Optimizing
the estrogen dose in oral contraceptives

Edited by J. R. Newton and M. op ten Berg

The Parthenon Publishing Group
International Publishers in Medicine, Science & Technology

Casterton Hall, Carnforth,
Lancs, LA6 2LA, UK

120 Mill Road, Park Ridge,
New Jersey, USA

Published in the UK and Europe by
The Parthenon Publishing Group Ltd.
Casterton Hall
Carnforth, Lancs, LA6 2LA

Published in North America by
The Parthenon Publishing Group Inc.
120 Mill Road
Park Ridge
New Jersey, NJ, USA

ISBN 1-85070-445-7

Typeset by AMA Graphics Ltd., Preston, Lancashire
Printed and bound in Great Britain by
Butler & Tanner Ltd., Frome and London

Contents

7

Double-blind comparative acceptability study with two combined oral contraceptives containing 20 μg ethinylestradiol plus desogestrel or norethisterone acetate

P. Lammers, W. J. Atsma, M. van den Heuvel and J. Picard

INTRODUCTION

Since the introduction of the first combined oral contraceptive on the contraceptive market, in 1960, the dosage and type of its two components, estrogen and progestogen, have changed considerably. Experience accumulated over the years has demonstrated that dose-dependent metabolic alterations as well as side-effects are associated with the use of oral contraceptives, and these changes may be induced by either the synthetic estrogen or progestogen used in these preparations, or even by both[1–4]. Estrogen-mediated side-effects like increase in body weight, nausea, headache and breast tenderness have been extensively studied and well-documented.

More important, however, are the serious side-effects associated with the use of synthetic estrogens. The dosage of estrogen in the pill was found to be directly related to the occurrence of thromboembolic events[5]. As a result of this, the estrogen dose has been brought down to 35 or 30 μg ethinylestradiol per tablet which is most commonly used in low-dose preparations.

Several attempts have been made to reduce the estrogen dose even further. These attempts have been rendered unsuccessful because of a loss of efficacy, poor cycle control, and the emergence of undesirable metabolic alterations[3,6–12]. The latter were the result of the intrinsic androgenic effects of the progestogens used in combined oral contraceptives on lipid and carbohydrate metabolism, that were not counteracted any more by such low estrogen dosages.

The availability of new, highly selective progestogens with minimal intrinsic androgenicity, like desogestrel, has created the possibility of combining these with a dosage of 20 μg of ethinylestradiol.

The study presented is a double-blind acceptability study comparing a monophasic preparation of 20 μg ethinylestradiol plus 1000 μg norethisterone acetate, with a recently developed combination of 20 μg ethinylestradiol plus 150 μg of desogestrel.

MATERIAL AND METHODS

Five university centers in Belgium participated in the study. A total of 270 women entered the study after having given verbal consent. Selection was made with the help of an eligibility check list based on the following inclusion and exclusion criteria: subjects had to be in good physical and mental condition, of reproductive age, to have regular menstrual cycles, and to be normally exposed to the risk of pregnancy. Excluded were women for whom the generally accepted contraindications for hormonal contraception were applicable. The women were randomly assigned to a 6-month treatment with one of two monophasic preparations: a combination of 20 μg ethinylestradiol plus 150 μg desogestrel (Mercilon®), or a combination of 20 μg ethinylestradiol plus 1000 μg norethisterone acetate (Loestrin-20®, Minestril-20®). The preparations were administered orally in a 28-day cyclic regimen, 3 weeks on medication followed by 1 week off.

Each woman was provided with a calendar on which she was instructed to record tablet-taking days as well as bleeding episodes. Bleeding episodes were subdivided into:

(1) Bleeding: any bleeding requiring more than one sanitary towel per day; and

(2) Spotting: a scanty bleeding requiring no or only one sanitary towel per day.

Bleeding cards were reviewed at each return visit, after the first, third and sixth cycle of treatment, respectively. Also the occurrence of side-effects was recorded and blood pressure and body weight were measured.

In the statistical analysis the following parameters were used for cycle control assessment:

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.