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A high cholecystectomy rate in a cohort of women who are Mexican-American, and postpartum, at the time of oral contraceptive pill initiation

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Abstract

Background—Opinions differ regarding the association between gallbladder disease and oral contraceptive (OCs). The objective of this paper is to quantify cholecystectomy rate among women initiating OCs.

Study Design—Women under age 25 years were enrolled at four sites in a randomized trial evaluating initiation of OCs. Hospitalizations while enrolled were elicited during follow-up interviews, and medical records of women who underwent cholecystectomy were reviewed.

Results—Eight of 757 women enrolled at University of Texas Southwestern Medical Center (UTSW) underwent cholecystectomy, a rate of 25.3/1000 woman-years (95% CI 8.1, 42.5). All eight were Mexican-American and postpartum when they initiated OCs. The expected rate is 4.2/1000 woman-years for US women aged 15–44.

Conclusions—Women enrolled at the UTSW site had an increased rate of cholecystectomy, and were more likely to be postpartum and Mexican-American than women enrolled at the other sites.

Keywords

Oral contraceptives; Mexican-American; postpartum; cholecystectomy; cholelithiasis; gallstones

1. Introduction

Conflicting opinions prevail regarding the association of gallbladder disease with the use of OCs. This is important because OCs are the most common form of reversible contraception used in the United States [1], and recently the reported annual cholecystectomy rate for women ages 15–44 was 4.2/1000 [2], a frequent operation in the U.S. A recent randomized clinical trial evaluating oral contraceptive initiation provided us the opportunity to analyze

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cholecystectomy rates among women initiating oral contraceptives [3]. The objective of this paper is to quantify cholecystectomy rate among women initiating OCs.

2. Materials and methods

2.1 Study design

This multicenter randomized trial was conducted between March 2003 and February 2005 at three University centers: Emory University, Atlanta; Mt. Sinai Medical Center, New York; and the University of Texas Southwestern Medical Center, Dallas (UTSW). Recruitment took place in their Family Planning and Teen Clinics. These clinics serve predominantly Latina and African-American populations; they are funded in part by Title X and by other federal and state grants.

Clinical Center Institutional Review Boards and the Columbia University (coordinating center) Institutional Review Board reviewed and approved the study. The study intervention was random assignment to immediate initiation of the OC at the time of study enrollment (quick start, intervention group) or conventional initiation of the OC with the next menstrual period (conventional start, control group). The results of the intervention and further details regarding study methods are reported elsewhere [3].

Young women requesting oral contraceptives were the target population for recruitment in this study. After the completion of clinical care following routine local protocols, health care providers referred women aged less than 25 years requesting OCs to study staff for screening. We excluded women with medical contraindications to oral contraceptives and women with lactational amenorrhea (because we could not reasonably instruct them to wait for the next menses to begin using OCs). In Texas, at the request of the local IRB, we excluded postpartum or post-abortion women younger than 18 years of age.

Subjects participated in three- and six-month telephone interviews to assess OC continuation, pregnancy since date of last interview, sexual activity (i.e., risk of pregnancy), and adverse events. We obtained medical records to validate all reported serious adverse events including hospitalizations. Medical records for the cholecystectomy admission and any antecedent pregnancy of the women who underwent cholecystectomy were reviewed in detail and pertinent data were abstracted. All gallbladder specimens were confirmed to have cholelithiasis on pathology reports.

2.1 Statistical analysis

Data collected for the QuickStart study was entered and maintained by the study statistical coordinating center at Columbia University.

Analysis included chi-square, Student's t-test, and Fisher's exact test. Rate and standard error of proportions were calculated for the UTSW cholecystectomy rate.

3. Results

Seven hundred fifty-seven women were enrolled at the UTSW site during the study period. Six hundred eighty-three (90.2%) completed the three-month follow-up interview and 633 (83.6%) completed the study by undergoing the six-month interview, resulting in 316.5 woman-years at the University of Texas. Eight women at the UTSW site reported undergoing a cholecystectomy. The two other clinical centers enrolled a total of 959 subjects; none of those women reported undergoing a cholecystectomy. BMI was similar at all the sites, and the average age of women at UTSW was 20.9 ± 2.1 years compared with 19 ± 2.7 years at the other two sites ($p < 0.01$).

At UTSW the women were more likely to be postpartum and of Mexican-American ethnicity than the women enrolled at the other sites. Six hundred women enrolled at UTSW identified themselves as Hispanic ethnicity (87.3%), 91% of whom called themselves Mexican-American, compared to 347 (36.2%) at the other two sites ($p<0.01$) reporting Hispanic ethnicity. Five hundred women (66.1%) enrolled at UTSW were postpartum when they initiated their oral contraceptives, compared to only 36 (3.8%) at the other two sites ($p<0.01$).

Eight women at UTSW reported undergoing cholecystectomy for symptomatic cholecystitis during the study follow-up period. All eight women were postpartum and of Mexican-American ethnicity (Table 1).

The cholecystectomy rate at UTSW was 25.3/1000 woman-years (95% CI 8.1/1000, 42.5/1000), compared to the expected rate in the United States of 4.2/1000 woman-years yields a rate ratio of 6.0 (95% CI 1.92, 10.11).

4. Discussion

Cholelithiasis requiring cholecystectomy was reported only at the UTSW Medical Center site, and all eight of those women were Mexican-American, and were postpartum at the time of OC initiation. There are numerous reports which provide conflicting conclusions regarding the risk of cholelithiasis and cholecystectomy when taking OCs [4–21], but none included women who were specifically postpartum. At least three studies have reported on an increased association of gallbladder disease and oral contraceptive use only during the first few years of OC use, suggesting that OC use may accelerate the course of pre-existing gallstone disease [10,23, 24].

The relationship between Hispanic ethnicity (specifically Mexican-Americans) and gallstones (as diagnosed by ultrasound) was reported in the NHANES III survey [25]. Among women, age-adjusted prevalence of gallstones was highest in Mexican-Americans (26.7%), followed by non-Hispanic whites (16.6%) and non-Hispanic blacks (13.9%). A chart review of a primarily Mexican-American outpatient population in San Antonio, found the prevalence of gallstone disease to be highest in the Mexican-American ethnic group [23]. Neither of these studies reported on postpartum women.

This study provides no information about symptoms suggestive of cholelithiasis in the entire study population. Our report includes only women who underwent cholecystectomy within 6 months of OC initiation. We have no information on women with cholelithiasis without hospitalization or women who had a later cholecystectomy.

At this hospital post-partum Mexican-American women had an increased risk of cholecystectomy after OC initiation compared to other women in the study. This was roughly six times the national rate for this age group [2]. While clinical decision-making at UTSW may have favored cholecystectomy compared to other study locations, an increased risk of this magnitude is unlikely to be due to clinical judgment alone. In addition all surgical cases were found to have cholelithiasis. Thus, this difference is likely real and clinically important.

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Table 1

Characteristics of the eight women who underwent cholecystectomy at UTSW compared to the remainder of the cohort at UTSW which did not undergo cholecystectomy

	Cholecystectomy (n =8) N (%)	No cholecystectomy(n =749) N (%)	p
Postpartum	8 (100)	492 (66)	.06
Mexican-American	8 (100)	590 (79)	.20