부인과 질환에서 LNG-IUS의 적용, 효과, 부작용 대처

부산의대 주종길

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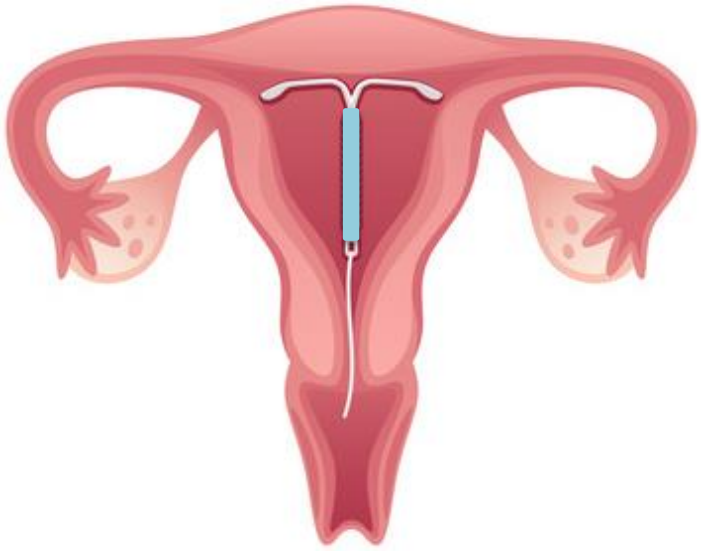
Introduction

LNG (levonorgestel)

Progestogenic	Anti-androgenic	Androgenic	Anti-mineralocorticoid
++	–	+	–

IUS (intrauterine system)



- ✓ 자궁내막 470-1500 ng/ml
- ✓ 자궁근육층 1.8-2.4 ng/ml
- ✓ 혈장 0.1-0.2 ng/ml

Introduction : LNG-IUS

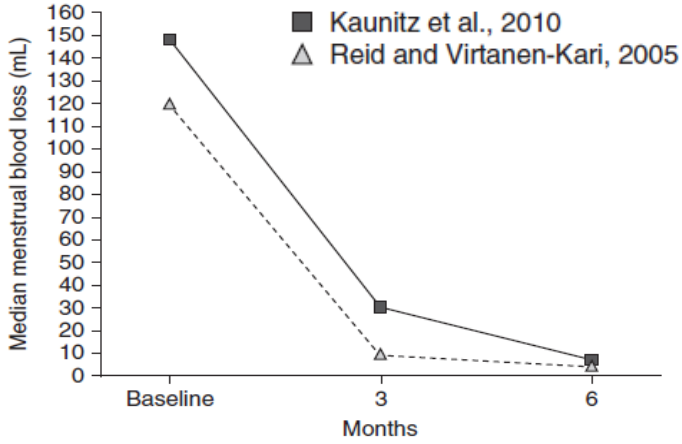
Types of LNG-IUS	Mirena (LNG-IUS 20)	Kyleena (LNG-IUS 12)	Jaydess (LNG-IUS 8)
T-frame dimensions	32mm x 32mm	28mm x 30mm	28mm x 30mm
Maximum duration of use	up to 5 years	up to 5years	up to 3 years
Total LNG content	total 52mg	total 19.5mg	total 13.5mg
Average release rate over 1st year	daily 20ug LNG	daily 12ug LNG	daily 8ug LNG
Color of removal thread	brown	blue	brown
적응증	피임, 월경과다 월경곤란증 ERT시 P 국소적용	피임	피임

LNG-IUS in GY disease

- Heavy menstrual bleeding
- Endometrial hyperplasia
- Endometrial polyps in user of tamoxifen
- Endometriosis
- Adenomyosis
- Endometrial protection during ERT

HMB : efficacy (non-structural)

RCT



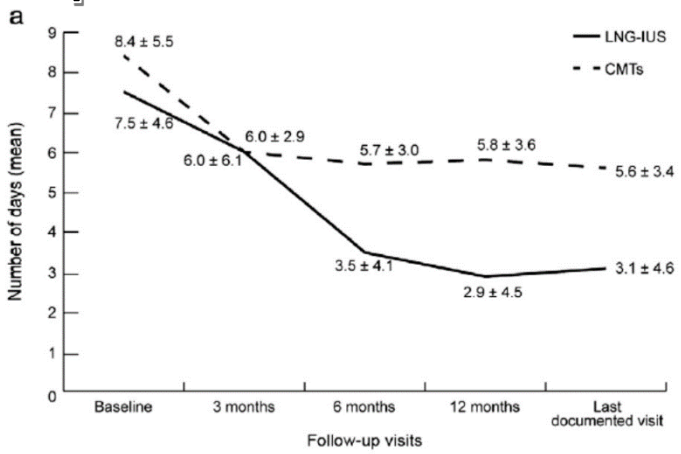
MBL reduction

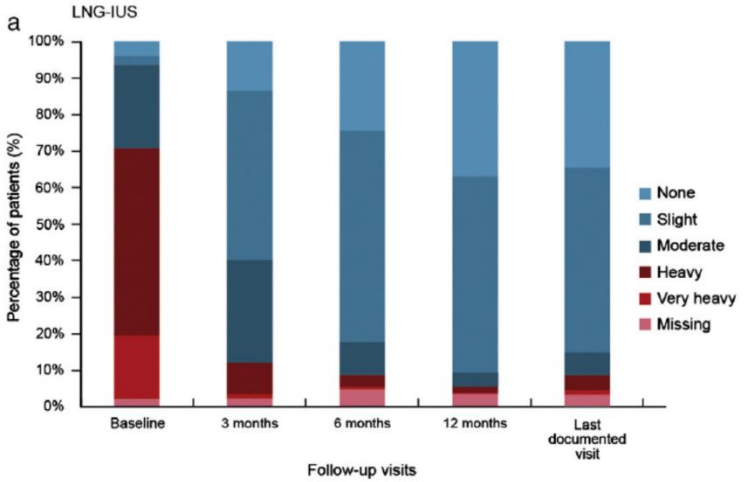
: 71% (6mo.) & 87% (12mo.)

: end of the 1st year → 3 years

(indirect assay)

Prospective observational





Kaunitz AM & Inki P. Drugs 2012; Lee BS et al., Int J Gynecol Obstet 2013

HMB-C (coagulopathy)

- Effective in reducing HMB with RCTs
  - 35% (6mo), 78% (9mo), 86% (33mo) in PBAC

- Special considerations
  - may benefit from removal & replacement prior to 5 years
  - at insertion, in selected cases

    prophylactic hemostatic cover considered

    : tranexamic acid (1 g), 1 h prior to procedure

    & continued every 6 h for 24 h

    : desmopressin, factor concentrate, PLT transfusion

Kaunitz AM & Inki P. Drugs 2012
Kadir RA et al., Contraception 2007

HMB : efficacy (LNG-IUS vs. others)

- Exclusion : intermenstrual or irregular bleeding, pathological causes
- Comparisons with placebo, medical Tx., endometrial destruction & hysterectomy

Authors' conclusions

The levonorgestrel-releasing intrauterine device (LNG IUS) is more effective than oral medication as a treatment for heavy menstrual bleeding (HMB). It is associated with a greater reduction in HMB, improved quality of life and appears to be more acceptable long term but is associated with more minor adverse effects than oral therapy.

When compared to endometrial ablation, it is not clear whether the LNG IUS offers any benefits with regard to reduced HMB and satisfaction rates and quality of life measures were similar. Some minor adverse effects were more common with the LNG IUS but it appeared to be more cost effective than endometrial ablation techniques.

The LNG IUS was less effective than hysterectomy in reducing HMB. Both treatments improved quality of life but the LNG IUS appeared more cost effective than hysterectomy for up to 10 years after treatment.

- **EFFECT** **hysterectomy > LNG-IUS = EA > oral medication**
- **LNG-IUS** **more cost effective than endometrial ablation, hysterectomy**

  more minor adverse effect than endometrial ablation

Lethaby A et al., Cochrane Database review 2015

HMB-A (adenomyosis)

- Effective treatment option of adenomyosis-associated HMB

- 48 pts., **large adenomyosis (≥ 12 wks, mean volume 253. 5mL)** in Korean
- 20 months (range, 3-50mo.) follow up of dysmenorrhea & HMB

Subjective symptomatic change before & after LNG-IUS insertion

	Before insertion	After insertion			
		3mo.	12mo.	24mo.	36mo.
No. of patients	48	36	31	15	9
Dysmenorrhea	58.1±29.6	28.6±28.0*	22.3±25.9*	19.3±19.8*	14.0±16.5*
HMB	69.4±26.1	**32.5±30.2***	**25.2±26.7***	**18.7±16.9***	**8.9±12.7***

Data are presented as mean±SD

Park DS et al., Taiwan J Obstet Gynecol 2015

HMB-L (leiomyoma)

Study	Tx. duration (no. of pts)	Inclusion criteria	Outcomes : mean PBAC ↓
Grigorieva et al., 2003	12mo. (69)	20-45yr **at least 2.5cm** **multiple 1.5cm**	67%, 77%, 84% (3, 6, 9mo)
Mercorio et al., 2003	12mo. (32)	Ut. : 8-10wks	40%. 50%, 65%, 69% (3, 6, 9, 12mo)
Murat et al., 2010	6mo. (46)	Ut. ≤12wks	85% (6mo)
Kriplani et al., 2012	48mo. (54)	**no submucous** **no adenomyosis**	97%, 99%, 99% (12, 24, 48mo)

Kaunitz AM & Inki P. Drugs 2012; Kriplani et al., Int J Gynecol Obstet 2012

HMB-L : myoma size

- Myoma size & treatment failure
- Thermal balloon ablation (n=67) & LNG-IUS (n=37)

Table 3. Treatment outcome of TBA and LNG-IUS according to myoma size

Myoma size (cm)	TBA			LNG-IUS			*P*-value
	Total	Success	Failure	Total	Success	Failure	
<2.5	33	29 (88)	4 (12)	21	18 (86)	3 (14)	1.000
≥2.5 and <5.0	25	18 (72)	7 (28)	14	10 (71)	4 (29)	1.000
≥5.0	9	4 (44)	5 (56)	4	3 (75)	1 (25)	0.486

Values are presented as number (%).

TBA, thermal balloon ablation; LNG-IUS, levonorgestrel-releasing intrauterine system.

Myoma size (2.5 cm) was associated with treatment outcome

Kim JY et al., Obstet Gynecol Sci 2013

Endometrial hyperplasia

- Off-label in many countries
- Mainly young women who wanted to preserve fertility

- ***Oral P vs. LNG-IUS***

: 24 observational studies (1001 women), regression rate

	Oral progestogens (95 % CI)	**LNG-IUS (95 % CI)**	**P-value**
Simple hyperplasia	89% (77-100)	96% (76-100)	0.41
Complex hyperplasia	66% (58-74)	92% (65-100)	**< 0.01**
Atypical hyperplasia	69% (58-83)	90% (62-100)	**0.03**

LNG-IUS

mode of progestogen delivery

higher patient satisfaction → higher compliance

Gallos ID et al., Am J Obstet Gynecol 2010

End. hyperplasia : IUS vs. conti or cyclic P

- Multi-center randomized trial in Norway
- 170 women aged 30–70 years
- LNG-IUS; MPA 10mg (10 days/cycle or continuous) for 6 months

Intervention	SH Fraction of regression (95% CI)	CH Fraction of regression (95% CI)	ACH Fraction of regression (95% CI)
LNG-IUS	6/6 = 1.0 (0.54-1.0)	41/41 = 1.0 (0.91-1.0)	6/6 = 1.0 (0.54-1.0)
Oral continuous	6/6 = 1.0 (0.54-1.0)	33/34 = 0.97 (0.84-1.0)	7/8 = 0.88 (0.47-1.0)
Oral cyclic	7/11 = 0.64 (0.31-0.89)	26/36 = 0.72 (0.55-0.86)	3/5 = 0.6 (0.14-0.95)
Total	19/30 = 0.64 (0.44-0.80)	100/111 = 0.90 (0.83-0.95)	16/19 = 0.84 (0.60-0.97)

SH, simple hyperplasia; CH, complex hyperplasia; ACH, atypical complex hyperplasia

LNG-IUS, continuous MPA > cyclic MPA

Orbo A et al., BJOG 2013

Endometrial hyerplasia

Royal College of Obstetricians & Gynaecologists

What should the first-line medical treatment of hyperplasia without atypia be?

Both continuous oral and local intrauterine (levonorgestrel-releasing intrauterine system [LNG-IUS]) progestogens are effective in achieving regression of endometrial hyperplasia without atypia. **A**

The LNG-IUS should be the first-line medical treatment because compared with oral progestogens it has a higher disease regression rate with a more favourable bleeding profile and it is associated with fewer adverse effects. **A**

without atypia → LNG-IUS : 1st line Tx.

What should the initial management of atypical hyperplasia be?

Women with atypical hyperplasia should undergo a total hysterectomy because of the risk of underlying malignancy or progression to cancer. **B**

with atypia → should hysterectomy

RCOG/BSGE. Guideline No. 67. Feb. 2016

Endometrial hyerplasia

Royal College of Obstetricians & Gynaecologists

How should women with atypical hyperplasia who wish to preserve their fertility or who are not suitable for surgery be managed?

Women wishing to retain their fertility should be counselled about the risks of underlying malignancy and subsequent progression to endometrial cancer.	✓
Pretreatment investigations should aim to rule out invasive endometrial cancer or co-existing ovarian cancer.	✓
Histology, imaging and tumour marker results should be reviewed in a multidisciplinary meeting and a plan for management and ongoing endometrial surveillance formulated.	✓
First-line treatment with the LNG-IUS should be recommended, with oral progestogens as a second-best alternative (see section 7.2).	B

with atypia & preserve fertility

→ LNG-IUS as 1st line Tx.

RCOG/BSGE. Guideline No. 67. Feb. 2016

Endometrial cancer

- 32 studies, 408 women with fertility-sparing treatment

  : ***progestin, LNG-IUS***, *AIs, hysteroscopic resection + GnRH ago or P*

- Regression rate of 76.2% ↔ Relapse rate of 40.6%

  Live birth rate of 28%

- LNG-IUS-based treatment of FIGO stage IA, grade 1
- Patients at high risk for perioperative complications

- Among 12 patients

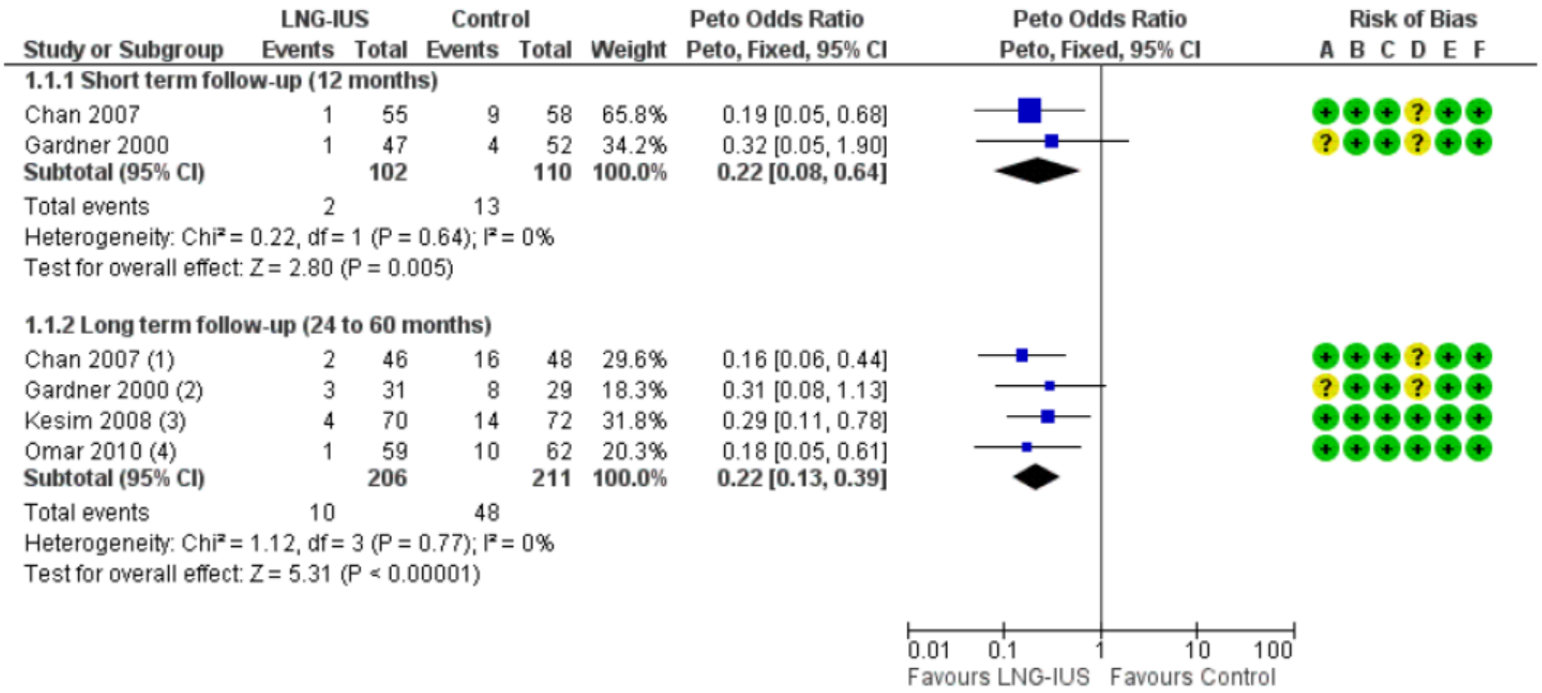
  : biopsy results were negative for 64% (6 mo.) & 75% (12 mo.)

Gallos ID et al., Am J Obstet Gynecol 2012; Montz FJ et al., Am J Obstet Gynecol 2002

Endometrial polyp in tamoxifen user (I)

- 4 RCTs involving 543 women from 317 studies

Figure 4. Forest plot of comparison: 1 LNG-IUS with endometrial surveillance versus endometrial surveillance alone, outcome: 1.1 Endometrial Polyps.



*제품설명서 : 다음 환자에는 투여하지 말 것, 유방암이 있거나 의심되는 경우

Dominick S et al., Cochrane Database Syst Rev 2015

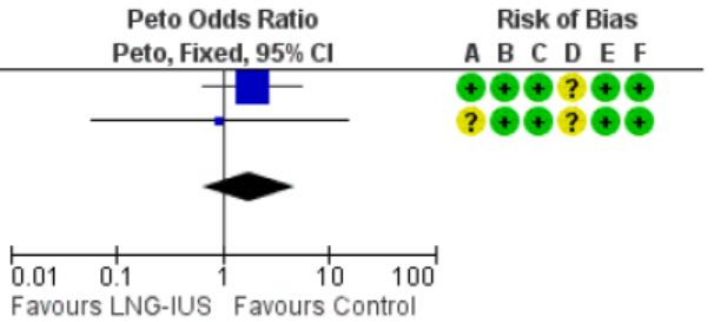
Endometrial polyp in tamoxifen user (II)

- 4 RCTs involving 543 women from 317 studies

Figure 8. Forest plot of comparison: 1 LNG-IUS with endometrial surveillance versus endometrial surveillance alone, outcome: 1.6 Breast Cancer Recurrence.

Study or Subgroup	LNG-IUS Events	LNG-IUS Total	Control Events	Control Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Chan 2007 (1)	10	46	6	48	87.2%	1.91 [0.65, 5.57]
Gardner 2000 (2)	1	31	1	29	12.8%	0.93 [0.06, 15.32]
Total (95% CI)		**77**		**77**	**100.0%**	**1.74 [0.64, 4.74]**
Total events	11		7			

Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0%
Test for overall effect: Z = 1.09 (P = 0.28)



benign endometrial polyps ↓

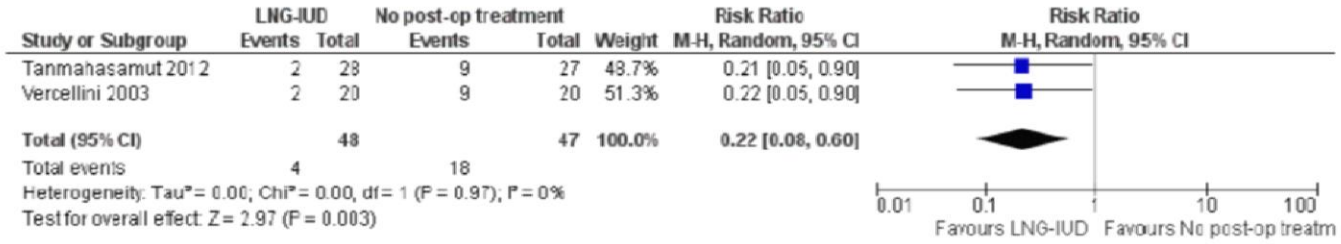
abnormal vaginal bleeding or spotting ↑

no clear evidence
prevents endometrial cancer
affects risk of breast ca. recurrence

Dominick S et al., Cochrane Database Syst Rev 2015

Endometriosis : pain

Figure 1. Forest plot of comparison 1 Postoperative use of LNG-IUD compared with expectant management in women with endometriosis, outcome 1.1: painful symptoms.

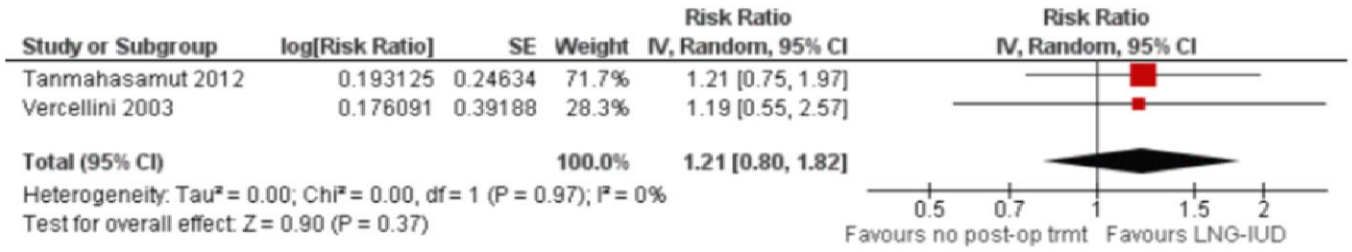


Painful symptoms

IUS vs. expectant

0.22 (0.05, 0.90)

Figure 2. Forest plot of comparison: 1 Postoperative use of LNG-IUD compared with expectant management in women with endometriosis, outcome: 1.2 Patient satisfaction.



Patient satisfaction

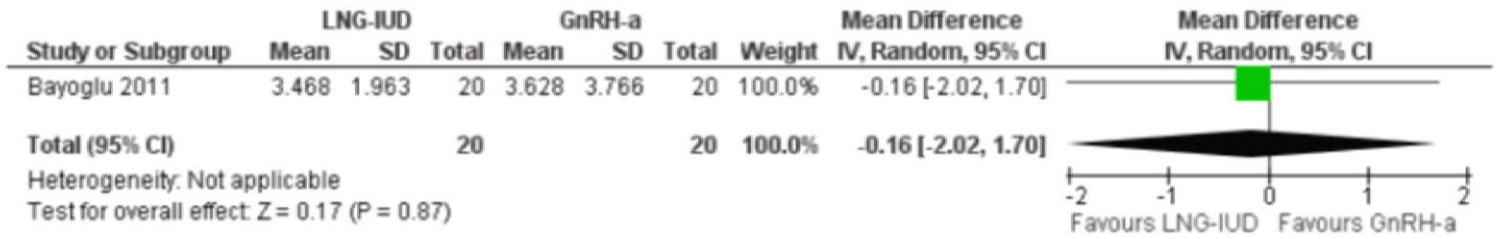
IUS vs. expectant

1.19 (0.55, 2.57)

Abou-Setta AM et al., Cochrane Database Syst Rev 2013

Endometriosis : LNG-IUS vs. GnRH ago

Figure 5. Forest plot of comparison: 2 Postoperative use of LNG-IUD compared with GnRH analogue in women with endometriosis, outcome: 2.1 Painful symptoms.



Painful symptoms : IUS vs. GnRH agonist, **-0.16 (-2.02, 1.70)**

Abou-Setta AM et al., Cochrane Database Syst Rev 2013

Eoma recurrence ; inconsistent

comparable to use of cyclic OC

long-term maintenance of LNG-IUS, not effective

Cho SH et al., Acta Obstet Gynecol Scand 2014; Chen YJ et al., Am J Obstet Gynecol 2017

Adenomyosis : pain

- 94 women who had moderate or severe dysmenorrhea associated adenomyosis
- VAS of dysmenorrhea, uterine volume, CA-125 at baseline, 3,6,12, 24,36 months

Satisfaction degree	0 months	12 months	24 months	36 months
Very satisfied		12 (16.9)	12 (18.8)	8 (15.7)
Satisfied		28 (39.4)	30 (46.9)	29 (56.9)
Uncertain		23 (32.4)	17 (26.6)	11 (21.6)
Dissatisfied		8 (11.3)	5 (7.8)	3 (5.9)
Very dissatisfied		0	0	0
VAS score	**77.9±14.7**	15.8±21.8	14.9±20.9	**11.8±17.9**
Uterine volume (mL)	**113.8±46.9**	87.7±35.8	88.2±37.1	**93.7±46.7**

70%

30%

Sheng J et al., Contraception 2009

Adenomyosis : volume & duration

Uterine volume

TABLE 1
Uterine volume, pain scores, and laboratory findings after treatment with the LNG-IUD

Variable	Before insertion (n = 44)	6 Mo (n = 44)	12 Mo (n = 44)	24 Mo (n = 44)	36 Mo (n = 32)
Before insertion	6 mo.	12 mo.	24 mo.	36 mo.	
156.85±49.79	127.17±46.85 ↓	118.64±41.36 ↓ ↓	128.84±48.70 ↑	139.87±29.93 ↑ ↑	

Decline of LNG concentration

- **32 pt. (> 36 months F/U) → 15 pt. had new LNG-IUD inserted**

  : dysmenorrhea (7 patients), increased vaginal bleeding (6 patients)

  increasing uterus size (2 patients)

Cho SH et al., Am J Obstet Gynecol 2008

End. protection during ERT

Study	*Population*	*Main inclusion criteria*	*Endpoints*	*Progestin therapy*	*Subjects (n)*	*ERT regimen*	*Treatment duration*
Pivotal trials for the LNG-IUS in ERT							
Suhonen *et al.*[48,49]; Phase II, non-comparative, open	Peri- and postmenopausal women; mean age 51.4 years	Stopped HRT for ≥2 weeks prior to study	Endometrial protection during ERT assessed by histology	LNG-IUS	36	Transdermal estradiol (50 µg/day) at weeks 1–4; thereafter, either 1 or 3 subcutaneous estradiol implants (12 or 36 µg/day)[a]	5 years
Varila *et al.*[33]; Phase II, non-comparative, open, prospective cohort	Postmenopausal women; mean age 55.0 years	Requirement for HRT because of climacteric symptoms, and no wish for withdrawal bleeding induced by cyclic HRT	Endometrial protection during ERT assessed by histology, bleeding pattern, evaluation of LNG-IUS placement/removal	LNG-IUS	40	Oral estradiol valerate (2 mg/day) or transdermal estradiol (50 µg/day)	1 year first phase; 5 years second phase
Boon *et al.*[30]; Phase III, comparative, open, randomized	Perimenopausal women; mean age 46.9 (LNG-IUS), 46.8 (oral NETA) years	Age 40–60 years, with an intact uterus, requesting HRT, with an irregular menstrual cycle but no amenorrhea for >12 months, or stopped HRT ≥6 weeks prior to study	Endometrial protection during ERT assessed by histology, bleeding pattern, efficacy, overall acceptability	LNG-IUS, oral NETA (1 mg on days 13–22)	97; 99	Oral estradiol (2 mg/day); oral estradiol (2 mg/day) on days 1–22, oral estradiol (1 mg/day) on days 23–28	2 years
Bayer HealthCare, data on file[c,e,e]; Phase III, comparative/non-comparative, open, randomized	Postmenopausal women; mean age: 53.3 (LNG-IUS), 52.7 (oral LNG) years	Normally shaped and sized uterus, amenorrhea for >6 months and FSH >30 IU/l (no previous HRT) or FSH >15 IU/l (previous HRT), no endometrial hyperplasia or atypia on biopsy	Endometrial protection during ERT assessed by histology	LNG-IUS; oral LNG (75 µg on days 17–28)	109; 58	Oral estradiol valerate (2 mg/day)	2 years comparative phase, 5 years non-comparative phase

Endometrial histology
Oral E2 or transdermal E2
Up to 5years

Depypere H & Inki P. Climacteric 2015

End. protection during ERT

Hampton *et al.*[22]; Phase III, non-comparative, open, prospective, outpatient	Postmenopausal women; mean age 47.9 years	Normally shaped and sized uterus, ≥ 3 menstrual periods and no amenorrhea for > 6 months in past year, FSH > 15 IU/l (FSH < 15 IU/l if aged > 48 years with menopausal symptoms)	Endometrial protection during ERT assessed by histology, bleeding pattern, continuation rate, menopausal symptoms, overall tolerability	LNG-IUS	82	Oral conjugated estrogen (1.25 mg/day, with reduction to 0.625 mg/day, if necessary)	5 years
Bayer HealthCare; data on file[6,7,8]; Phase III, non-comparative, open	Perimenopausal women; mean age 50.8 years	Intact uterus, using transdermal ERT and oral norethisterone (1 mg/day) or dydrogesterone (10 mg/day) for 10 days per month for ≥ 6 months	Endometrial protection during ERT assessed by histology	LNG-IUS	23	Transdermal estradiol (50 µg/day)	1 year
Other key trials of the LNG-IUS in ERT							
Andersson *et al.*[50]; comparative, open, randomized	Perimenopausal women; mean age 48.1 (LNG-IUS), 48.7 (oral HRT) years	Seeking treatment for climacteric symptoms, no signs of pelvic pathology, last menstrual period at < 12 months	Climacteric symptoms, bleeding pattern, endometrial protection during ERT assessed by histology	LNG-IUS; oral LNG (250 µg on days 11–21)	18; 19	Oral estradiol valerate (2 mg/day); oral estradiol valerate (2 mg/day) on days 1–21	1 year
Antoniou *et al.*[12]; comparative, open, randomized	Postmenopausal women; mean age 59.5 years	Parous, no estrogen use for ≥ 3 months, confirmed postmenopausal status	Climacteric symptoms, bleeding pattern, endometrial protection during ERT assessed by histology and transvaginal ultrasound	LNG-IUS; vaginal progesterone suppository (100 mg on days 1–7)	28; 28	Transdermal estradiol (50 µg/day); vaginal estradiol ring (2 mg micronized estradiol/3 months)	1 year

Bleeding pattern, health-related QoL

Depypere H & Inki P. Climacteric 2015

End. protection during ERT : benefit

- Provides effective **endometrial protection** from hyperplasia during ERT
- Provides simultaneous **contraceptive effect**
- Does not interfere with the ability of ERT to **improve climacteric symptoms**
- High rate of **amenorrhea**
- Well tolerated; comparable **safety profile** for contraception
- **No relevant effects** on **plasma lipids** or other **cardiovascular risk factors**
- **Convenient** form of progestin administration

Depypere H & Inki P. Climacteric 2015

End. protection during ERT : risks

- **Placement** may be more challenging,

  particularly in postmenopausal women

  with advanced uterine atrophy

- Associated with **initial spotting** during first months of use

- Unresolved issue: **risk of breast cancer** is not established

Depypere H & Inki P. Climacteric 2015

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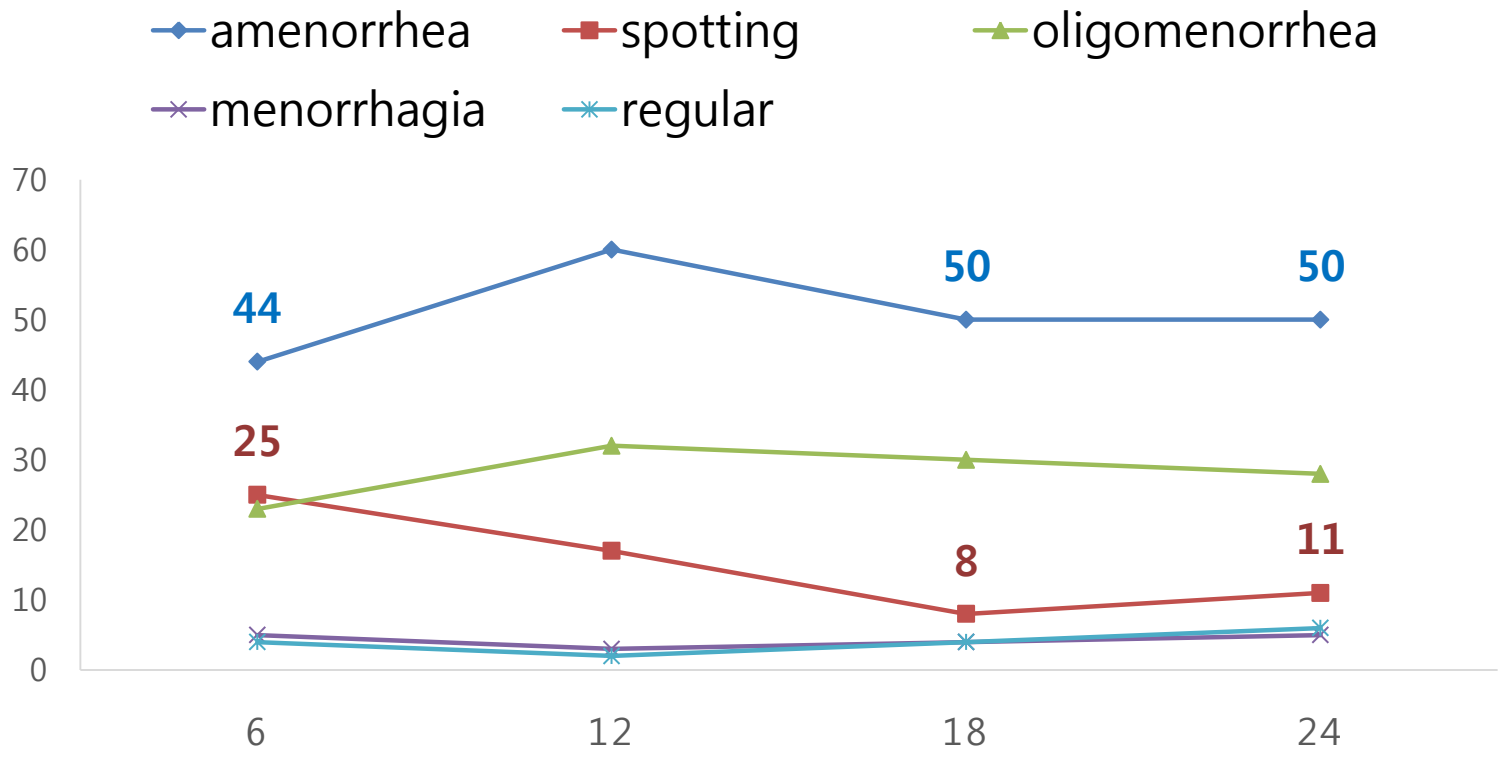
Side effect & management

- Bleeding
- Perforation & embedment
- Expulsion
- Ovarian cyst formation
- Pelvic inflammatory disease

+ Contraindication

LNG-IUS : bleeding pattern

- Bleeding patterns up to 2 years



- Discontinuation rate for menstrual disturbance : **5.9%**

Hidalgo M et al., Contraception 2002

Bleeding in LNG-IUS

- Structured direct **counseling before initiation**
- **Pregnancy** should be excluded first
- Verify **proper placement** in IUD

  with irregular bleeding & pelvic pain
- **Infections** or **pathologic causes**

  like cervical & endometrial cancer

LNG-IUS : bleeding control

- NSAIDs : naproxen 500mg bid 5days
- Tranexamic acid 500mg tid until bleeding stop
- Antiprogestin (mifepristone) 100mg/day/month for 3cycles
- Estrogen in atrophic endometrium ???

Perforation & embedment

- **Perforation**
  - primary (insertion pressure)

    or secondary (imbalance of IUD size & uterine cavity) is possible

  → must be located & removed

- **Embedment** in the myometrium may occur
  - may decrease contraceptive effectiveness & result in pregnancy
  - should be removed

    : in some cases surgical removal may be necessary

Mirena insert paper. Bayer HealthCare Pharmaceuticals Inc.

Perforation

Overall risk remains low !!!

- EURAS-IUD : 61,448 women (70% LNG-IUS, 30% Cu-IUD)

- 58 complete perforations : lactating vs. non-lactating
  - incidence (/1000 insertions) : *4.5 (30 cases) vs. 0.6 (28 cases)*
  - *relative risk :* 7.7 (95% CI: 4.6–12.9)

- Time since delivery

Perforations per 1000 insertions and risk ratios stratified by breastfeeding status and time since last delivery interval

Perforation per 1000 insertions (95% CI)		Breastfeeding[a]		
		Yes *n*=30	No *n*=28	RR (95% CI)
Time since last delivery	≤36 weeks *n*=35	4.8 (3.2–6.9)	1.0 (0.4–2.2)	4.7 (2.0–11.4)
	>36 weeks *n*=23	1.6 (0.0–9.1)	0.5 (0.3–0.8)	3.1 (0.4–23.2)
	RR (95% CI)	2.9 (0.4–21.4)	1.9 (0.8–4.8)	

Heinemann K et al., Contraception 2017

Expulsion of LNG-IUS

- 2,138 patients (2008-2011), mean F/U 37±11 months
- 5,403 patients (2007-2011), mean F/U 22.6±11 months

  : overall, 6% (2nd expulsion :14%) – 10%

  : adolescence - HR 2 – 3

- Counselling for higher risk of expulsion

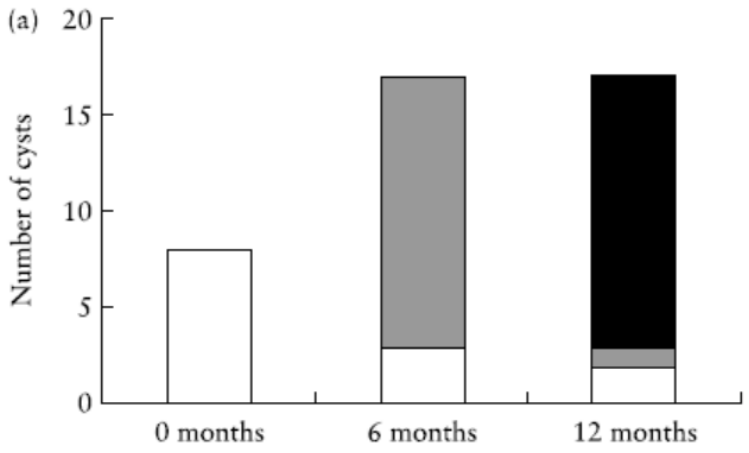
  : adolescence, previous expulsion, leiomyomas

- Should not restrict IUD use in high expulsion risk group

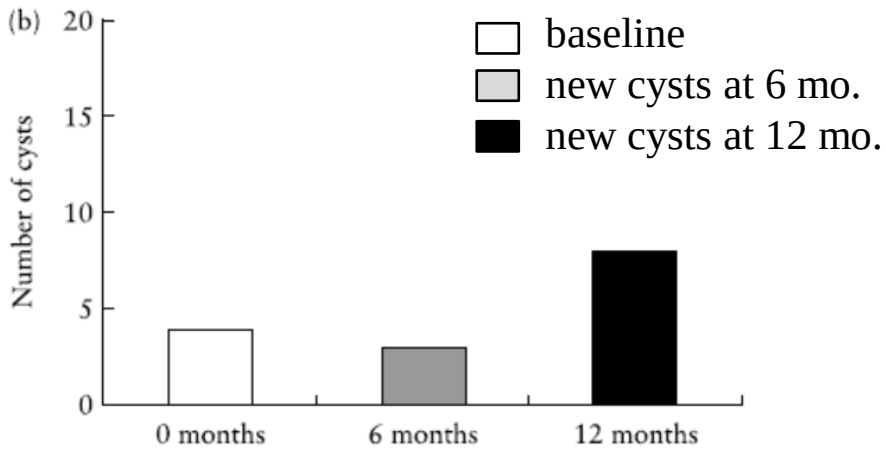
Madden T et al., Obstet Gynecol 2014; Aoun J et al., Obstet Gynecol 2014

Ovarian cyst formation

- Prospective, RCT trial in 236 women (age range 35–49 years)



during LNG-IUS



after hysterectomy

LNG-IUS use was associated with

development of ovarian cysts,

but, symptomless & high rate of spontaneous resolution

Inki P et al., Ultrasound Obstet Gynecol 2002

PID

- 1.6 cases per 1,000 women-years / protective effect ?
- During insertion procedure
  - no beneficial effect of prophylactic antimicrobials
  - screening for cervical infection at the time of insertion
- STI or PID while IUD in place
  - standard treatment / removal of IUD : not required
  - refractory to standard Tx. : removal should be considered

Russo JA et al., J Adolesc Health 2013; Stoddard A et al., Drugs 2013

Contraindication of LNG-IUS

MEC categories for contraceptive eligibility	
1	A condition for which there is no restriction for the use of the contraceptive method
2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks
3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method
4	A condition which represents an unacceptable health risk if the contraceptive method is used

http://www.who.int/reproductivehealth/publications/family_planning/Ex-Summ-MEC-5/en/

Medical eligibility criteria

Condition	WHO	CDC
Pregnancy / Puerperal sepsis / Immediate post-septic abortion	4	
Positive APA	3	
Unexplained vaginal bleeding	I=4 / C=2	
Cervical / endometrial cancer	I=4 / C=2	
Current & Hx. of IHD	I=2 / C=3	
Breast cancer, current / Distortion of uterine cavity	4	
Breast cancer, past & no evidence of current disease for 5 yr	3	
PID & STI, current	I=4 / C=2	
Severe cirrhosis / hepatocellular adenoma / hepatoma	3	
Acute DVT/PE	**3**	**2**
Migraine with aura, at any age	**I=2 / C=3**	**1**
Ovarian cancer	**I=3 / C=2**	**1**

I=initiation, C=continuation

Summary (I)

Gynecological condition	Main non-contraceptive benefits	Possible disadvantages
AUB	Substantial reduction in **bleeding** & improvement of **QoL** Less invasive & cost-effective compared with hysterectomy	Unpredictable spotting
IDA	Higher Hb & serum ferritin levels	Empiric Tx.
Coagulopathies	Reduction of **bleeding**	Poor literature
End. hyperplasia	**High regression rates** with simple & atypical hyperplasia 2nd -line Tx., if surgery unavailable	Risk of malig. Strict follow-up

Sabbioni L et al., Gynecol Endocrinol 2017

Summary (II)

Gynecological condition	Main non-contraceptive benefits	Possible disadvantages
Leiomyomas	Reduction of **bleeding** (depending on localization)	Less effective without fibroids High expulsion rates
Adenomyosis	Reduction of **bleeding & dysmenorrhea** Reduction in thickness of myometrial junctional zone & total **ut. volume**	Less efficient in more severe cases
Endometriosis	Endometrial glands apoptosis ↑ Reduction of recurrence of moderate or severe **dysmenorrhea** after conservative surgery	Irregular & intolerable bleeding associated with persistent pain

Sabbioni L et al., Gynecol Endocrinol 2017


경청해 주셔서
감사합니다.