DRAFT 5

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Program title: Zoely (NOMAC/E2) – The choice of natural estrogen in combination with nomegestrol acetate for oral contraception.

Audience:

Primary: Obstetricians/gynaecologists

Secondary: GPs

Tertiary: Pharmacists/nurses

Format: Product Brief – single edition newsletter:

- 1 issue (15 mins reading time)
- This Product Brief is unaccredited

Faculty:

1. A/Prof Gino Pecoraro – Obstetrician & Gynaecologist

2. Dr Ginni Mansberg – GP, Women's Health Advocate

Introduction

Contraceptive choices for Australian women

The combined oral contraceptive (COC) pill is the most commonly-used contraceptive method among Australian women.[1,2] When taken correctly, COCs have a high rate of efficacy.[2] Clinicians can, at times, find it challenging to choose between the various formulations as the choices seem innumerable and interchangeable.[2] Clinically-consequential differences do, however, exist between the various formulations of COCs. It is therefore important that providers utilise shared decision-making in choosing the right COC to address patient preferences, health risks and patient concerns.[3]

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What are the common health risks and patient concerns with the use of COCs?

Health risks in women of reproductive age who request COCs may include cardiovascular disease, hypertension, venous thromboembolism, migraine, and diabetes mellitus.[2] Zoely (nomegestrol acetate [NOMAC]/17β-estradiol/ - E2) is a formulation with a good safety profile that may allow for use in patient groups in which COCs may have been previously avoided.[4]

Concerns voiced by women who request COCs include acne, weight gain, headaches, breakthrough bleeding, breast tenderness, nausea, pre-menstrual symptoms and contraceptive reliability.[3] Patient education can cover the message that contraceptive reliability is based largely on correct use of COCs and these symptoms generally improve with increasing length of COC use.[3]

It is important to keep in mind that the majority of studies that assess COCs are limited to women aged 18 to 50 with a body mass index (BMI) between 17 and 35 kg/m^2.[5] As such, prescribing practices should note these patient parameters.

The unique approach of nomegestrol acetate and 17β-estradiol (NOMAC/E2)

Most oral contraceptives available today contain ethinyl estradiol (EE).[6] EE is a manufactured, synthetic estrogen. In contrast, a natural form of oestrogen- 17β-estradiol (E2), is structurally and biologically identical to human oestrogen and believed to have fewer adverse effects than EE.[7,8] In the past, 17β-estradiol was recognised as causing significant irregular bleeding, which has been avoided by combining it with a potent progestogen, such as nomegestrol acetate (NOMAC).[7] Oestrogen primarily stabilises the bleeding pattern, while progestogen provides the major contraceptive effect.[9] Zoely is the only COC available in Australia containing 17β-estradiol combined with NOMAC (NOMAC/E2).[10]

A significant benefit of the NOMAC/E2 combination is that it minimises the risk of breakthrough bleeding.[11] The mean number of days of vaginal bleeding or spotting with a NOMAC/E2 combination pill is markedly reduced compared to an EE-containing COC, as shown below.[5]

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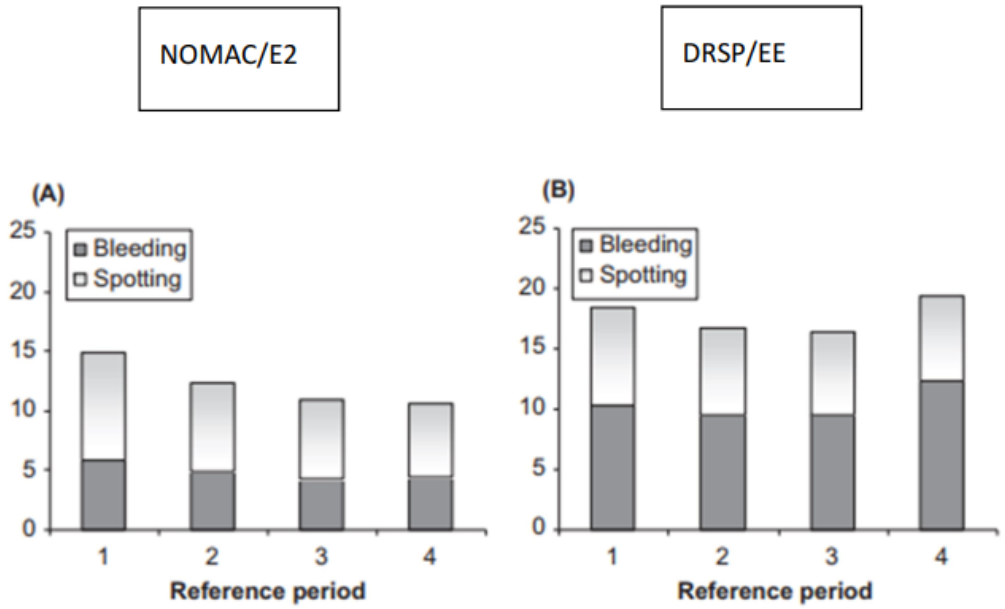

Note to MDBC designer: under each of the 4 columns for both graphs (currently showing '1,2,3,4') lower axis should read:

"Day 1-91" "Day 92-182" "Day 182-273" , "Day 274-364"

Figure 1: Mean number of bleeding-spotting days per 91-day reference periods for (A) NOMAC/E2 acetate and (B) drospirenone/ethinylestradiol (EE/DRSP). [[MDBC to seek permission to reproduce copyright material]]

17β-estradiol may show evidence for a more favourable cardiovascular risk profile compared to LNG/EE and DRSP/EE formulations, paving the way for better safety profile in the use of oral contraception.[12] NOMAC/E2 exhibits less metabolic impact compared to other COCs, and specifically demonstrates no clinically-relevant effect on glucose and lipid metabolism.[12] A low metabolic impact experienced with NOMAC/E2 may be more favourable for patients with elevated cardiovascular and diabetic risk profiles, providing contraceptive choice for these women. An additional benefit of NOMAC/E2 in these patient populations is the avoidance of unplanned pregnancy due to its contraceptive efficacy.[5]

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In addition, the NOMAC/E2 combination showed statistically significant favourable results on haemostatic markers compared to the traditional EE/LNG, making it a promising option to avoid increasing venous thromboembolic risk associated with other COC use.[4,12]

The progestogen NOMAC is metabolically neutral in that NOMAC/EE demonstrated no effect on glucose tolerance and insulin sensitivity, no clinically-relevant effects were observed on lipid metabolism and haemostasis.[7,8] There is clinical evidence to show NOMAC/E2 on acne, and in one study, the COC NOMAC/E2 demonstrated marked improvement on acne through its anti-androgenic effect.[5] The NOMAC/E2 combination also demonstrated no effect on blood pressure or body weight.[5]

NOMAC/E2 COC provides a 24 hour missed pill window compared to 12 hours in the majority of available COCs, due to the long half-life of 46 hours for NOMAC.[2] Evidence suggests up to 60% of COC users report irregular pill use, therefore a formulation with a longer half-life can reduce failure rates.[2] This provides improved contraceptive assurance and it is more forgiving of missed pill events.[2] This feature can be reassuring for clinicians and patients alike.

How does a 24/4 monophasic regimen benefit your patient?

COC formulations are either monophasic or multiphasic, and feature a combination of varying doses of oestrogen and progestogen, each with its own set of potential benefits for the individual patient.[6] Monophasic COCs are more commonly chosen initially, as multiphasic pills require more careful adherence to the specific sequence of pills in each cycle and cannot be adjusted for extended use.[3]

When asked about their cycle, the majority of women report they would prefer a shorter, light menses and/or amenorrhea.[13] Compared to the traditional 21/7 COC regimen, there is a trend in favour of a 24/4 regimen, which provides a shorter duration of lighter withdrawal bleeding, addresses the concerns of menorrhagia and dysmenorrhoea,[3,8] as well as inducing fewer cycle-related symptoms, such as bloating, headaches and breast tenderness.[2,7] It is important to remind patients that breakthrough bleeding and irregular bleeding will improve over time with use of COCs.[9]
Importantly, the 24/4 regimen provides a shortened hormone-free interval which has evidence of increased efficacy through improved ovarian suppression.[2,7] A short hormone-free interval results in lighter and shorter bleeding, and less hormone-withdrawal symptoms related to COC use.[11] For some women, this can lead to complete amenorrhoea with ongoing use.[5,8]

The 24/4 monophasic regimen has demonstrated a well-accepted safety and tolerability profile that may benefit a wide patient population.[5,7]

ZOELY – a modern choice in oral contraception

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- A well-accepted safety, efficacy and tolerability profile for a wide patient population[7]
- 24/4 monophasic regimen induces lighter, shorter vaginal bleeding with increased contraceptive assurance, compared with other COC formulations[2,12]
- Benefits of a lower impact on haemostasis parameters[12]
- Neutral effect on cardiovascular and carbohydrate metabolism parameters[12]
- Improvement in acne[5]

Take home message:

Zoely is a unique, modern oral contraceptive, combining the specific biological advantages of both natural oestrogen and the long-acting metabolically neutral progestogen (NOMAC) in the form nomegestrol acetate and 17β-estradiol.

The fresh and purpose-built design of this product means Zoely users can expect shorter episodes of vaginal bleeding with less intermenstrual bleeding and measurable improvement in acne.

By using the body's own 17β-estradiol, Zoely is able to avoid the negative cardiovascular and carbohydrate metabolic effects of traditional artificial oestrogen-containing contraceptives.

In addition to proven contraceptive efficacy, Zoely has the enviable distinction of offering a 24 hour missed pill window compared with the shorter 12 hour window associated with older contraceptives.

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