Contraceptive practices and cervical screening in women with cystic fibrosis

C. Rousset Jablonski1,2,3,*, Q. Reynaud1,4, M. Perceval1, R. Nove-Josserand1, S. Durupt1, J.C. Lega1,4, and I. Durieu1,4

1Cystic Fibrosis Adult Referral Centre, Department of Internal Medicine, Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, 69495 Pierre Benite Cedex, France 2Department of Obstetrics and Gynecology, Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, 69495 Pierre Benite Cedex, France 3Department of Surgical Oncology, Centre Léon Bérard, 28 rue Laennec, 69008 Lyon, France 4Lyon 1 Claude Bernard University, Lyon, France

*Correspondence address. Tel: +33-478861354; E-mail: christine.rousset-jablonski@chu-lyon.fr

Submitted on April 6, 2015; resubmitted on July 8, 2015; accepted on August 11, 2015

STUDY QUESTION: Is gynaecological management of women with cystic fibrosis (CF) adequate?
SUMMARY ANSWER: Gynaecological care (frequency of follow-up, cervical screening and contraceptive use among sexually active women) in women with CF fails to reach the recommended level.
WHAT IS KNOWN ALREADY: Little is known about gynaecological follow-up and cervical screening in CF. Only few studies have described contraceptive practices in cohorts of CF women.

STUDY DESIGN, SIZE, DURATION: We did a cross-sectional study in a cohort of 155 CF women attending the Lyon adult centre. Women attending the CF adult centre in 2014 completed a written questionnaire about their contraceptive choices, frequency of gynaecological follow-up and cervical screening. Other clinical data were collected from the CF adult centre registry.

PARTICIPANTS/MATERIALS, SETTING, METHODS: One hundred and twenty women (100%) answered the questionnaire, among whom two were post-menopausal (46 and 59 years of age), and five were pregnant.

MAIN RESULTS AND THE ROLE OF CHANCE: Seventy-four per cent of the women declared they had undergone gynaecological follow-up (89% of the women with transplantation), and only 55% reported having at least one previous Pap smear test. Among the transplanted patients, only 58% had had a Pap smear test, despite immunosuppressive treatment. The overall rate of contraception was only 64% and in diabetic women, it was 61%. Among contraception users; 65% used oral contraception, predominantly combined estrogen–progestagen (47%); among diabetic patients, 26% used progestin-only contraception. Intrauterine device accounted for 10% of patients using contraception, and tubal ligation only 4%.

LIMITATIONS, REASONS FOR CAUTION: This study is limited by its cross-sectional design. Despite an internal validation of the questionnaire showing an almost perfect agreement, the risk of recall bias has to be taken into account.

WIDER IMPLICATIONS OF THE FINDINGS: This study of practices highlights the importance of improved information regarding sexuality, fertility and reproductive health in young women with CF. A regular gynaecological follow-up and cervical screening is mandatory in this population. Better gynaecological care and contraceptive advice would help to avoid unplanned pregnancies, and optimize contraceptive selection in relationship to specific clinical conditions.

STUDY FUNDING/COMPETING INTEREST(S): None.

Key words: cystic fibrosis / contraception / gynaecological follow-up / screening / Pap smear / counselling

Introduction

With significant improvement in the survival of patients with cystic fibrosis (CF), ~50% of the patients on the national registry in France are adult patients (Cystic Fibrosis French Registry, 2012). Reproductive healthcare and contraception are of great importance in the management of adolescent and adult CF women (Frayman and Sawyer, 2015).

Literature is scarce regarding gynaecological follow-up and cervical screening in this specific population, although some of them will need a transplantation, which is associated with a higher risk of cervical dysplasia due to the use of immunosuppressive treatments.

Despite various causes of fertility impairment, many women with CF are able to conceive spontaneously (Thorpe-Beeston, 2009), and previous studies have underlined that knowledge regarding fertility issues...
among CF patients is insufficient (Fair et al., 2000; Korzeniewska et al., 2009). Providing CF patients with advice regarding safe and efficient contraception to avoid unplanned pregnancies is strongly recommended (Tsang et al., 2010).

A recent review on sexual and reproductive healthcare in CF women has underlined that little is known regarding their contraceptive practices (Frayman and Sawyer, 2015). Only few studies have described contraceptive practices in cohorts of CF women (Plant et al., 2008; Gatiss et al., 2009; Korzeniewska et al., 2009). Since these studies, some papers have related estrogen treatment to pulmonary status (Chotirmall et al., 2012; Saint-Criq and Harvey, 2014). However, there is no evidence that oral contraceptives might affect the severity of CF (Kerman et al., 2013). Moreover, there are now many CF patients with clinical conditions such as a previous pregnancy, diabetes mellitus and pulmonary transplantation who need specific attention for contraceptive selection and gynaecological monitoring.

To learn about the contraceptive practices and gynaecological care for our patients, we performed a cross-sectional study of the entire CF female population attending the Lyon University Adult CF centre during 2014. We discuss how the results can be used to recommend improvements in the care of CF women in general and in those with specific clinical conditions.

Materials and Methods

All the women attending the Lyon University adult CF centre between 1 January and 31 December 2014 were asked to complete a self-report written questionnaire (see Supplementary Material). The questionnaire was filled in by the patients in presence of a clinical nurse. The gynaecological healthcare options and contraceptive choices were recorded. All following questions were closed-ended (answer yes/no): use of contraception; use of contraceptive pill; use of contraceptive implant; use of intrauterine device; use of tubal sterilization; use of mechanical contraception; use of other type of contraception; previous delivery (term pregnancy); gynaecological follow-up; previous Pap smear. In case of a positive answer to one of these questions, more details were requested (depending on the situation: name of the contraception, date of delivery, frequency of the gynaecological follow-up, date of the last pap smear). An internal validation of the questionnaire was performed on a subgroup of patients. Data on contraception, previous pregnancies and cervical screening were recorded for the 42 patients (of the 120 patients) who underwent a gynaecological consultation within the past three years in the University Hospital Network of Lyon. Cohen’s kappa values for the three items contraception, previous term pregnancy and previous Pap smear were 0.93, 1 and 0.85, respectively. Concordance about type of contraception, number of previous pregnancies, date of the last Pap smear (when known) was 96, 100 and 100%, respectively.

All patients attending the CF adult centre are included in a registry, which records data including: BMI and Forced Expiratory Volume (FEV1), as well as the presence of diabetes mellitus, hepatic cirrhosis, transplantation and a history of previous pregnancies (term pregnancies, miscarriages, abortions).

The local ethics committee was informed of the study and approved it.

Statistical analysis: we performed a descriptive study. Statistical analyses to compare patients with and without oral contraception were performed using Student’s t-test (Excel software) and significance was set at α < 0.05.

Results

The entire cohort of women attending the Lyon CF centre comprises 155 women. The questionnaire was offered to all 120 women who attended the clinic in 2014 (77%) and they all answered it (response rate = 100%). The remaining 35 women did not attend the centre in 2014. The characteristics of the women are summarized in Table I. Among the 35 remaining patients, 15 were transplanted ones. Their age and BMI were similar as the 120 responder patients. Their FEV1% was slightly better (median FEV1% 80%), and the proportion of diabetic patients slightly higher (40%). The mean duration of diabetes in diabetic responder women was 115 months (range = 11–324).

Eighty-nine patients (74%) declared that they had a regular clinical gynaecological follow-up, predominantly by a specialist (gynaecologist) (Table II). Among the 89 patients with a regular follow-up, 47 (53%) reported being followed yearly, 5 (6%) were followed less frequently and the information was not available for 37 (41%) patients. The proportion of patients with a regular gynaecological follow-up in the transplanted patients was 89%.
Table III  Pap smear cervical screening.

<table>
<thead>
<tr>
<th>Pap smear test: ever</th>
<th>All patients (N = 120)</th>
<th>Diabetic patients (N = 34)</th>
<th>Transplanted patients (N = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>Mean age (years)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Yes</td>
<td>72 (55)</td>
<td>30.3</td>
<td>16 (47)</td>
</tr>
<tr>
<td>No</td>
<td>25 (19)</td>
<td>27.4</td>
<td>11 (32)</td>
</tr>
<tr>
<td>Unknown</td>
<td>23 (18)</td>
<td>30.9</td>
<td>7 (21)</td>
</tr>
</tbody>
</table>

Table IV  Contraceptive practices.

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 113)</th>
<th>Diabetic patients (n = 31)</th>
<th>Transplanted patients (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No contraception</td>
<td>41 (36)</td>
<td>12 (39)</td>
<td>7 (37)</td>
</tr>
<tr>
<td>Contraceptive use</td>
<td>72 (64)</td>
<td>19 (61)</td>
<td>12 (63)</td>
</tr>
<tr>
<td>Oral contraception</td>
<td>47 (65)</td>
<td>13 (68)</td>
<td>8 (67)</td>
</tr>
<tr>
<td>Combined oral contraceptive pill</td>
<td>34 (47)</td>
<td>8 (42)</td>
<td>—</td>
</tr>
<tr>
<td>Second-generation combined OC</td>
<td>25</td>
<td>8</td>
<td>—</td>
</tr>
<tr>
<td>Third-generation combined OC</td>
<td>5</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Drospirenone-containing combined OC</td>
<td>3</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Other (cyproterone acetate-containing combined OC)</td>
<td>1</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Progesterin-only oral contraception</td>
<td>13 (18)</td>
<td>5 (26)</td>
<td>8 (67)</td>
</tr>
<tr>
<td>Progesterin-only mini-pill</td>
<td>12</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>High-dose progesterin</td>
<td>1</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Condom</td>
<td>13 (18)</td>
<td>4 (21)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Intrauterine device (copper or levonorgestrel)</td>
<td>7 (10)</td>
<td>2 (11)</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Tubal sterilization</td>
<td>3 (4)</td>
<td>—</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Vaginal ring</td>
<td>2 (3)</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Data are n (%), percentages for individual methods are of contraceptive users only.

*After exclusion of the post-menopausal and pregnant women.

(Table II). The characteristics of the cervical screening are detailed in Table III. Seventy-two (55%) of all the patients had a history of having a Pap smear test, and 51 (42.5%) reported having had a Pap smear test in the previous 3 years. Two patients had a Pap smear test more than 3 years ago, and 19 patients could not remember precisely the date of their last Pap smear. Twenty-three (18%) patients could not remember if they had ever had a Pap smear and 25 (19%) reported never having had a Pap smear. Among these 25 patients, 13 were younger than 25 years of age. Among the transplanted patients, 11 (58%) had had a Pap smear test. Six of the eight transplanted patients without a history of having a Pap smear were older than 25.

Among the 120 women, two of the respondents were post-menopausal (46 and 59 years of age), and five were pregnant. The contraceptive users in the remaining 113 women are reported in Table IV. Four patients declared that they were trying to become pregnant at the time of the study.

The overall rate of contraception was 64% in all the women, and 61% in the diabetic women. No significant difference was found between the contraceptive users and the non-contraceptive users when considering the median age, BMI or FEV1. Among the diabetic women using combined oral contraception, the mean duration of diabetes was 60.6 months (range = 12–135).

Among the 19 transplanted patients, 7 were not using any contraception (among whom 5 were single, and 2 were trying to become pregnant). Five of these women had a pregnancy before their transplantation.

Twenty-seven women had at least one previous term pregnancy. A total of 43 pregnancies and 46 children born were recorded. Among these 27 women, the rate of contraceptive use was 81%. Oral contraceptives represented 55% (12/22), intrauterine devices (IUDs), 22% (5/22), and tubal sterilization, 14% (3/22) of the types of contraception used by these women. We counted, in addition to the term pregnancies, five abortions (one in a context of a prenatal diagnosis of CF) and six miscarriages. However, two of the term pregnancies were unintended ones.

Discussion

This is the first study to our knowledge to assess frequency of gynaecological follow-up and cervical screening among CF women. In our cohort, 74% of the patients reported having a regular gynaecological follow-up,
but only 53% attended yearly, despite recommendation of a yearly examination in the general population.

A Pap smear test is an efficient, affordable and acceptable test for cervical cancer screening. In France, a Pap smear is recommended every 3 years for women aged 25–65, after two consecutive yearly normal Pap smear tests (HAS, 2010). The screening coverage rate in France from 2007 to 2009 was estimated at ~56.6% (HAS, 2010), which is insufficient (Boulanger et al., 2007). Only 42.5% of our patients reported having had a Pap smear test in the previous 3 years, illustrating insufficient cervical screening. One explanation could be that CF patients already have significant medical follow-up and treatment and thus pay less attention to their gynaecological care. The high proportion of missing data in the reported information by patients regarding their follow-up underline a lack of interest for this aspect of their health. Another explanation could be the young age of the women in our cohort. However, among the 25 patients who had never had a Pap smear, only 13 were <25 years old, and the remaining 12 should have had this screening. Among the transplanted patients, 58% reported ever having had a Pap smear, and six of the eight transplanted patients who had never had a Pap smear were older than 25 years of age. Considering the use of immunosuppressive treatment in these patients and the high rate of cervical dysplasia after transplantation (Malouf et al., 2004), greater attention should be focused on cervical screening in this population. Human Papilloma Virus vaccination is a primary prevention tool against cervical cancer, which is recommended in France in girls 11–14 years old, and possible in girls up to 19 years old (Heard and Floret, 2013). This recommendation should be particularly respected in CF patients.

Only 64% of the premenopausal and non-pregnant women were using contraception. This proportion is close to those observed in other cohorts (Fair et al., 2000; Plant et al., 2008; Tsang et al., 2010). A British cohort found a high proportion of women using no contraception (50%), but some of them were not sexually active or were wishing a pregnancy (Gatiss et al., 2009).

Women trying to become pregnant know that they have to inform their doctors about their goals in order to organize genetic counselling and disease monitoring. Thus, we believe that the number of women considered as trying to become pregnant is accurate. The proportion of CF adult women being sexually active is similar to that of general population (Sawyer et al., 1995; Korzeniewska et al., 2009). The proportion of our patients using no contraception and not trying to become pregnant was high compared with the French population (Bajos et al., 2014). This could reflect the fact that many CF patients are aware of their risk of infertility related to an increased thickness of the cervical mucus (Oppenheimer et al., 1970) and a higher frequency of ovulation disorders (Galli-Tsinoportun et al., 2006). Thus, some patients do not consider themselves to be at risk of pregnancy. Previous abortions and unintended pregnancies were recorded among our patients, similarly to previous studies finding risky sexual behaviour (Korzeniewska et al., 2009) and a high proportion of unplanned pregnancies (Gatiss et al., 2009) among CF women. Women should be aware of their potential fertility and of the necessity to use efficient contraception.

No transplanted woman took the risk of unintended pregnancy. Considering the risks of pregnancy in this condition, efficient contraception is needed (Gyi et al., 2006; Vos et al., 2014).

The proportion of condom users in our cohort was similar to that in the general population. Despite its weak contraceptive efficacy (Trussell, 2007), its use is recommended for prevention of sexually transmitted infections that can jeopardize future lung transplantation (Frayman and Sawyer, 2015).

The young age and the high proportion of nulliparous women can explain the low proportion of women using IUDs compared with French women (Bajos et al., 2014), although it can be used safely in this population. Two transplanted patients were using an IUD. There are some concerns on copper IUDs efficiency under immunosuppressive treatment (Zerner et al., 1981), although prevention of fertilization due to copper might not be affected. Attention should be paid to the risk of pelvic infection following IUD insertion (Martínez and López-Arrequí, 2009).

The young age of the women and the popularity of oral contraception in France (Moreau et al., 2013) could explain the high proportion of oral contraception compared with American or British CF cohorts (Plant et al., 2008; Gatiss et al., 2009).

Tubal ligation was rarely used in the entire cohort and among transplanted patients, probably because of their young age. This efficient permanent contraceptive option must be discussed in this last specific complicated condition (Vos et al., 2014).

The proportion of progestin-only OCs is higher than that among French women [26% (12/47) versus 16%] (Bajos et al., 2014). This difference could be explained by the specificities of contraception among the diabetic and transplanted patients. Combined OC can usually be used among with CF, except in case of specific contra-indication (Deerojanawong et al., 1998; Frayman and Sawyer, 2015). Combined OCs are not systematically contra-indicated in cases of diabetes, except in case of a diabetic complication, of a longer duration of diabetes (≥20 years), or in case of any additional risk factor for cardiovascular disease (World Health Organization, 2010). The mean duration of diabetes in our population (<10 years) can explain the relatively high prevalence of combined estrogen—progestagen use. None of the transplanted patients was using a combined OC, although there is no specific contra-indication in uncomplicated transplantation patients (Krajewski et al., 2013; Vos et al., 2014). Unlike in other CF cohorts (Plant et al., 2008; Gatiss et al., 2009), no patient were using injectable progesterone, as this contraception is rarely used in France, where other progestogen-only contraception are usually preferred.

Studies have suggested that estradiol and oestriol have a deleterious effect on the disease, and that hormonal contraception could have a potential beneficial effect (Chotirmall et al., 2012). Data from the CF Irish Registry showed a decreasing tendency to require antibiotics in women receiving OCs (Chotirmall et al., 2012). Another retrospective cohort study found no difference in the disease severity in case of OC exposure (Kerman et al., 2013). The type of OC was not recorded in these studies, and the hormonal profiles of contraception type show such wide variations that these data must be interpreted cautiously. Thus, these data are not sufficient to recommend hormonal contraception for its beneficial effect on the disease or to influence contraceptive choice.

Our study has some limitations. The cross-sectional design limits its significance. The high proportion of transplanted patients among the 35 women who did not attend the centre in 2014 can be explained by the fact that they are also regularly followed in the department of transplantation. The slight differences in FEV and in the proportion of diabetic patients might not affect the validity of our study. The use of questionnaire is associated with a risk of recall bias. Nevertheless, the internal validation on a subgroup of patients showed an almost perfect agreement between the questionnaire and the gynaecological record.
Conclusion
This preliminary study concerning gynaecological follow-up and contraceptive practices in an adult French CF centre highlights the importance of better information regarding reproductive health, sexuality and fertility in CF adolescents and young women. The regular gynaecological follow-up schedule appeared to be insufficient, although Pap smear cervical screening and prevention is mandatory in this specific population.

Therefore, easy access to specific gynaecological consultations should be discussed in the CF adult centres. Better gynaecological care and contraceptive advice could help to avoid unplanned pregnancies and to optimize the selection of contraceptives in relation to specific clinical conditions. The possible influence of hormonal status on respiratory exacerbations supports the suggestion to include information regarding the contraceptive practices of our patients in the patient registries.

Supplementary data
Supplementary data are available at http://humrep.oxfordjournals.org/.

Author’s roles
C.R.J., I.D. and R.N.J. planned and designed the study. I.D., R.N.J., S.D., M.P., Q.R. and J.C.L. contributed to the acquisition of data. C.R.J., M.P. and I.D. analysed the data. C.R.J. and I.D. provided a draft manuscript. All authors were involved in revising the manuscript and approved the final version.

Funding
No external funding was used for this study.

Conflict of interest
None.

References
Tsang A, Moriarty C, Towns S. Contraception, communication and counselling for sexuality and reproductive health in adolescents and young adults with CF. Peadiatr Respir Rev 2010;11:84–89.