

Review article

Contraception in women with cystic fibrosis: a systematic review of the literature

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Abstract

Objective: To perform a systematic review of the literature to examine original research on contraception in women with cystic fibrosis (CF) with a specific focus on safety, efficacy, non-contraceptive benefits, and utilization patterns in this population.

Study design: We searched PubMed and Embase databases for any peer-reviewed original research in English on the use of contraception in women with CF.

Results: We identified 241 unique citations. After title review and exclusion of articles not reporting original data, 18 publications were included in the final review, with at least two articles for each area of focus. Limited evidence indicates that oral contraceptive pills are likely safe and efficacious in women with CF. Hormonal contraception may reduce pulmonary exacerbation rates and decrease need for antibiotics, suggesting non-contraceptive benefits. Women with CF utilize birth control at similar rates as the general population, and oral contraceptive pills and condoms are the most commonly used methods.

Conclusions: Data on the safety, efficacy, and non-contraceptive benefits of hormonal contraception in women with CF are scant. Based on the limited data, hormonal contraception seems to be safe and efficacious and may provide noncontraceptive benefits. Further high-quality data from disease-specific research are required to better inform contraceptive decision-making among women with CF.

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1. Introduction

Cystic fibrosis (CF) is the most common lethal genetic disorder in the Caucasian population. It results from a mutation in the CF transmembrane conductance regulator protein and leads to extensive pulmonary, infectious, gastrointestinal, and endocrine consequences. CF is diagnosed in 1 in 3500 newborns annually and currently affects 30,000 people in the United States [1].

Advances in medical treatment of CF have markedly increased life expectancy for those with the disease. In the 1980s, only 30% of individuals with CF survived beyond the age of 18 years, compared to 50% today, and the median age of survival now approaches 41 years [1]. Consequently,

more women with CF are living through their reproductive years and are at risk of becoming pregnant; thus, their reproductive health and family planning needs require greater attention.

Women with CF are sexually active at rates similar to the general population [2], and 70–85% plan to have children at some point in their lives [3,4]. Nevertheless, one quarter of pregnancies among women with CF are unplanned [5]. Normal physiologic changes of pregnancy can negatively impact the health of women with CF, especially at times when health status is suboptimal. Although pregnancy has not been shown to affect long-term survival [6], it can be associated with increased hospitalizations, infection, chronic hypoxia, fetal growth restriction, preterm delivery, diabetes, cardiac decompensation, and even death [7,8]. Improving utilization of effective contraception would reduce rates of unintended pregnancy and enable women with CF to optimize their health prior to attempting pregnancy.

Published data on appropriate contraceptive methods for women with CF are inadequate. Safety data and interactions

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with disease processes have not been well outlined, and the *US Medical Eligibility Criteria for Contraceptive Use* does not specify guidelines for offering contraception to women with CF [9]. Given the need for comprehensive information regarding contraception in this population, we conducted a systematic review of the literature on the use, safety, efficacy, and therapeutic effects of hormonal contraception in women with CF. We emphasize gaps in knowledge and areas for further research.

2. Methods

This systematic review was performed according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. We searched the PubMed and Embase databases for peer-reviewed original research on the use of contraception in women with CF. Search terms included both keywords and official vocabulary for each database, for example, ‘contracept*’ and ‘cystic fibrosis’ (keywords) and “Contraceptives, Female” [MeSH] and “Cystic Fibrosis” [MeSH] (controlled vocabulary). The search was restricted to English language publications only. No date restrictions were applied. The search included all manuscripts available for search in March 2015.

The search strategy identified 241 unique citations. These were screened by relevance to contraception and CF, and 35 citations were selected for full-text review. Of these, studies of any design type reporting original data on contraceptive efficacy, safety, use and preferences in women with CF were eligible for inclusion; review articles were excluded. Two independent reviewers identified 18 publications that met these criteria (Fig. 1). These studies varied not only by methodology but also by area of inquiry. The primary author extracted data from each of these publications (Table 1). Our summary and analysis of the studies is organized according to topic: contraceptive efficacy, contraceptive safety, non-contraceptive benefits, and contraceptive use in the CF population.

3. Results

3.1. Contraceptive efficacy

The data on contraceptive efficacy in women with CF are scant. There is a single pharmacokinetics study that compared plasma levels of orally administered hormones in 6 women with CF and 6 controls [10]. In the CF group, ethinyl estradiol had increased bioavailability but also increased clearance, resulting in similar plasma levels in the two participant groups. No significant differences in levonorgestrel pharmacokinetics were found between the two groups. These results indicate that women with CF have absorption of oral contraceptives that is similar to other women, but with such a small sample size, it is difficult to draw definitive conclusions.

Pancreatic insufficiency is common in women with CF, and as a result, there are theoretical concerns regarding hormonal absorption. One retrospective chart review did note that, of 18 women using the oral contraceptive pill over the course of 1 year, 94% had pancreatic insufficiency and none suffered contraceptive failures [11]. However, this was an incidental finding without a control group, and contraceptive failure was not a primary endpoint of the study.

3.2. Contraceptive safety

The first published data on safety of contraceptives in women with CF, a case series published in 1974, raised concerns about side effects and worsening disease [12]. Three of 4 patients who started combined oral contraceptives developed cervical polyps, and 2 had pulmonary deterioration with one dying within 7 months. It should be noted that this case series was published at a time when patients with CF had fewer treatment options and overall shorter expected survival than in the present day.

More recent case reports have noted other possible complications of hormonal contraception in women with CF. One describes a patient who developed a 3-cm benign, mucinous cervical mass 4 months after initiating a progestin-only pill [13]. Another reports that a woman with CF and a patent foramen ovale developed a transient ischemic attack 2 months after starting the combined oral contraceptive pill [14]. However, small case studies such as these are subject to selective reporting, and clinical decisions cannot be made on the basis of this evidence alone.

A prospective study of 10 female CF patients documented their pulmonary function at baseline and over 6 months following the initiation of a combined oral contraceptive pill [15]. During this time, pulmonary function studies and disease exacerbation frequency were noted to be stable, although the study interval was short and there was no comparison group.

A large retrospective cohort study of 114 women, comparing users and nonusers of oral contraceptives (type of pill not specified), showed similar disease severity, as measured by annual change in forced expiratory volume and body mass index, as well as total days of intravenous antibiotic use, over 5 years [16]. Baseline values were equivalent between the two groups. An additional inpatient crossover analysis was performed using a subgroup of 50 women who had used oral contraceptives for 3 consecutive years followed by 3 years of nonuse (or the reverse), again with no difference in the above parameters. Because there are no large prospective studies of women with CF using hormonal contraceptives, this study may provide the best evidence of oral contraceptive safety in this population.

3.3. Noncontraceptive benefits

Hormonal contraception has also been investigated for its possible therapeutic benefit in women with CF. In a small

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