Women's Health Research Review

Making Education Easy

Issue 27 – 2018

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Abbreviations used in this issue

ACOG = American College of Obstetricians and Gynecologists
BMI = body mass index
FDA = Food and Drug Administration
IUD = intrauterine device
IUS = intrauterine system
LNG-IUS = levonorgestrel-IUS
NICE = National Institute for Health and Care Excellence
POP = pelvic organ prolapse
RCOG = Royal College of Obstetricians and Gynaecologistsm

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NZMA New Zealand Medical Association

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Welcome to the latest issue of Women's Health Research Review.

This month a systematic review reports that progestogen-only contraceptives do not cause depression, a meta-analysis determines the risk of endometrial cancer in women with postmenopausal bleeding, a US study reports that few young women know about the IUD for emergency contraception, and a Mayo clinic study finds that moderate to severe vasomotor symptoms may be disruptive in women well beyond the natural age of menopause. US researchers report that pelvic pain before global endometrial ablation is an independent risk factor for failure, Spanish investigators report a high success rate with a vaginal ring pessary for advanced POP, and a multicentre case-control study determines that fatigue is a common symptom of endometriosis.

We hope you find these and the other selected studies interesting, and welcome any feedback you may have.

Kind regards,

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The relationship between progestin hormonal contraception and depression

Authors: Worly B et al.

Summary: This systematic review investigated the association between progestogen-only contraception and depression. A search of PubMed, Ovid and Web of Science identified 26 English-language studies (5 randomised controlled trials, 11 cohort studies and 10 cross-sectional studies) that reported progestogen-only contraception and depression. Analysis of the data found minimal association between progestogen-only contraceptive methods and depression. No correlation with depression was found in 5 progestogen subdermal implant studies, 4 out of 5 LNG-IUS studies, 3 depot medroxyprogesterone acetate (DMPA) injection trials, and 2 progestogen-only contraceptive pill studies. Only 1 good-quality, medium-bias study showed an association between progestogen-only pills, IUDs and depression.

Comment (HR): Good to have an updated analysis of the association between progestogen-only contraception and depression. The results from the Depo Provera® study are particularly helpful as there still seems to be a misconception that it cannot be used in women with depression. The comment from the 2 largest studies (n=495 and n=608) says "Although these studies were not randomised, large sample sizes and use of validated scales provide convincing evidence that DMPA does not increase the risk of depression". The other worry in the past has been the potential loss of bone mineral density (BMD) with the injection. However, the systematic review undertaken by NICE concluded that DMPA use is associated with a small loss of BMD, which is largely recovered when DMPA is discontinued. In addition, another systematic review of 10 observational studies published between 1996 and 2006 found that following discontinuation of DMPA, BMD returned towards baseline or to baseline values in women of all ages. Women using DMPA until the menopause do not experience further significant bone loss because they have already undergone loss associated with the hypoestrogenic effects of DMPA. There has been no evidence that the injection increases fracture risk.

Reference: Contraception 2018;97(6):478-89

Abstract

Independent commentary provided by Honorary Associate Professor Helen Roberts MB, MPH, FAChSHM

After my medical degree at Trinity College Dublin, I worked at the Rotunda Hospital and then King's College Hospital in London. In 1983 I came to New Zealand and joined Family Planning, becoming the Medical Director and National Medical Spokesperson from 1988-1992. In 1991 I completed the MPH at Yale University in New Haven and on my return took up an academic position in the Department of Obstetrics and Gynaecology, University of Auckland. I was Associate Professor Women's Health until my retirement at the end of 2017. At present I continue my contraception and menopause clinic at Greenlane clinical centre and work as a certifying consultant at Epsom Day Unit.

Association of endometrial cancer risk with postmenopausal bleeding in women

Authors: Clarke M et al.

Summary: This systematic review and meta-analysis determined the risk of endometrial cancer in women with postmenopausal bleeding (PMB). A search of PubMed and Embase identified 129 observational studies that reported either the prevalence of PMB in women with endometrial cancer (n=6358) or the risk of endometrial cancer in women with PMB (n=34,432). The pooled prevalence of PMB among women with endometrial cancer was 91%, irrespective of tumour stage. The pooled risk of endometrial cancer among women with PMB was 9%, with estimates varying by use of hormone therapy (range 7–12%) and geographic region (from 5% in North America to 13% in Western Europe).

Comment (HR): It is recommended that women are advised at menopause to present if they have PMB i.e., bleeding 1 year after the last period. Although the commonest cause of PMB is vaginal atrophy, usually presenting in older women, the conclusion here says that "early detection strategies focused on women with PMB have the potential to capture as many as 90% of endometrial cancers". A recent NZ study looked at this. The GPs were following the Canterbury HealthPathways algorithm for management of PMB. This included doing a pipelle for those women with endometrial thickness >5mm. They found that "the clinical pathway disseminated on HealthPathways was a safe and promising alternative model of care for women with PMB that does not expose them to the risk of undue delay or missed diagnoses of endometrial cancer. However, there are potential concerns regarding the efficiency of this pathway, mainly regarding the high inadequacy rate of pipelle biopsies carried out in primary care, requiring further investigations in secondary care. This indicates that targeted education of general practitioners on pipelle biopsies is necessary".

Comment (AS): This systematic review and meta-analysis of 129 studies is timely given the increasing incidence of endometrial cancer (mainly due to the obesity epidemic) and rising mortality from this disease. The study lends considerable support to the ongoing assessment and appropriate investigation of all women with PMB as 90% of women diagnosed with endometrial cancer had PMB. Of course the chance of having endometrial cancer if one has PMB remains low (most of the causes are benign). Indeed in the studies that were assessed the pooled estimate of the risk of PMB being due to endometrial cancer was 9%. So for the time being (until more elegant tests are developed) all women with PMB need investigation.

Reference: JAMA Intern Med 2018;178(9):1210-22
Abstract

Time spent reading this publication has been approved for CME for Royal New Zealand College of General Practitioners (RNZCGP) General Practice Educational Programme Stage 2 (GPEP2) and the Maintenance of Professional Standards (MOPS) purposes, provided that a Learning Reflection Form is completed. Please **CLICK HERE** to download your CPD MOPS Learning Reflection Form.

Time spent reading this publication has been approved for CNE by The College of Nurses Aotearoa (NZ) for RNs and NPs. For more information on how to claim CNE hours please **CLICK HERE**.

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The intrauterine device as emergency contraception: how much do young women know?

Authors: Goodman S et al.

Summary: This US study evaluated young women's awareness of the use of IUDs for emergency contraception. 1500 women aged 18–25 years who were receiving contraceptive counselling within a larger cluster-randomised trial in 40 Planned Parenthood health centres in 2011–2013 were included. The health centres were randomised to receive enhanced training on contraceptive counselling and IUD placement, or to provide standard care. The intervention did not focus specifically on IUDs for emergency contraception. At 6-month follow-up, only 7.5% of the women visiting the health centres had heard of IUDs as emergency contraceptives. However, if they needed emergency contraception, 68% of them said they would want to learn about IUDs in addition to emergency contraceptive pills (ECPs), especially those who would be very unhappy to become pregnant. 91% of them reported that a doctor or nurse would be their most trusted source of emergency contraception information.

Comment (HR): It is likely that older women also may not know about the postcoital IUD. The Faculty of Sexual and Reproductive Health Guidelines on Emergency Contraception were updated in December 2017. They remind us that the IUD is the most effective method of emergency contraception and should be considered by all women who have had unprotected sexual intercourse (UPSI) and do not want to conceive.The IUD Is the only method of emergency contraception that is effective after ovulation has taken place, unlike the ECP. It can be inserted for emergency contraception within 5 days after the first UPSI in a cycle, or within 5 days of the earliest estimated date of ovulation, whichever is later. It also has the advantage of providing immediately effective ongoing contraception. Some groups of women in particular should consider the IUD for emergency contraception e.g., those with BMI >26, as evidence suggests that the ECP is not effective for these women. The ECP is also less effective for women using enzyme-inducing medications and although we can offer them double-dose ECP there is not a lot of information about efficacy.

Reference: Contraception 2018; published online Apr 18
Abstract

Vasomotor symptoms in women over 60: results from the Data Registry on Experiences of Aging, Menopause, and Sexuality (DREAMS)

Authors: David P et al.

Summary: This analysis of the DREAMS study investigated the frequency of moderate to severe vasomotor symptoms (msVMS) in women aged ≥60 years. Data were collected for women presenting to the Mayo Clinic for menopause consultation in 2006–2014. Women were classified as having msVMS bother if they reported "quite a bit" or "extremely" compared with women reporting "not at all" or "a little bit". Of the 4,956 women presenting for menopause consultation, 921 were aged ≥60 years. Of these, 379 (41.2%) reported msVMS bother. Women with msVMS were more likely to have a history of nonspontaneous menopause and report their health as fair. Women reporting current use of hormone therapy (21%) were less likely to report msVMS than women not taking hormone therapy.

Comment (HR): VMS (hot flushes or night sweats) are normal during the menopause transition and affect around 80% of women. The mechanisms of vasomotor symptoms are poorly understood, but are thought to reflect disturbances of the hypothalamic thermoregulatory system after oestrogen exposure then withdrawal. The results of this study show that 41% of women over the age of 60 years were still having flushes. The SWAN longitudinal study in 2015 also suggested that for some women flush duration was longer than originally thought. It found the average duration of VMS to be around 7.4 years and those who start flushing before their final menstrual period may have the most persistent symptoms. Around 10% have symptoms lasting for as long as 12 years and symptoms may persist for many decades in some women. What would be the safest combination of hormone therapy for these older women? Transdermal oestrogen (Estradot® 25mcg patch) will not have the same venous thromboembolism or stroke risk as oral oestrogen. For those women with a uterus who require endometrial protection then oral Utrogestan® 100mg has been shown to have less breast cancer risk than progestogens.

Reference: Menopause 2018;25(10):1105-9
Abstract

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) Fellows may claim 1 PD point per hour in the 'Self-Education' component of any of the three domain for any self-educational O&G activities completed (including reading of relevant Research Reviews).

Prescribing bioidentical menopausal hormone therapy: a survey of physician views and practices

Authors: Dubaut J et al.

Summary: This US study investigated prescribing practices for compounded bioidentical menopausal hormone therapy (MHT). An internet-based 38-item survey was sent to 1349 obstetrician-gynaecologists and family medicine physicians in Kansas; 164 (12.2%) responded to the survey, and 128 (9.5%) responses were included in the final analysis. In the past year, 96.1% of respondents had prescribed conventional MHT, 93.0% had prescribed FDA-approved bioidentical MHT, and 66.1% had prescribed compounded bioidentical MHT. When asked about factors influencing MHT-prescribing practices, 16.7% of physicians felt that FDA regulation was not important and 68.5% felt that customisation was important.

Comment (HR): While there may be varying levels of disagreement regarding prescribing compounded hormones, for many women cost will be the deciding factor. Compounded hormones are expensive. When I last looked, progesterone cream was around $91 for 3 months' supply and Biest cream was $153. This compares to $5 for a 3-month prescription for Progynova®, Estradot® patch or Provera® tablets. If a woman really wants bioidentical hormones she could be prescribed Estradot® patch (17-ß oestradiol) along with oral Utrogestan® (progesterone). The latter isn't subsidised and will be about $82 for 3 months.

Reference: J Womens Health (Larchmt) 2018;27(7):859-66
Abstract

Twelve-month discontinuation rates of levonorgestrel intrauterine system 13.5 mg and subdermal etonogestrel implant in women aged 18–44

Authors: Law A et al.

Summary: This retrospective analysis investigated 12-month discontinuation rates for LNG-IUS 13.5mg and subdermal etonogestrel implant in the US. Women aged 18–44 years who had an LNG-IUS or etonogestrel implant inserted were identified from the MarketScan Commercial claims database. They were required to have 12 months of continuous insurance coverage prior to the insertion (baseline) and for at least 12 months after (follow-up). A total of 3680 LNG-IUS and 23,770 etonogestrel implant users met the selection criteria. Prior to insertion, 56.6% and 42.1% of the respective users had used contraceptives, with oral contraceptives being most common. Rates of discontinuation were similar during the 12-month follow-up (24.9% for LNG-IUS and 24.0% for etonogestrel implant).

Comment (HR): This study shows similar discontinuation rates at one year (24/25%) for the small IUS (Jaydess®) and the etonogestrel implant (Implanon®/Nexplanon®). Compared to Mirena®, Jaydess® has a lower total levonorgestrel content (13.5mg vs 52mg), a shorter maximum on-label duration of use (3 years vs 5 years), a smaller T-frame (28×30mm vs 32×32mm) and a smaller diameter placement tube (3.8mm vs 4.4mm). Jaydess® can be distinguished from Mirena® by ultrasound as the device has a silver ring just below the transverse arms. However, what this study does not tell us is the reasons for discontinuation – "discontinuation cannot be accurately obtained from the data source". One reason for stopping use is of course irregular bleeding and we need to support women to return as soon as this is a problem. Early intervention such as use of the combined pill for a few months can be helpful to promote continuation of the method. Previous studies have shown that younger women are more likely to discontinue these methods and they may need extra discussion at insertion regarding potential irregular bleeding and how it can be helped.

Reference: Contraception 2018; published online Apr 21
Abstract

Pain is an independent risk factor for failed global endometrial ablation

Authors: Cramer M et al.

Summary: This retrospective cohort study determined whether pain is an independent risk factor for failure of global endometrial ablation. 5818 women who underwent an endometrial ablation with radiofrequency ablation (63.7%), hydrothermablation (30.7%), or uterine balloon ablation (5.6%) in 2003–2015 at an academic-affiliated community hospital were included in the analysis. Of the 5818 ablations, 7.5% involved pain (i.e., pelvic pain, dysmenorrhoea, dyspareunia, lower abdominal pain, endometriosis, or adenomyosis) before ablation, in addition to abnormal uterine bleeding. Pain as part of the preoperative diagnoses before endometrial ablation was a significant risk factor for subsequent hysterectomy compared with all other diagnoses (19.2% vs 13.5%; p=0.001).

Comment (AS): This study adds further evidence to the notion that endometrial ablation is mainly indicated for the treatment of abnormal uterine bleeding and not as successful if pelvic pain is a cofactor. The numbers reviewed were high and it was quite clear that pre-existing pelvic pain was associated with higher chances of subsequent hysterectomy for 'failed endometrial ablation'. Indeed the indications for hysterectomy were more likely to include pelvic pain. Whilst endometrial ablation offers significant advantages over hysterectomy including reduced morbidity and a much quicker recovery, women with pelvic pain, including adenomyosis or endometriosis (whether known or suspected) should be appropriately counselled regarding the likely outcomes including efficacy and failure rate with endometrial ablation. That's not to say it is necessarily contraindicated as there was still a 'success' rate for ablation of over 80% for women with pre-existing pelvic pain.

Reference: J Minim Invasive Gynecol 2018;25(6):1018-23
Abstract

Effectiveness of a continuous-use ring-shaped vaginal pessary without support for advanced pelvic organ prolapse in postmenopausal women

Authors: Dueñas J & Miceli A

Summary: This prospective Spanish study investigated the efficacy of a continuous-use ring pessary without support for the treatment of advanced POP. 94 non-hysterectomised postmenopausal women with symptomatic POP (stages III and IV) were fitted with a vaginal pessary at Macarena Hospital in Spain in 2013–2015. During a median 27-month follow-up, pessary use was continued by 80.8% of patients. Half of the discontinuations occurred within the first week after device insertion. Complications included extrusion of the pessary (18.4%), bleeding or excoriation (10.5%), and pain or vaginal discharge (2.6%). No major complications were reported.

Comment (AS): This prospective study showed a relatively high rate of successful use of ring pessaries by non-hysterectomised patients with significant prolapse. There was a remarkably high compliance shown, with around 80% ongoing use and a low rate of pain/discharge (2.6%). It did fall out in around 1/5 patients (usually with defaecation). Around 10% have vaginal bleeding. No specific mention was made regarding sexual activity and pessary-caused dyspareunia and hispareunia. Almost all patients were said to have mild stress urinary incontinence but said to respond to pelvic floor exercises (I believe this needed better assessment for study purposes). In summary, ring pessaries seemed to be well tolerated and a reasonable alternative to surgery in many women. The general time interval for pessary removal/replacement or change was 6 months. The issue of sexual function and patient approval of a long term 'forever' management plan also needs clarification.

Reference: Int Urogynecol J 2018;29(11):1629-36
Abstract

Fatigue – a symptom in endometriosis

Authors: Ramin-Wright A et al.

Summary: This multicentre case-control study in Switzerland, Germany and Austria investigated whether fatigue is a common symptom of endometriosis. 560 women with endometriosis were matched with 560 women without endometriosis. Frequent fatigue was experienced by approximately half the women with endometriosis (50.7%) compared with 22.4% of controls (p<0.001). Fatigue in endometriosis was associated with insomnia (odds ratio [OR], 7.31; p<0.001), depression (OR, 4.45; p<0.001), pain (OR, 2.22; p<0.001), and occupational stress (OR, 1.45; p=0.037), but was independent of age, time since first diagnosis and stage of the disease.

Comment (AS): Fatigue is a common symptom of this common disease. This case-control study found that 'frequent fatigue' was prevalent in over 50% of women with surgically and histologically diagnosed endometriosis against 22% of women in the control group. The association between endometriosis and fatigue remained after controlling for confounders including pain, insomnia, stress at work, depression, raised BMI and motherhood. However, given the significant chance of women with endometriosis having frequent fatigue, it would be worthwhile targeting fatigue with alternate approaches as well as appropriate medical/surgical interventions. These could include widespread lifestyle changes including exercise, nutrition review, sleep medicine, and counselling to name a few.

Reference: Hum Reprod 2018; published online Jun 26
Abstract

Independent commentary provided by
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Having delivered over 5,000 babies, Anil now works in gynaecology and colposcopy from Ascot Central and Ascot Hospital.
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