life activities				
E. Your home responsibilities				

Scoring

The following criteria must be present for a diagnosis of **PMDD**

1) at least one of #1, #2, #3, #4 is **severe**
2) in addition at least four of #1 – #14 are **moderate to severe**
3) at least one of A, B, C, D, E is **severe**

The following criteria must be present for a diagnosis of **moderate to severe PMS**

1) at least one of #1, #2, #3, #4 is **moderate to severe**
2) in addition at least four of #1 – #14 are **moderate to severe**
3) at least one of A, B, C, D, E is **moderate to severe**

NAPS MENSTRUAL DIARY

	JAN	FEB	MAR	APR	MAY	JUN	JULY	AUG	SEPT	OCT	NOV	DEC
1												
2												
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Keeping a chart

A chart will accurately reflect your symptoms and will show the days on which they occur, the days they are absent, the days of menstruation and the duration of the cycle. A symbol can be chosen for your two or three worst symptoms and used to record them on the chart. For instance

- H = Headache B = Bloating I = Irritability

The chart should be completed for at least three months and then can be used during consultations with your GP to reflect the symptoms you have experienced.

- Record the days of menstruation with a P for period or M for menstruation

Below are a suggested list of Psychological, Behavioural and Physical Symptoms you may experience.

Mood swings and depression
Tearfulness or feeling 'low
Tiredness, fatigue or lethargy
Tension or unease
Irritability
Clumsiness/poor co-ordination
Difficulty in concentrating
Altered interest in sex
Sleep disorders
Food cravings
Aggression

Breast tenderness
Swollen/bloated feelings
Puffiness of face, abdomen or fingers
Weight gain
Headaches
Appetite changes
Acne or other skin rashes
Constipation or diarrhoea
Muscle or joint stiffness
General aches and pains – backache
Abdominal pain/cramps

(4-2) Risk factor

- FHx, Obesity (*3), Smoking (*2), Stress, Trauma …

(4-3) Differential Diagnosis (ACOG)

- Depression, Anxiety, Panic disorder
- Peimenopause
- Endometriosis, fibroids etc.
- Chronic fatigue syndrome
- IBS
- Thyroid disease

(4-4) Test to DDx

- BP, pulse rate
- Breast & Thyroid exam
- Pelvic exam
- CBC, TFT, FSH

(5) Multidisplinary approach

- Referral to a gynecologist should be considered
  when simple measures (COCs, VB6, SSRIs) have been explored, failed
  when the severity of the PMS justifies gynecological intervention.

- Women with severe PMS may benefit from being managed
  by a multidisciplinary team
  comprising a general practitioner,
  a gynecologist – general or special interest in PMS,
  a mental health professional
  (psychiatrist, clinical psychologist or counsellor)
  a dietician.

(6) Managements - CAM

- Women with PMS should be informed that there is conflicting evidence to support the use of some complementary medicines.

- An integrated holistic approach should be used when treating women with PMS.

  particularly important for women in whom hormonal therapy is contraindicated.
  In PMS Tx, there is a 36–43% placebo response.

- Interactions with conventional medicines should be considered.

Complementary therapy	Benefit	Types of studies	Numbers in the study	Note
Exercise[22–25]	Some benefit	Nonrandomised and randomised	72 (4 published studies)	High quality studies recommended.
Reflexology[26]	Some benefit	Randomised	35	
Vitamin B6[27–39]	Mixed results	Double-blind Randomised Cross-over	1067 (13 published studies)	Peripheral neuropathy v high doses (most studies performed using higher doses). Department of Health restricts the daily dose to 10 mg.
Magnesium[37,40,41]	Mixed results	Double-blind Randomised Cross-over	153 (3 published studies)	Used in premenstrual phase.
Multivitamins[42–45]	Unknown	–	400 (several published studies)	Unclear which are the active ingredients.
Calcium/ vitamin D[46,47]	Yes	Double-blind Randomised Cross-over	499 (2 published studies)	
Isoflavones[48,49]	Mixed results	Double-blind Randomised Cross-over	72 (2 published studies)	May benefit menstrual migraine.
Vitex agnus castus L.[19,39,50–54]	Yes	Double-blind Randomised	923 (7 published studies)	There is no standardised
St John's Wort[20,21,55,56]	Mixed results	Double-blind Placebo-controlled	402 (4 published studies)	May benefit physical and behavioural symptoms. Many withdrew from one study due to adverse effects. Significant interactions with conventional medicines. The British National Formulary advises avoid concomitant use with SSRIs.
Ginkgo biloba[57,58]	Some benefit	Double-blind Placebo-controlled	233 (2 published studies)	
Saffron[59]	Yes	Double-blind Placebo-controlled	47	Further data before recommendation.
Evening primrose oil[15,60–63]	Some benefit	Double-blind Placebo-controlled Cross-over	215 (4 published studies)	May benefit women with cyclical breast symptoms.

Interactions

breast symptom

Mood change, fluid retentdion

= chaste berry (Prefemin®)

E, OCS, antipsychotics

Breast pain, swelling, food craving, cramping

depression

OCS, SSRI

breast symptom, mood, bloating, weight

Bleeding with Warfarin

Complementary therapy	Benefit	Types of studies	Numbers in the study	Note
Acupuncture[64–73]	Some benefit	Case–control	235 (10 published studies)	High risk of bias. Further data before recommendation.
Lemon balm[74]	Some benefit	Double-blind Placebo-controlled	100 (1 published study)	PMS severity quantified by PSST. Further data before recommendation.
Curcumin[75]	Some benefit	Double-blind Placebo-controlled	70 (1 published study)	PMS severity quantified by an unvalidated symptom score. Further data before recommendation.
Wheat germ[76]	Some benefit	Triple-blind Placebo-controlled	84 (1 published study)	PMS severity quantified by an unvalidated symptom score. Further data before recommendation.

- Avoid : refined sugar, saturated fat, caffeine, salt, chocolate, alcohol, smoking, stress
- More : exercise
- NSAIDs for pain
- Diuretics for fluid retention and bloating
- Firm supportive bra, support stockings

(6) Managements – CBT (cognitive behavioral therapy)

- When treating women with severe PMS,
  CBT should be considered routinely as a treatment option.

RCT : fluoxetine, CBT, combination for 6M
- benefit was similar
- fluoxetine showed quicker improvements
  CBT showed better maintenance of treatment effects

meta-analysis of CBT : significant reduction in depression, anxiety, behavioral problems

(6) Management – Hormones (DRSP OCS)

- When treating women with PMS,
  drospirenone-containing COCs may represent effective Tx for PMS
  and should be considered as a first-line pharmaceutical intervention.

Progestogens in second-generation pills (levonorgestrel or norethisterone)
regenerating PMS-type symptoms.

(Cochrane CD006586) 5 trials, 1920 women
drospirenone 3 mg plus ethinyl estradiol 20 μg for 3M
: less severe premenstrual symptoms (MD −7.92; 95% CI −11.16 to −4.67).
greater mean decreases in impairment of productivity (MD −0.31; 95% CI −0.55 to −0.08),
social activities (MD −0.29; 95% CI −0.54 to −0.04),
relationships (MD −0.30; 95% CI −0.54 to −0.06).
side effects is more common – nausea, intermenstrual bleeding, breast pain.

Licensed in Europe and the USA for PMDD but only in women requiring oral contraception.

(6) Management - Hormones

- When treating women with PMS, emerging data suggest use of the contraceptive pill continuously rather than cyclically.

Phase I study
better Sx improvement : 6M extended regimen > standard 21/7-day regimen

Phase II
better mood, headache, pelvic pain scores : continuous 13M > standard 21/7-day regimen

Phase II
high satisfaction : 24/4-day regimen > standard 21/7-day regimen

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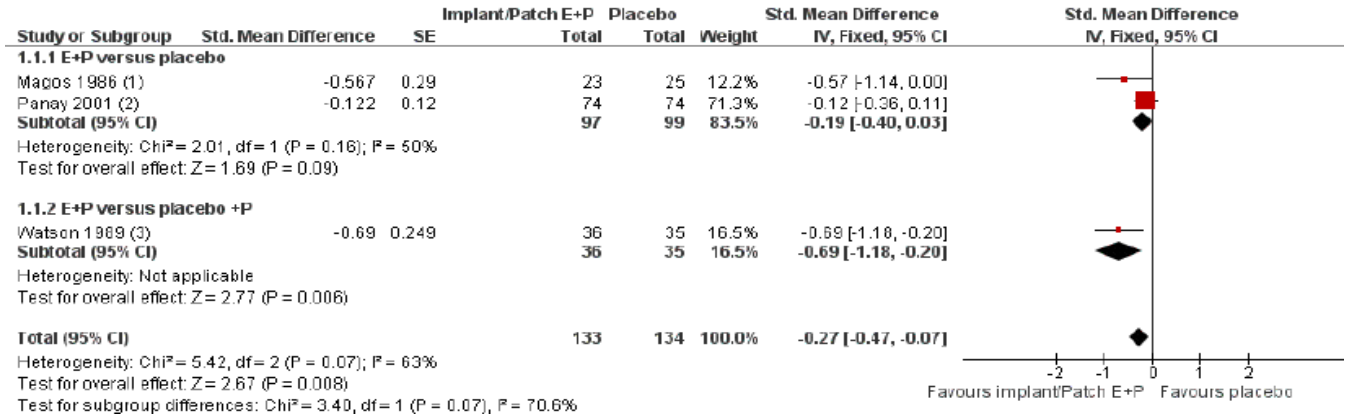
(6) Management – Hormones (Td E + P)

– Percutaneous estradiol combined with cyclical progestogens
has been shown to be effective for the management
of physical and psychological symptoms of severe PMS.

(Cochrane CD010503)
Luteal-phase oral unopposed oestrogen is probably ineffective and possibly detrimental for controlling the symptoms of PMS.

100mg estradiol implant or 200 micrograms transdermal estradiol patches + P : effective



– When treating women with PMS,
alternative barrier or intrauterine methods of contraception
should be used when estradiol is used to suppress ovulation.

(6) Management – Hormones (avoid PMS induced by P)

- When using transdermal estrogen to treat women with PMS,
  the lowest possible dose of progesterone or progestogen
  is recommended to minimise progestogenic adverse effects.

  Use of continuous estradiol necessitates the addition of cyclical progesterone or progestogens (10–12 days/cycle) to avoid endometrial hyperplasia in women who have a uterus.

- Women should be informed that low levels of levonorgestrel released
  by the LNG-IUS 52 mg can initially produce PMS-type adverse effects
  (as well as bleeding problems).

- Micronized progesterone is
  theoretically less likely to reintroduce PMS-like symptoms and
  should therefore be considered as first line for progestogenic
  opposition rather than progestogens.

  Micronized oral progesterone (100 or 200 mg)
  : fewer androgenic and unwanted adverse effects (than NETA, LNG)

  Vaginal administration : better tolerated by avoiding first-pass hepatic metabolism.
  avoiding allopregnanolone formation.

(6) Management – Hormones (effect on EM, breast)

- When treating women with percutaneous estradiol,
  a cyclical 10–12 day course of oral or vaginal progesterone
  or long-term progestogen with the LNG-IUS 52 mg
  should be used for the prevention of endometrial hyperplasia.

- When using a short duration of progestogen therapy,
  or in cases where only low doses are tolerated,
  there should be a low threshold for investigating unscheduled bleeding

  Oral dose (micronised progesterone 100 mg or norethisterone 2.5 mg)
  for days 17–28 of each calendar month should be sufficient.

- When treating women with PMS using estradiol,
  women should be informed that there are insufficient data
  to advise on the long-term effects on breast and endometrial tissue.

- Due to the uncertainty of the long-term effects of opposed estradiol Tx,
  treatment of women with PMS should be on an individual basis,
  taking into account the risks and benefits.

  Discontinuation of treatment could allow a return of premenstrual symptoms.

(6) Management - Danazol

- Women with PMS should be advised that,
  although treatment with low dose danazol (200 mg twice daily)
  is effective in the luteal phase for breast symptoms,
  it also has potential irreversible virilising effects.

  Danazol does have A/Es (acne, weight gain, hirsutism, deepening of the voice),
  which may interfere with the usual symptom-free late follicular phase of women with PMS.
  ➔ limit danazol treatment to the luteal phase only.

- Women treated with danazol for PMS
  should be advised to use contraception during treatment
  due to its potential virilising effects on female fetuses.

  Danazol during pregnancy : cliteromegaly, labial fusion, urogenital sinus abnormalities
  in female fetuses.

(6) Management - GnRHa

- GnRH analogues are highly effective in treating severe PMS.
  When treating women with PMS, GnRH analogues should usually be reserved for women with the most severe symptoms and not recommended routinely unless they are being used to aid diagnosis or treat particularly severe cases.

  Meta-analysis of seven trials (71 women)
  : overall standardised mean difference (SMD) : 1.19 (95% CI 1.88 to 0.51).
  OR for benefit : 8.66 (95% CI 2.52-30.26).

- When the diagnosis of PMS is unclear from 2 months' prospective DRSP charting, GnRH analogues can be used to establish and/or support a Dx of PMS.

  If GnRH analogue therapy does not result in elimination of premenstrual symptoms, a lack of efficacy suggests a questionable diagnosis rather than a limitation of the therapy.

(6) Management – GnRHa (add-back)

- When treating women with severe PMS using GnRH analogues for more than 6 months, add-back hormone therapy should be used.

- When add-back hormone therapy is required, continuous combined HRT or tibolone is recommended.

- Women should be provided with general advice regarding the effects of exercise, diet and smoking on BMD.

- Women on long-term treatment should have measurement of BMD (DEXA) every year. Treatment should be stopped if bone density declines significantly.

The overall SMD favoured neither GnRH alone nor GnRH with add-back (SMD 0.12, 95% CI 0.34 to 0.59), demonstrating there is no reversal of the beneficial effect of GnRH when using add-back.

(6) Management – Progestogen

- There is good evidence to suggest that
  treating PMS with progesterone or progestogens is not appropriate.

- There is no evidence to support
  the use of the LNG-IUS 52 mg alone to treat PMS symptoms.
  Its role should be confined to opposing the action of estrogen therapy on the endometrium.

  (Cochrane CD003415) 17 studies – 280 participants.
  The trials did not show that progesterone is an effective treatment for PMS nor that it is not.

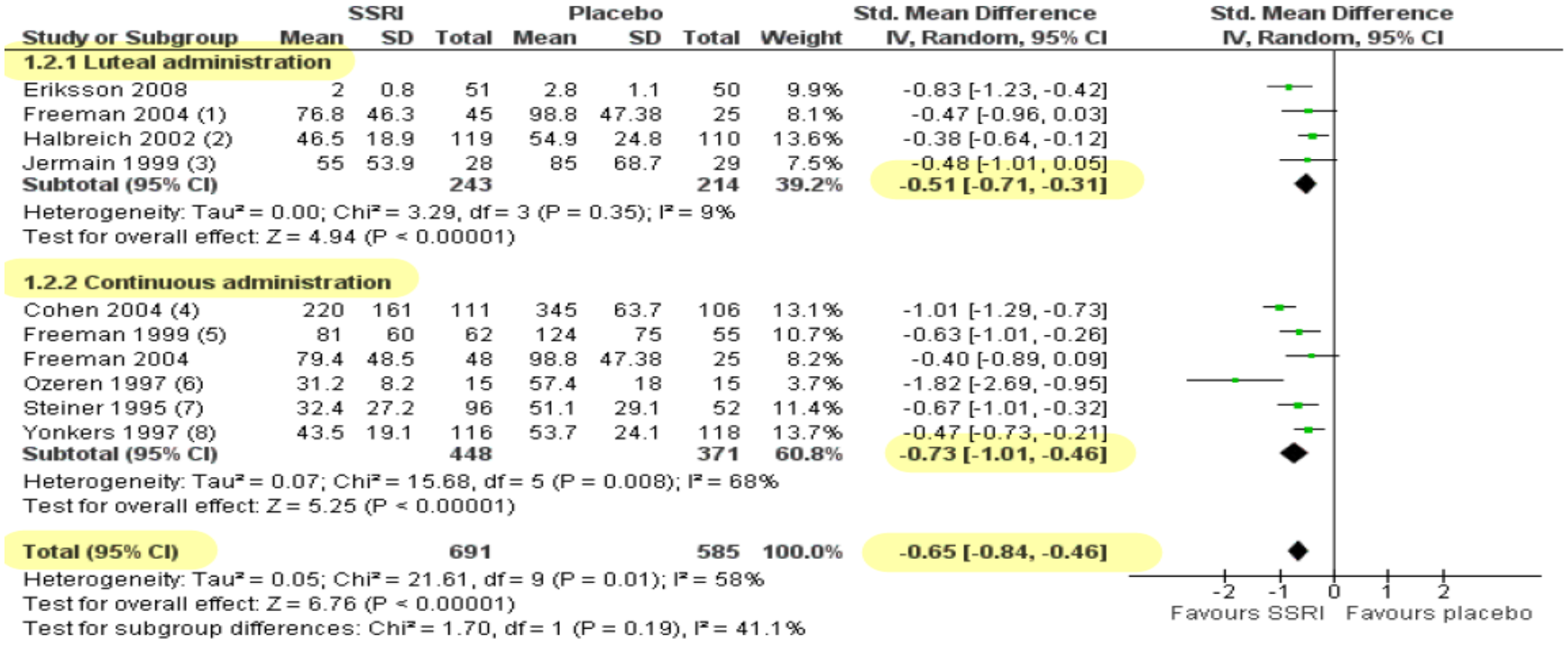
(6) Management – SSRI

- SSRIs should be considered
  one of the first-line pharmaceutical management options
  in severe PMS.

  Currently, most SSRIs are licensed in the USA for PMDD, but not in the UK.

- When treating women with PMS,
  either luteal or continuous dosing with SSRIs can be recommended.

  (Cochrane CD001396) 31 studies.



(6) Management – SSRI (A/E)

- SSRIs should be discontinued gradually to avoid withdrawal symptoms, if given on a continuous basis.

  Most common features of abrupt withdrawal of an SSRI or marked reduction of the dose
  : GI disturbances, headache, anxiety, dizziness, paraesthesia, sleep disturbances, fatigue, influenza-like symptoms, sweating

  The dose should be tapered over a few weeks to avoid these effects.

- Women with PMS treated with SSRIs should be warned of the possible adverse effects such as nausea, insomnia, somnolence, fatigue and reduction in libido.

  (Cochrane CD001396)
  Most common A/E : nausea, asthenia, somnolence, fatigue, decreased libido, sweating.

  Discontinue treatment due to adverse effects - OR 2.55 (95% CI 1.84-3.53).

  All of these adverse effects are dose- dependent.

Table 1. Classification of SSRI doses used by included studies

SSRI	Low dose	Moderate dose	High dose
Fluoxetine*	10 mg daily	20 mg daily	60 mg daily
Sertraline*	25-50 mg daily	100 -105 mg daily	
Paroxetine*	10-12.5 daily	20-30 daily	
Citalopram**		20-50 daily	
Escitalopram**	10 mg daily	20 mg daily	

* Based on suggested doses for PMDD (Micromedex 2013)

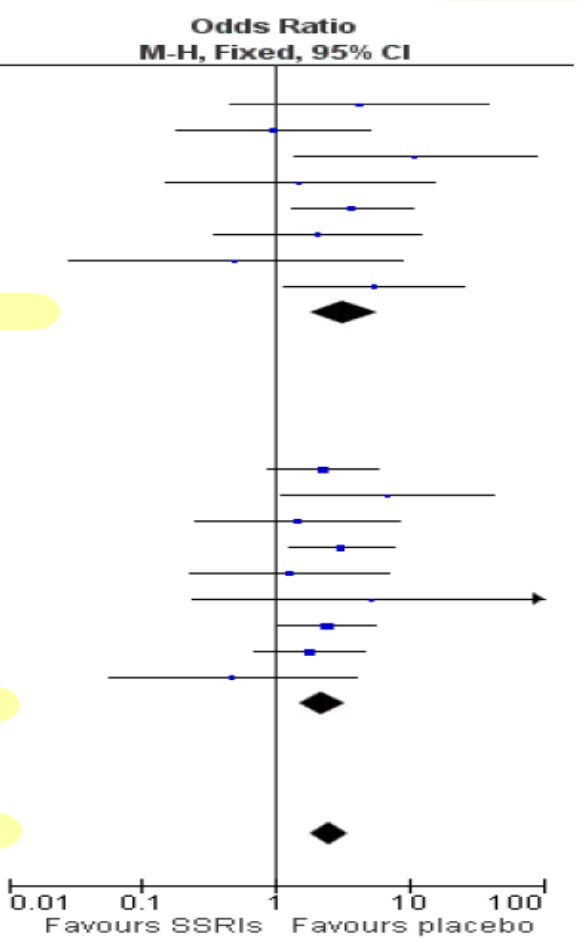
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Placebo	SSRIs				
Low dose SSRI versus placebo Luteal or continuous administration	53 per 1000	91 per 1000 (60 to 135)	OR 1.76 (1.13 to 2.75)	1301 (7 studies)	⊕⊕⊕○ moderate[1]	Withdrawal due to adverse effects was significantly more common in the SSRI groups
Mod dose SSRI versus placebo Luteal or continuous administration	45 per 1000	107 per 1000 (79 to 142)	OR 2.55 (1.84 to 3.53)	2447 (15 studies)	⊕⊕⊕○ moderate[2]	
High dose SSRIs versus placebo Continuous administration	72 per 1000	457 per 1000 (207 to 1000)	RR 6.35 (2.88 to 14)	231 (1 study)	⊕⊕⊕○ moderate[3]	

(6) Management – SSRI (A/E)

- When using SSRIs to treat PMS,
  efficacy may be improved and adverse effects minimised
  by the use of luteal-phase regimens with the newer agents.

(Cochrane CD001396) 31 studies.

Study or Subgroup	SSRIs Events	SSRIs Total	Placebo Events	Placebo Total	Weight	Odds Ratio M-H, Fixed, 95% CI
3.2.1 Luteal administration						
Cohen 2002	4	86	1	88	1.9%	4.24 [0.46, 38.76]
Eriksson 2008	3	53	3	51	5.9%	0.96 [0.18, 4.99]
Halbreich 2002	11	119	1	110	1.9%	11.10 [1.41, 87.48]
Landen 2007 (1)	3	59	1	29	2.6%	1.50 [0.15, 15.08]
Steiner 2005	16	119	5	123	8.7%	3.67 [1.30, 10.36]
Steiner 2008	4	36	2	35	3.7%	2.06 [0.35, 12.06]
Wikander 1998	1	19	1	10	2.5%	0.50 [0.03, 8.95]
Yonkers 1997	10	116	2	118	3.7%	5.47 [1.17, 25.55]
Subtotal (95% CI)		**607**		**564**	**30.8%**	**3.23 [1.82, 5.73]**
Total events	52		16			
Heterogeneity: Chi² = 6.30, df = 7 (P = 0.51); I² = 0%						
Test for overall effect: Z = 4.02 (P < 0.0001)						
3.2.2 Continuous administration						
Cohen 2004	15	113	7	111	12.5%	2.27 [0.89, 5.81]
Eriksson 1995	3	27	2	111	1.4%	6.81 [1.08, 43.02]
Glaxo 1996	5	31	2	17	4.4%	1.44 [0.25, 8.37]
Glaxo 2001	19	117	7	118	11.9%	3.07 [1.24, 7.62]
Landen 2007	5	60	2	30	5.0%	1.27 [0.23, 6.98]
Ozeren 1997	2	18	0	17	0.9%	5.30 [0.24, 118.89]
Pearlstein 2005	20	125	9	125	15.4%	2.46 [1.07, 5.63]
Steiner 1995	11	102	8	125	13.0%	1.77 [0.68, 4.58]
Wikander 1998	2	19	2	10	4.8%	0.47 [0.06, 3.97]
Subtotal (95% CI)		**612**		**664**	**69.2%**	**2.24 [1.50, 3.34]**
Total events	82		39			
Heterogeneity: Chi² = 5.17, df = 8 (P = 0.74); I² = 0%						
Test for overall effect: Z = 3.96 (P < 0.0001)						
Total (95% CI)		**1219**		**1228**	**100.0%**	**2.55 [1.84, 3.53]**
Total events	134		55			
Heterogeneity: Chi² = 11.95, df = 16 (P = 0.75); I² = 0%						
Test for overall effect: Z = 5.62 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.06, df = 1 (P = 0.30), I² = 6.1%						



(6) Management – SSRI (pregnancy)

- Women should be provided with prepregnancy counselling at every opportunity. They should be informed that PMS symptoms will abate during pregnancy and SSRIs should be discontinued prior to and during pregnancy.

- Women should be informed how to safely stop SSRIs.

- Women with PMS who become pregnant while taking an SSRI/SNRI should be aware of the possible, although unproven, association with congenital malformations.
  They should be reassured that if such an association does exist, it is likely to be extremely small, compared to the general population.

Cardiovascular birth defects and other major congenital defects (e.g. anal atresia, cystic kidneys, clubfoot, gastroschisis, hypospadias, limb reduction and omphalocele)

Multinational population-based study from five Nordic countries
- 36772 infants exposed to SSRIs/SNRI during 1st trimester vs 2266875 nonexposed infants
- cardiac defects (OR 1.15, 95% CI 1.05-1.26), other major defects (OR 1.13, 95% CI 1.06-1.20)

→ (가족력, life style 등 변수 보정 후)
cardiac defects (OR 0.92, 95% CI 0.72-1.17), other major defects (OR 1.06, 95% CI 0.91-1.24).

Discontinue treatment soon after the first missed period rather than later in the first trimester.

(6) Management – Spironolactone

- Spironolactone can be used in women with PMS to treat physical symptoms.

  Spironolactone 100 mg improves in both mood and physical symptoms, in particular reduced weight gain.

(6) Management – Surgery

- When treating women with severe PMS,
  hysterectomy and bilateral oophorectomy has been shown
  to be of benefit.

  Hysterectomy and bilateral oophorectomy is a permanent form of ovulation suppression. .

- When treating women with PMS,
  hysterectomy and bilateral oophorectomy can be considered
  when medical management has failed,
  long-term GnRH analogue treatment is required or
  other gynaecological conditions indicate surgery.

- When treating women with PMS,
  surgery should not be contemplated
  without preoperative use of GnRH analogues as a test of cure and
  to ensure that HRT is tolerated.

  It would seem important, particularly in women younger than 45 years of age and for PMS alone

(6) Management – Surgery + HRT

- Women being surgically treated for PMS should be advised to use HRT, particularly if they are younger than 45 years of age.

  Following hysterectomy, avoidance of progestogen prevents PMS-type adverse effects.

  Consideration should also be given to replacing testosterone to prevent hypoactive sexual desire disorder.

- When treating women with severe PMS,
  endometrial ablation and hysterectomy with conservation of ovaries are not recommended.

  Conservation of the ovaries will lead to persistence of PMS (PMDs with absent menstruation).

- Bilateral oophorectomy alone (without removal of the uterus) will necessitate the use of a progestogen as part of any subsequent HRT regimen and this carries a risk of reintroduction of PMS-like symptoms (progestogen-induced PMD).


Summary
GOYA

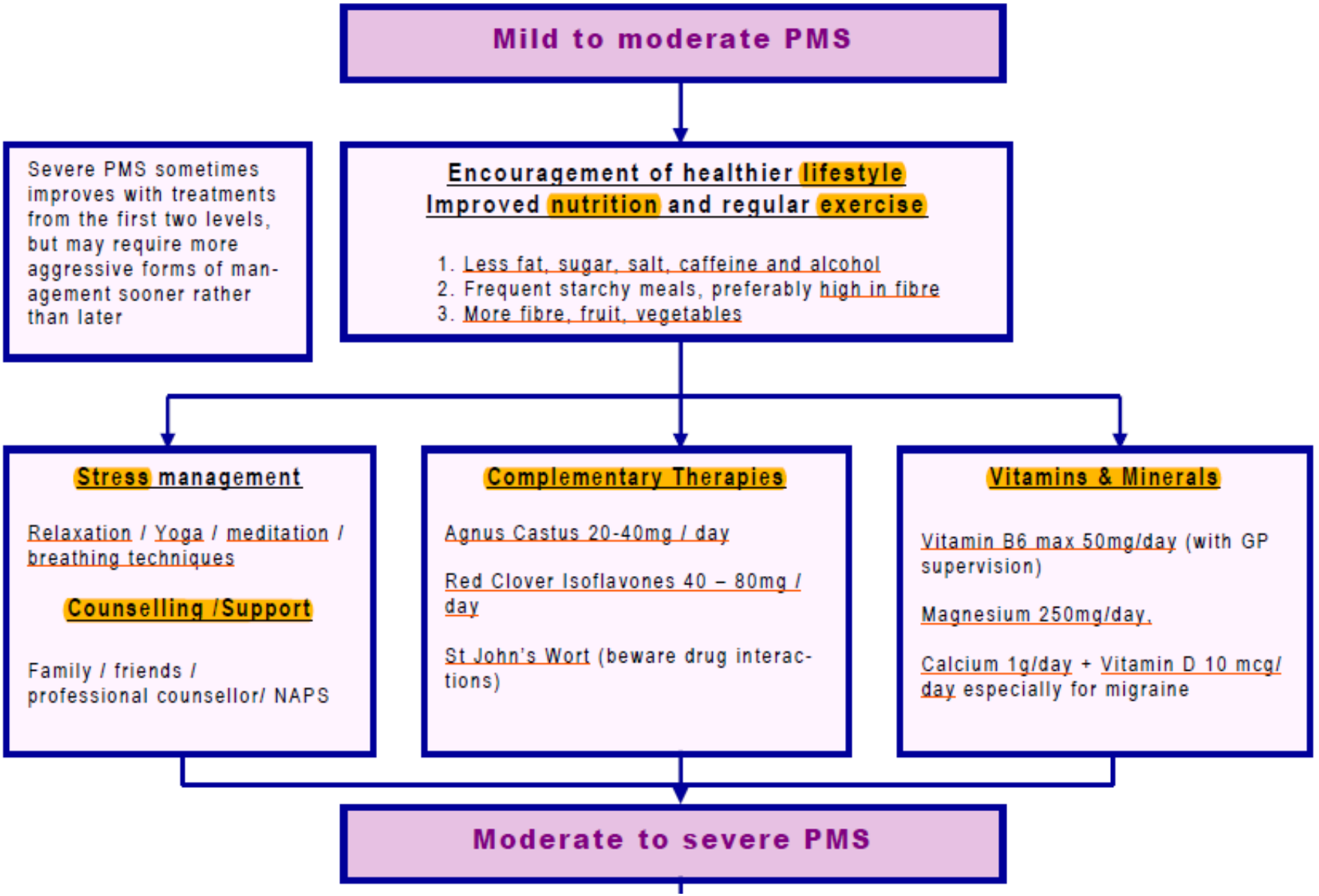
Summary

- 100% of women referred with PMS should have this diagnosis formally confirmed by completion of at least 2 consecutive months of a prospective symptom diary, usually the DRSP.

- 100% of women with PMS should not be offered progestogen therapy alone.

- 100% of women being considered for surgical treatment should have a trial of GnRH analogue therapy.

Managements (NAPS, 2011)



Moderate to severe PMS

PSYCHOLOGICAL APPROACH

Selective serotonin reuptake inhibitor antidepressants
Fluoxetine (Prozac) 20-40 mg/day
Citalopram (Cipramil) 10-20mg/day,
Escitalopram (Cipralex) 10-20mg/day
Continuous or in luteal phase

Cognitive Behavioural Therapy

CYCLE SUPPRESSION

Some combined oral contraceptive pills (e.g. Yasmin/Yaz)

Suppression of cycle with transdermal estradiol (100mcg patches or 4 doses oestrogel 0.06%)

+

Progestogenic opposition (utrogestan 200mg D17-D28 or Mirena)

Resistant PMS or persistent progestogenic side-effects — refer to gynaecologist

GnRH analogues + Add-back HRT
e.g. goserelin 3.6mg sc/month or triptorelin 3.0mg sc/month with add-back continuous combined HRT or Tibolone

Surgery

Hysterectomy and BSO + oestradiol +/- testosterone HRT

Transdermal estradiol 50-100mcg or 50-75mg estradiol implants+/- 100mg testosterone implants 6 monthly

Managements (RCOG, 2016)

Appendix IV: How PMS is treated – a decision-making algorithm[132]

First line Exercise, cognitive behavioural therapy, vitamin B6
Combined new generation pill (cyclically or continuously)
Continuous or luteal phase (day 15–28) low dose SSRIs, e.g. citalopram/escitalopram 10 mg

↓

Second line Estradiol patches (100 micrograms) + micronised progesterone (100 mg or 200 mg [day 17–28], orally *or* vaginally) or LNG-IUS 52 mg
Higher dose SSRIs continuously or luteal phase, e.g. citalopram/escitalopram 20–40 mg

↓

Third line GnRH analogues + add-back HRT (continuous combined estrogen + progesterone [e.g. 50–100 micrograms estradiol patches *or* 2–4 doses of estradiol gel combined with micronised progesterone 100 mg/day] or tibolone 2.5 mg)

↓

Fourth line Surgical treatment ± HRT


경청해 주셔서 감사합니다