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Original research article

Comparison of rates of and charges from pregnancy complications in users of extended and cyclic combined oral contraceptive (COC) regimens: a brief report☆

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Abstract

Objective: To evaluate pregnancy complication rates and related charges in users of 84/7, 21/7 and 24/4 combined oral contraceptives (COCs).
Study design: Data were obtained from the i3 InVision Data Mart™ retrospective claims database. Subjects were aged 15–40 years, first prescribed a COC between 1/1/2006 and 4/1/2011 and continuously insured for ≥ 1 year. 84/7 users were matched 1:1 to 21/7 and 24/4 users.
Results: Pregnancy-related complication rates and associated charges were significantly lower with 84/7 vs. 21/7 and 24/4 regimens.
Conclusion: Preliminary data suggest 84/7 regimens may be associated with fewer pregnancy complications and lower related charges.

Keywords: Hormonal contraception; Pregnancy rates; 84/7, 21/7, 24/4 regimens

1. Implications statement

In this analysis of data from a retrospective claims database, rates of pregnancy complications and related charges were lower with 84/7 regimens vs. 21/7 and 24/4 COC regimens, suggesting that 84/7 regimens may be more efficacious and cost effective than traditional cyclic regimens.

2. Introduction

Extended 84/7 combined oral contraceptives (COCs), which provide 84 days of COCs plus 7 days of placebo pills or 7 days of low-dose estrogen in place of placebo, and 24/4 regimens, which reduce the number of hormone-free pills from 7 to 4, were designed to increase ovarian suppression and, possibly, improve contraceptive efficacy, compared with traditional 21/7 regimens [1,2]. Extended 84/7 COCs also reduce the number of annual withdrawal bleeds from 13 to 4 vs. 21/7 regimens [3].

Preliminary observational data suggest that unintended pregnancy rates are reduced with 24/4 vs. 21/7 regimens [4]. However, estimates of efficacy from different clinical studies of COC regimens, including extended 84/7 regimens, cannot be compared due to wide variations in COC trial design [5].

We recently conducted a retrospective observational analysis of insurance claims data to identify possible differences in real-world pregnancy rates among users of 84/7, 21/7 and 24/4 regimens, and we demonstrated that pregnancy rates were significantly lower with 84/7 regimens (4.4%) than with either 21/7 (7.3%) or 24/4 regimens (6.9%) at 1 year ($p<.0001$) [6]. Because rates of pregnancy complications are influenced by the frequency of pregnancy, we used the same database to compare rates of pregnancy-related complications as well as their related charges among users of 84/7 COCs vs. users of 21/7 and 24/4 COCs.

☆ Conflicts of interest: Brandon Howard is an employee of Teva Global Medical Affairs. Elizabeth Grubb is an employee of Teva Pharmaceuticals, Inc. Maureen Lage is the managing member of Health Metrics Outcomes Research and was compensated by Teva Branded Pharmaceutical Products, R&D for her work on this project.

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3. Materials and methods

Data for this study were obtained from the i3 InVision Data Mart™ database, a retrospective claims database that spans from January 1, 2006, through March 31, 2012. This database captures person-specific patient characteristics, enrollment dates, inpatient and outpatient medical claims and outpatient pharmaceutical claims throughout the US and is fully compliant with the Health Insurance Portability and Accountability Act.

Women were included in the study if they received a prescription for an 84/7 COC, a 21/7 COC or a 24/4 COC (with the first date of prescription identified as the index date), were aged 15–40 years as of the index date and had continuous insurance coverage from the index date through 1-year post-index date within the period of observation. The 84/7 cohort was matched to the 21/7 and 24/4 cohorts using 1:1 matching without replacement based on year of birth, region of residence, insurance business type, insurance product and year of index date. Mean scripts filled and mean days' COC supply were also evaluated for each cohort.

Complication rates were based on receipt of an *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code for the following pregnancy-related diagnoses: molar pregnancy, missed abortion, ectopic pregnancy, spontaneous abortion, hemorrhage in early pregnancy, placenta previa, placental abruption, hypertension complicating pregnancy, pre-eclampsia, eclampsia, hyperemesis gravidarum, preterm labor, gestational diabetes and premature rupture of membranes. Mean per-patient charges related to complications in 2011 US dollars were also collected using the medical component of the Consumer Price Index. Charges represent per-member charges related to the complication averaged over the entire population.

Statistical analyses of COC supply, complication rates and complication charges were conducted using SAS, version 9.2. Findings with associated p values $<.05$ were considered statistically significant.

4. Results

Of the 1,041,586 COC users identified, 845,360 (81.2%) were prescribed 21/7 regimens, 169,879 (16.3%) were prescribed 24/4 regimens and 26,347 (2.5%) were prescribed 84/7 regimens. Demographic characteristics of women in the study following matching have been previously presented [6]. Mean age was 27.3 years in the 84/7 vs. 21/7 analysis (n=26,332 in each group) and 27.8 years in the 84/7 vs. 24/4 analysis (n=25,347 in each group).

Women in the 84/7 group filled fewer scripts than women prescribed the 28-day regimens (2.7 vs. 5.7 with 24/4 and 7.3 with 21/7; p<.0001 for both comparisons) and had a lower medication supply than women prescribed 21/7 regimens (225.5 vs. 248.9, p<.0001). However, medication supply was higher with 84/7 regimens than with 24/4 regimens (225.5 vs. 185.5, p<.0001).

Use of 84/7 COCs resulted in significantly lower complication rates compared with 21/7 (1.69% vs. 3.00%) and 24/4 (1.68% vs. 2.81%) regimens (Tables 1 and 2) (p<.0001 for both comparisons). Mean charges were $195 lower with 84/7 regimens than with 21/7 regimens ($95 vs. $290, p<.0001) and were $200 lower with 84/7 regimens than with 24/4 regimens ($112 vs. $312, p=.0011). When we stratified by age (15–24, 25–34, 35+), the results by age group (data not shown) mirrored the results for the overall population. There was no clear trend reflecting an increase in risk of complications in either the younger or the older age groups.

Table 1
Complications and related charges with 84/7 vs. 21/7 regimens (n=26,332 per group)

ICD-9 Code	Complication	Rates of complications			Complication-related charges[a]		
		84/7, *n* (%)	21/7, *n* (%)	p value	84/7 mean charges	21/7 mean charges	p value
630, 631	Molar pregnancy	27 (0.10)	31 (0.12)	.60	$3	$3	.82
632	Missed abortion	108 (0.41)	203 (0.77)	<.0001	$19	$40	.0004
633	Ectopic pregnancy	28 (0.11)	42 (0.16)	.094	$9	$14	.38
634	Spontaneous abortion	103 (0.39)	132 (0.50)	.058	$6	$13	.065
640	Hemorrhage in early pregnancy	273 (1.04)	455 (1.73)	<.0001	$13	$24	.0004
641.0, 641.1	Placenta previa	25 (0.09)	60 (0.23)	.0001	$2	$19	.048
641.2	Placental abruption	4 (0.02)	10 (0.04)	.11	$1	$11	.16
642	Hypertension complicating pregnancy	33 (0.13)	90 (0.34)	<.0001	$17	$83	.0001
642.4, 642.5, 642.9	Pre-eclampsia	11 (0.04)	44 (0.17)	<.0001	$8	$48	.0017
642.6	Eclampsia	1 (0.00)	1 (0.00)	1.00	<$1	<$1	.50
643.1	Hyperemesis gravidarum	9 (0.03)	13 (0.05)	.39	$1	$2	.42
644.0	Preterm labor	43 (0.16)	122 (0.46)	<.0001	$7	$34	.022
648.0	Gestational diabetes	11 (0.04)	27 (0.10)	.0094	$2	$6	.090
658.1	Premature rupture of membranes	7 (0.03)	40 (0.15)	<.0001	$11	$50	.012
All of the above	Total complications or charges	445 (1.69)	789 (3.00)	<.0001	$95	$290	<.0001
	Differences in total charges per woman					$195	<.0001

[a] Charges rounded to the nearest dollar.