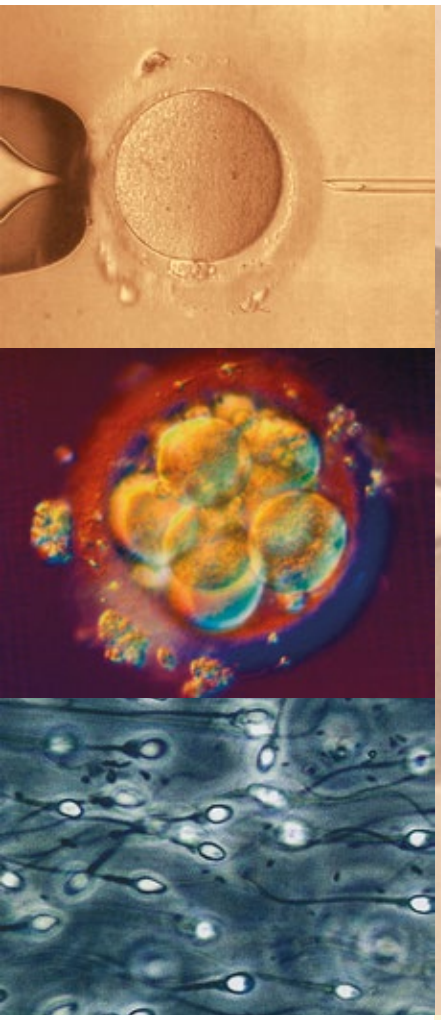
Journal für

Reproduktionsmedizin und Endokrinologie

– Journal of Reproductive Medicine and Endocrinology –

Andrologie • Embryologie & Biologie • Endokrinologie • Ethik & Recht • Genetik
Gynäkologie • Kontrazeption • Psychosomatik • Reproduktionsmedizin • Urologie



Contraception in Obese Women

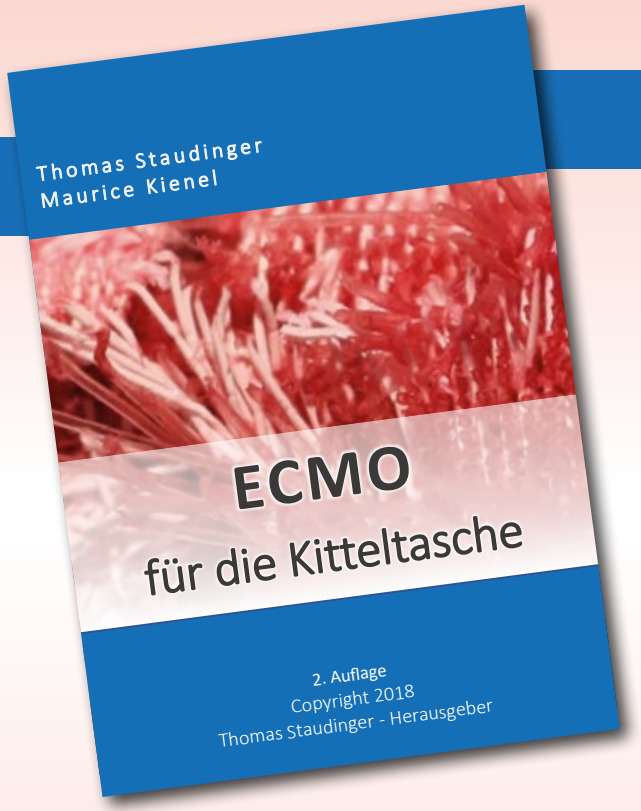
Merki Feld G

J. Reproduktionsmed. Endokrinol 2015; 12 (4), 241-245

Offizielles Organ: AGRBM, BRZ, DVR, DGA, DGGEF, DGRM, DIR, EFA, OEGRM, SRBM/DGE

Indexed in EMBASE/Excerpta Medica/Scopus

Krause & Pachernegg GmbH, Verlag für Medizin und Wirtschaft, A-3003 Gablitz



Ab sofort in unserem Verlag

Thomas Staudinger
Maurice Kienel

ECMO

für die Kitteltasche

2. Auflage Jänner 2019
ISBN 978-3-901299-65-0
78 Seiten, div. Abbildungen
19.80 EUR

Krause & Pachernegg GmbH

Bestellen Sie noch heute Ihr Exemplar auf

www.kup.at/cd-buch/75-bestellung.html

Contraception in Obese Women

G. S. Merki-Feld

Today obesity is an epidemic. Within Europe the prevalence of obesity is 20–30% with a tendency to increase further. Obesity is associated with severe complications like diabetes mellitus, cardiovascular disease increased risk for venous thromboembolism (VTE) and metabolic syndrome. Especially availability of efficient methods which do not further enhance the cardiovascular and thromboembolic risk in obese women is an important point. Using contraception to prevent unwanted pregnancies is recommended to all women whatever their weight, as it reduces the risks of unplanned pregnancy, which is higher in women with overweight. Progestin-only contraceptives and IUDs have no or minimal metabolic effects and are first choices options, also it has to be taken in account that oral progestins and the implant might have lower efficacy in very obese women. CHC are associated with a higher risk for VTE in obese women,but should be used if other methods are not acceptable. A long-cycle or use of preparations with 30 mcg EE can contribute to improve efficacy. **J Reproduktionsmed Endokrinol_Online 2015; 12 (4): 241–4.**

Key words: contracepiton, obesity, cardiovascular risk, contraceptive pill, vaginal ring

Introduction

Today obesity is an epidemic. Within Europe, the prevalence of obesity is 20–30% with a tendency to increase further. Understanding the influence of body weight on contraceptive effectiveness is critical for health-care professionals. Obesity is associated with severe complications like diabetes mellitus, cardiovascular disease, increased risk for venous thromboembolism (VTE) and metabolic syndrome. Pregnancies can be associated with severe morbidities for the mother and the unborn child. Consequently use of safe and effective contraceptive methods is of paramount importance. Not only epidemiology of obesity differs across continents, but also compliance with contraception and availability and access to the variety of contraceptive methods. Availability of efficient methods which do not further enhance the cardiovascular and thromboembolic risk in obese women is not given everywhere. In 2014 the *European Society for Contraception* published a statement for the use of contraception in obese women [1].

Definition of Obesity

Obesity is defined based on body mass index (BMI kg/m^2). The degree of adiposity associated with a given level of BMI varies by age, sex, and racial and ethnic group. Although BMI is not a perfect indicator of body fat, it is reliable, inexpensive and easy to perform in a clinical setting. BMI categories are defined by the Centers for Disease Control (CDC) and Prevention and the World Health Organization (WHO) [2, 3] as

- Underweight < 18.5 kg/m^2
- Normal 18.5–24.9 kg/m^2
- Overweight 25–29.9 kg/m^2
- Obese 30–39.9 kg/m^2 or Class I obesity 30–34.9 kg/m^2/Class II obesity 35–39.9 kg/m^2
- Very obese ≥ 40 kg/m^2 or otherwise referred to as severe, extreme, morbid or Class III obesity

Combined Hormonal Contraceptives (CHC)

CHC do not typically cause weight increase [4]. There is a controversial discussion about the efficacy of these methods in obese women and there is concern with regard to safety (thromboembolic and cardiovascular risk) especially in CHC containing ethinylestradiol (EE). Recently published pharmacokinetic studies in obese women have improved our understanding of potential efficacy problems.

Efficacy of Combined Hormonal Pills, Ring and Patch in Obese Women

Observational studies have reported a higher failure rate of CHCs in overweight women [5, 6]. In contrast a large randomized trial including patients with BMI > 25 kg/m^2 was associated with a non-significantly increased relative risk for pregnancy (1.4 and 1.8) in women using the oral contraceptives (OC) under investigation [7]. An important limitation of this study with regard to obesity is the exclusion of women with BMI > 32.4 kg/m^2. The conclusion of a Cochrane Review addressing this issue was that there is no general evidence of an association between BMI and decreased efficacy with COCs, but the quality of available studies is limited [8].

Pharmacokinetic studies should help to clarify this issue. The pharmacokinetics of COCs in obese women have been studied for a pill containing EE 30 mcg/levonorgestrel (LNG) 150 mcg and a lower dosed COC (EE 20 mcg/LNG 100 mcg) [9, 10]. With the higher-dose COC, lower maximal values for EE but not LNG levels were found in the obese group in one study (BMI 30–39.9 kg/m^2), however, this did not translate into more ovarian follicular activity [9]. For the 20 mcg EE/100 mcg LNG pill a study over the whole pill cycle (mean BMI 39.9 kg/m^2) demonstrated delayed time to reach steady-state of the progestin concentration after the hormone-free interval [10, 11]. Interestingly the changes in half-life of LNG and time to reach steady-state in obese women were not correlated with follicular suppression in ovary. These findings in addition to the high interindividual variability in plasma levels (ranging from 24–62%) make it difficult to decide in individual cases what might be the adequate hormonal dosage for an obese individual. A recently published study compares dosages of 20 mcg EE/100 mcg LNG in a long cycle with 30 mcg EE/

Received and accepted: February 23rd, 2015

From the Clinic for Reproductive Endocrinology, Zürich

Correspondence: PD Dr. Gabriele S. Merki-Feld, Clinic for Reproductive Endocrinology, Department of Gynaecology and Obstetrics, University Hospital, CH-8091 Zürich, Frauenklinikstraße 10; e-mail: gabriele.merki@usz.ch

150 mcg LNG in an intermittend regimen (21/7) [10]. Also in this study time to reach steady-state was significantly longer in obese women in comparison to normal weight controls. Plasma levels of the hormones however were higher with the 30 mcg EE/150 mcg LNG regimen. Even if changes in pharmacokinetics did not correlate with end-organ suppression the women using the higher dosage experienced better ovarian suppression. However, both regimen were with regard to pharmacokinetic parameters superior in comparison to an intermittend 20 mcg EE/100 mcg LNG regimen. These data allow only cautious and preliminary recommendations with regard to COC use in obese patients:

- Pharmacokinetic data are only available for COCs containing the progestin levonorgestrel.
- Use condoms for 10–14 days in COC newstarters until steady-state is achieved.
- 30 mcg EE/150 mcg LNG might be more effective than 20 mcg EE/100 mcg LNG.
- Continuous use of 20 mcg EE/100 mcg LNG is better than a 21/7 regimen, but breakthrough bleeding has to be taken into account and should not limit compliance.

It seems reasonable to postulate that extended-regimen is an option to reduce contraceptive failures in obese women. Prospective studies on extended-cycle preparations in normal weight populations do not indicate an increased efficacy [12, 13]. Across European countries extended regimen are off-label. A disadvantage of these regimen is the unpredictable bleeding pattern, which might further compromise adherence in less compliant women.

Ethinylestradiol serum levels are lower in obese women in comparison to normal weight controls with use of the combined hormonal contraceptive vaginal ring (CVR) (EE/etonogestrel) [14]. Etonogestrel levels, which are believed to be of higher importance for the efficacy of CHC do not differ and are maintained over more than 4–6 weeks of use, in a range higher than with the use of the etonogestrel-releasing contraceptive implant. Follicular development was minimal in both groups [15]. These results are reassuring that the CVR is effective in obese women. For the combined contraceptive patch no kinetic data in obese women are available. However, in an observational study increased body weight was associated with an increased rate of pregnancy. The higher pregnancy rate affected women with a weight of ≥ 90 kg (≥ 198 lb) [6]. Potentially variations in the plasma levels of the steroids norelgestromin and ethinylestradiol between obese and normal weight users cause the increased pregnancy rate. The patch study included women of a wider range of body weights (± 35% ideal body weight) than most CHC studies (± 20% ideal body weight) [6]. Therefore, it remains unclear if there is indeed a difference between the patch and COCs with regard to efficacy in women ≥ 90 kg. Nevertheless, the patch label indicates a cut-off of ≥ 90 kg (≥ 198 lb) as a concern for increased failure risk.

Safety of CHC: Risk for VTE and Arterial Events in CHC Users

Baseline risk for VTE in obese women ranges from 6–11/10,000 women years (WY) [16–19]. The risk is 2–4 fold increased in comparison to normal weight women and increases further with age [20–23]. Age has to be considered as a strong additional risk factor for VTE in obese and non-obese women [16, 18]. In obese or very obese women the VTE risk is 2–3-fold in comparison to normal weight CHC users [22, 24].

Long-term use of CHC does not induce atherosclerosis in animal models [25]. Previous studies indicated that CHC with desogestrel and gestodene might be associated with a lower increase in cardiovascular risk in comparison to COCs containing levonorgestrel (LNG) [26]. This could not be confirmed in a recent cohort study [27]. There were only minor risk variations between the patch and the vaginal ring and combined pills. In a large prospective cohort study, vaginal ring use and combined COC use were associated with a similar risk of arterial thromboembolic events (ATE) [28]. Obesity was associated with an additional 1.5–4.2 fold increased risk for ischemic stroke in users of CHC [18, 29]. There is no clear evidence whether obese women have an increased risk of myocardial infarction [24].

CHC do further increase the risk for VTE and ATE in obese women. Therefore they should only be used if no other acceptable contraceptive methods like progestin-only contraceptives or intrauterine devices are available or acceptable – or if benefits still outweigh the risks [1]. Obese women should be informed of their risk of thrombosis and should be counseled on the added risk of taking combined hormonal contraceptives.

Progestin-Only Methods

Progestogen-only contraceptives (POC) include progestogen-only pills (POP) with norethisterone, levonorgestrel or desogestrel; levonorgestrel-releasing intrauterine systems (LNG-IUS); injections with depot-medroxy-progesterone acetate and subcutaneous implants releasing etonogestrel or levonorgestrel. From the standpoint of venous and arterial thrombosis, progestin-only agents are the safest hormonal methods [30]. The mode of action ranges from full ovulation suppression to a local barrier to sperm transport by increasing viscosity of cervical mucus. Non-contraceptive benefits of the LNG-IUS and depot-medroxy-progesterone acetate include the reduction of the intensity and duration of menstrual bleeding, inhibition of the growth of myoma and a positive effect on endometriosis [31–34]. A special benefit of the desogestrel-only pill is a positive effect on menstrual migraine, as well as non-menstrual migraine headaches [35–37]. A disadvantage of DMPA is the unpredictable weight-gain in a subset of women [38]. There is limited evidence of weight-gain in users of progestin-only pills [39]. This drawback and the unpredictable bleeding pattern of most POC may limit the acceptability of these methods in some women. There is limited data on the efficacy of Desogestrel 75mcg in obese women. This might restrict the use. Ovarian ultrasound might help the clinician to decide whether an obese patients is sufficient protected from pregnancy with this pill. Desogestrel 75 mcg is not associated with an increased risk for thromboembolic events or arterial embolic events [27–40]. The impact of desogestrel 75 mcg on plasma lipids and glucose metabolism is minimal [41, 42].

In the CHOICE study the efficacy of the etonogestrel-releasing implant was not reduced in obese women [43]. Plasma levels of etonogestrel (ENG) are lower in

obese women and come close to the concentration, which is necessary to effectively prevent ovulation [44–46]. As individual plasma levels vary widely the implant might not be efficient in all obese women over the duration of three years. Preliminary epidemiologic data do not suggest an increased risk for thrombotic stroke or myocardial infarction with this implant [27]. Even if epidemiologic and clinical data at present do not indicate a decreased efficacy in obese women caution is recommended. As etonogestrel plasma levels decline over time an earlier replacement of the implant after 24 months instead of 36 months may be considered in some obese women.

Several studies found that depot-medroxyprogesterone acetate (DMPA) intramuscular and subcutaneous (sc) are highly effective in normal weight and overweight women [47, 48]. Jain et al demonstrated no difference in efficacy in obese DMPA-sc users, but showed a trend towards decreasing through MPA levels as the BMI increases [49, 50]. This observation caused uncertainty in regard to the effectiveness in women with BMI > 35 kg/m^2. DMPA is frequently used all over the world in women with obesity and other cardiovascular risk factors. Hemostatic risk markers do not indicate changes and therefore do not suggest an increased risk for VTE [51]. One observational study reported an elevated VTE risk with DMPA, but was limited by a small number of cases [52]. DMPA-intramuscular and sc are effective contraceptives in overweight and obese women. When balancing risks vs. benefits of this contraceptive method it should be considered, that in comparison to CHC, safety and efficacy of DMPA are higher.

Intrauterine Devices (IUD) and Intrauterine Systems (IUS)

Copper-IUD or the levonorgestrel-releasing device are highly recommended efficient and safe options in obese women.

Copper-IUDs do neither affect metabolic parameters, nor the risk for VTE. They are highly efficient and efficacy is not affected by weight or BMI, because the contraceptive acts locally in the uterus [43, 53]. Contraindications (CI) like ongoing pregnancy, uterus malformation, active pelvic inflammatory disease must be excluded. Increased STD risk, hysterometer > 9 cm and nulliparity need precautions before prescription and insertion and have to be weighed against other benefits. With the levonorgestrel-releasing device LNG-plasma levels are lower in obese women in comparison to non-obese [54]. Because of the local effects of this system in the uterine cavity the efficacy should not be compromised in obese women. The system is not associated with an increased risk of VTE [40]. In an observational study the removal rate was > 20 % in obese women [55]. For women with heavy menstrual bleeding the IUS is the better option.

Emergency Contraception (EC)

Insertion of a copper-IUD is the most efficient method for EC, but access is not available everywhere, the insertion is uncomfortable and costs are high. Many women who demand EC are not at high risk for a pregnancy and in those cases IUD-insertion might be an overtreatment. Ulipristal-acetate (UPA) 30 mg, a progesterone-receptor modulator, appeared superior to Levonorgestrel (LNG) 1.5 mg, especially when administered after the LH surge and between 72 and 120 h following unprotected intercourse [56, 57]. Besides the lower pregnancy rate the longer window for use and the higher capacity to prevent ovulation in the presence of follicles measuring 18–20 mm are important additional advantages of UPA [58]. Side effects are similar with both methods [59]. One meta-analysis indicated that in obese women the efficacy of both methods is reduced, but the efficacy of LNG was more reduced than that of UPA (OR 4.4; CI: 2.0–9.4 vs OR 2.6; CI: 0.9–7.0) in comparison to women with normal BMI [59].

Conclusion

In summary using contraception to prevent unwanted pregnancies is recommended to all women whatever their weight, as it reduces the risks of unplanned pregnancy, which is higher in women with overweight. Progestin-only contraceptives and IUDs have no or minimal metabolic effects and are first choices options, also it has to be taken in account that oral progestins and the implant might have lower efficacy in very obese women. CHC are associated with a higher risk for VTE in obese women, but should be used if other methods are not acceptable. A long-cycle or use of preparations with 30 mcg EE can contribute to improve efficacy.

Conflict of Interest

During the past years G. S. Merki-Feld had financial relationship (lecturer, member of advisory boards and/or consultant) with Bayer-Schering Pharma, MSD and HRA Pharma.

References:

1. Merki-Feld GS, Skouby S, Serfaty D, et al. European society of contraception statement on contraception in obese women. Eur J Contracept Reprod Health Care 2015; 20: 19–28.

2. Oliveros E, Somers VK, Sochor O, Goel K, Lopez-Jimenez F. The concept of normal weight obesity. Prog Cardiovas Dis 2014; 56: 426–33.

3. The Centers for Disease control and Prevention. BMI categories, 2008. http://www.cdc.gov/nccdphp/dnpa/healthweight; http://wwwcdcgov/nccdphp/dnpa/healthweight.

4. Hani D, Imthurn B, Merki-Feld GS. [*Weight gain due to hormonal contraception: myth or truth?*]. Gynäkol Geburtshilfliche Rundsch 2009; 49: 87–93.

5. Holt VL, Scholes D, Wicklund KG, Cushing-Haugen KL, Daling JR. Body mass index, weight, and oral contraceptive failure risk. Obstet Gynecol 2005; 105: 46–52.

6. Zieman M, Guillebaud J, Weisberg E, Shangold GA, Fisher AC, Creasy GW. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: the analysis of pooled data. Fertil Steril 2002; 77: S13–S18.

7. Burkman RT, Fisher AC, Wan GJ, Barnowski CE, LaGuardia KD. Association between efficacy and body weight or body mass index for two low-dose oral contraceptives. Contraception 2009; 79: 424–7.

8. Lopez LM, Grimes DA, Chen M, et al. Hormonal contraceptives for contraception in overweight or obese women. Cochrane Database Syst Rev 2013; 4: CD008452.

9. Westhoff CL, Torgal AH, Mayeda ER, Pike MC, Stanczyk FZ. Pharmacokinetics of a combined oral contraceptive in obese and normal-weight women. Contraception 2010; 81: 474–80.

10. Edelman AB, Cherala G, Munar MY, et al. Prolonged monitoring of ethinyl estradiol and levonorgestrel levels confirms an altered pharmacokinetic profile in obese oral contraceptives users. Contraception 2013; 87: 220–6.

11. Edelman AB, Carlson NE, Cherala G, et al. Impact of obesity on oral contraceptive pharmacokinetics and hypothalamic-pituitary-ovarian activity. Contraception 2009; 80: 119–27.

12. Bonnema RA, Spencer AL. The new extended-cycle levonorgestrel-ethinyl estradiol oral contraceptives. Clin Med Insights Reprod Health 2011; 5: 49–54.

13. Anderson FD, Gibbons W, Portman D. Safety and efficacy of an extended-regimen oral contraceptive utilizing continuous low-dose ethinyl estradiol. Contraception 2006; 73: 229–34.

14. Westhoff CL, Torgal AH, Mayeda ER, et al. Pharmacokinetics and ovarian suppression during use of a contraceptive vaginal ring in normal-weight and obese women. Am J Obstet Gynecol 2012; 207: 39 e31–e36.

15. Dragoman M, Petrie K, Torgal A, Thomas T, Cremers S, Westhoff CL. Contraceptive vaginal ring effectiveness is maintained during 6 weeks of use: a prospective study of normal BMI and obese women. Contraception 2013; 87: 432–6.

16. Trussell J, Guthrie KA, Schwarz EB. Much ado about little: obesity, combined hormonal contraceptive use and venous thrombosis. Contraception 2008; 77: 143–6.

17. Nightingale AL, Lawrenson RA, Simpson EL, Williams TJ, MacRae KD, Farmer RD. The effects of age, body mass index, smoking and general health on the risk of venous thromboembolism in users of combined oral contraceptives. Eur J Contracept Reprod Health Care 2000; 5: 265–74.

18. Gronich N, Lavi I, Rennert G. Higher risk of venous thrombosis associated with drospirenone-containing oral contraceptives: a population-based cohort study. CMAJ 2011; 183: E1319–E1325.

19. van Hylckama Vlieg A, Helmerhorst FM, Vandenbroucke JP, Doggen CJ, Rosendaal FR. The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. BMJ 2009; 339: b2921.

20. Parkin L, Sweetland S, Balkwill A, Green J, Reeves G, Beral V. Body mass index, surgery, and risk of venous thromboembolism in middle-aged women: a cohort study. Circulation 2012; 125: 1897–904.

21. Wattanakit K, Lutsey PL, Bell EJ, et al. Association between cardiovascular disease risk factors and occurrence of venous thromboembolism. A time-dependent analysis. Thromb Haemost 2012; 108: 508–15.

22. Pomp ER, le Cessie S, Rosendaal FR, Doggen CJ. Risk of venous thrombosis: obesity and its joint effect with oral contraceptive use and prothrombotic mutations. Br J Haematol 2007; 139: 289–96.

23. Parkin L, Sharples K, Hernandez RK, Jick SS. Risk of venous thromboembolism in users of oral contraceptives containing drospirenone or levonorgestrel: nested case-control study based on UK General Practice Research Database. BMJ 2011; 342: d2139.

24. Shaw KA, Edelman AB. Obesity and oral contraceptives: a clinician's guide. Best Pract Res Clin Endocrinol Metab 2013; 27: 55–65.

25. Adams MR, Anthony MS, Manning JM, Golden DL, Parks JS. Low-dose contraceptive estrogen-progestin and coronary artery atherosclerosis of monkeys. Obstet Gynecol 2000; 96: 250–5.

26. Consensus conference on combination oral contraceptives and cardiovascular disease. Fertil Steril 1999; 71: 1S–6S.

27. Lidegaard O, Lokkegaard E, Jensen A, Skovlund CW, Keiding N. Thrombotic stroke and myocardial infarction with hormonal contraception. N Engl J Med 2012; 366: 2257–66.

28. Dinger J, Mohner S, Heinemann K. Cardiovascular risk associated with the use of an etonogestrel-containing vaginal ring. Obstet Gynecol 2013; 122: 800–8.

29. Kemmeren JM, Tanis BC, van den Bosch MA, et al. Risk of Arterial Thrombosis in Relation to Oral Contraceptives (RATIO) study: oral contraceptives and the risk of ischemic stroke. Stroke 2002; 33: 1202–8.

30. Edelman AB, Jensen JT. Obesity and hormonal contraception: safety and efficacy. Semin Reprod Med 2012; 30: 479–85.

31. Koh SC, Singh K. The effect of levonorgestrel-releasing intrauterine system use on menstrual blood loss and the hemostatic, fibrinolytic/inhibitor systems in women with menorrhagia. J Thromb Haemost 2007; 5: 133–8.

32. Bahamondes L, Petta CA, Fernandes A, Monteiro I. Use of the levonorgestrel-releasing intrauterine system in women with endometriosis, chronic pelvic pain and dysmenorrhea. Contraception 2007; 75: S134–S139.

33. Dinger J, Minh TD, Buttmann N, Bardenheuer K. Effectiveness of oral contraceptive pills in a large U.S. cohort comparing progestogen and regimen. Obstet Gynecol 2011; 117: 33–40.

34. Cheewadhanaraks S, Choksuchat C, Dhanaworavibul K, Liabsuetrakul T. Postoperative depot medroxyprogesterone acetate versus continuous oral contraceptive pills in the treatment of endometriosis-associated pain: a randomized comparative trial. Gynecol Obstet Invest 2012; 74: 151–6.

35. Merki-Feld GS, Imthurn B, Langner R, Sandor PS, Gantenbein AR. Headache frequency and intensity in female migraineurs using desogestrel-only contraception: a retrospective pilot diary study. Cephalalgia 2013; 33: 340–6.

36. Merki-Feld GS. Headache Frequency and Intensity in female Migraineurs using Desogestrel-only Contraception: A retrospective Pilot Diary Study. Cephalalgia 2013; 3: 340–6.

37. Nappi RE, Sances G, Allais G, et al. Effects of an estrogen-free, desogestrel-containing oral contraceptive in women with migraine with aura: a prospective diary-based pilot study. Contraception 2011; 83: 223–8.

38. Vickery Z, Madden T, Zhao Q, Secura GM, Allsworth JE, Peipert JF. Weight change at 12 months in users of three progestin-only contraceptive methods. Contraception 2013; 88: 503–8.

39. Lopez LM, Edelman A, Chen M, Otterness C, Trussell J, Helmerhorst FM. Progestin-only contraceptives: effects on weight. Cochrane Database Syst Rev 2013; 7: CD008815.

40. Lidegaard O, Nielsen LH, Skovlund CW, Skjeldestad FE, Lokkegaard E. Risk of venous thromboembolism from use of oral contraceptives containing different progestogens and oestrogen doses: Danish cohort study, 2001–9. BMJ 2011; 343: d6423.

41. Kivela A, Ruuskanen M, Agren U, Dieben T. The effects of two progrestogen-only pills containing either desogestrel (75 microgram/day) or levonorgestrel (30 microgram/day) on carbohydrate metabolism and adrenal and thyroid function. Eur J Contracept Reprod Health Care 2001; 6: 71–7.

42. Barkfeldt J, Virkkunen A, Dieben T. The effects of two progestogen-only pills containing either desogestrel (75 microg/day) or levonorgestrel (30 microg/day) on lipid metabolism. Contraception 2001; 64: 295–9.

43. Xu H, Wade JA, Peipert JF, Zhao Q, Madden T, Secura GM. Contraceptive failure rates of etonogestrel subdermal implants in overweight and obese women. Obstet Gynecol 2012; 120: 21–6.

44. Mornar S, Chan LN, Mistretta S, Neustadt A, Martins S, Gilliam M. Pharmacokinetics of the etonogestrel contraceptive implant in obese women. Am J Obstet Gynecol 2012; 207: 110 e111–e116.

45. Diaz S, Pavez M, Moo-Young AJ, Bardin CW, Croxatto HB. Clinical trial with 3-keto-desogestrel subdermal implants. Contraception 1991; 44: 393–408.

46. Ciangura C, Corigliano N, Basdevant A, et al. Etonorgestrel concentrations in morbidly obese women following Roux-en-Y gastric bypass surgery: three case reports. Contraception 2011; 84: 649–51.

47. Fotherby K, Koetsawang S. Metabolism of injectable formulations of contraceptive steroids in obese and thin women. Contraception 1982; 26: 51–8.

48. Smit J, Botha J, McFadyen L, Beksinska M. Serum medroxyprogesterone acetate levels in new and repeat users of depot medroxyprogesterone acetate at the end of the dosing interval. Contraception 2004; 69: 3–7.

49. Jain J, Jakimiuk AJ, Bode FR, Ross D, Kaunitz AM. Contraceptive efficacy and safety of DMPA-SC. Contraception 2004; 70: 269–75.

50. Jain J, Dutton C, Nicosia A, Wajszczuk C, Bode FR, Mishell DR, Jr. Pharmacokinetics, ovulation suppression and return to ovulation following a lower dose subcutaneous formulation of Depo-Provera. Contraception 2004; 70: 11–8.

51. Goldstein J, Cushman M, Badger GJ, Johnson JV. Effect of depomedroxyprogesterone acetate on coagulation parameter: a pilot study. Fertil Steril 2007; 87: 1267–70.

52. van Hylckama Vlieg A, Helmerhorst FM, Rosendaal FR. The risk of deep venous thrombosis associated with injectable depot-medroxyprogesterone acetate contraceptives or a levonorgestrel intrauterine device. Arterioscler Thromb Vasc Biol 2010; 30: 2297–300.

53. Winner B, Peipert JF, Zhao Q, et al. Effectiveness of long-acting reversible contraception. N Engl J Med 2012; 366: 1998–2007.

54. Seeber B, Ziehr SC, Gschliebetaer A, et al. Quantitative levonorgestrel plasma level measurements in patients with regular and prolonged use of the levonorgestrel-releasing intrauterine system. Contraception 2012; 86: 345–9.

55. Vilos GA, Marks J, Tureanu V, Abu-Rafea B, Vilos AG. The levonorgestrel intrauterine system is an effective treatment in selected obese women with abnormal uterine bleeding. J Minim Invasive Gynecol 2011; 18: 75–80.

56. Glasier AF, Cameron ST, Fine PM, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. Lancet 2010; 375: 555–62.

57. Creinin MD, Schlaff W, Archer DF, et al. Progesterone receptor modulator for emergency contraception: a randomized controlled trial. Obstet Gynecol 2006; 108: 1089–97.

58. T.C.f.D.C.a. Prevention (ed). Manual for the surveillance of vaccine-preventable diseases. 4th edition, Atlanta, USA, 2008.

59. Glasier A, Cameron ST, Blithe D, et al. Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel. Contraception 2011; 84: 363–7.

Mitteilungen aus der Redaktion

Besuchen Sie unsere Rubrik

☑ Medizintechnik-Produkte

Neues CRT-D Implantat
Intica 7 HF-T QP von Biotronik

Artis pheno
Siemens Healthcare Diagnostics GmbH

Philips Azurion:
Innovative Bildgebungslösung

Aspirator 3
Labotect GmbH

InControl 1050
Labotect GmbH

e-Journal-Abo

Beziehen Sie die elektronischen Ausgaben dieser Zeitschrift hier.

Die Lieferung umfasst 4–5 Ausgaben pro Jahr zzgl. allfälliger Sonderhefte.

Unsere e-Journale stehen als PDF-Datei zur Verfügung und sind auf den meisten der marktüblichen e-Book-Readern, Tablets sowie auf iPad funktionsfähig.

☑ Bestellung e-Journal-Abo