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Short Communication

Drugs during pregnancy and breast feeding in women diagnosed with Cystic Fibrosis - An update

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1. Introduction

Over the past decades life expectancy of people with Cystic Fibrosis (CF) has significantly improved as a result of improved antimicrobial treatment, management strategies aimed at improved nutritional status and facilitating mucus clearance, neonatal screening and standardization of care in multidisciplinary CF care centers. The median age of CF patients in developed countries has increased to over 40 years. Improved survival and overall health has led to an increased number of women reaching reproductive age. In contrast to men, the majority of women with CF have near-normal fertility. Correspondingly, the number of pregnancies in women with CF has been rising during the last decades [1]. The pregnancy rate remained constant the last years resulting in 25,5 pregnancies per 1000 woman-years [2]. To insure the best outcomes for mother and baby, well planned management of pregnancy becomes increasingly important, including knowledge of medication safety during pregnancy and breast feeding.

In 2008, Edenborough et al. published guidelines for the management of pregnancy in women with CF [3]. They address many aspects of pregnancy, from the preconceptual period until after delivery. Appendix C of their paper discusses the risks of drug use during pregnancy and lactation in CF patients along with recommendations. Since this paper, new prescription medications have been approved for treating CF resulting in the need of an update of Appendix C. This report provides an update on recommendations for safe use of prescription medication in CF patients during pregnancy and breast feeding.

2. Methods

All prescription medication mentioned in Appendix C of the Edenborough paper were evaluated whether or not new information about their safety during pregnancy and lactation was available. When new information was found, a new recommendation was formulated. Newly registered prescription medication after the publication of Edenborough et al. have been added to offer an up-to-date evaluation of safety data for the most current prescription medication used in CF patients.

The Cystic Fibrosis Foundation, FDA, EMA EPAR and uptodate.com provided information on prescription medication registered for CF. This provided an insight in the current use of prescription medication on the market and showed which prescription medication are currently in clinical trial stage 3. After the initial review of prescription medication that were acknowledged for treating CF, a thorough PubMed search using the MeSH terms ‘drug name’, ‘drug class’, ‘pregnancy’, ‘breastfeeding’ and ‘breast milk’ was conducted. Abstracts were included up to April

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Table 1
Overview and recommendations on drug use in pregnant and breast feeding patients diagnosed with CF. New recommendations have been displayed in *italics*.

	Risk in first trimester	Risk in second/ third trimester	Risk at delivery	Recommendation	Breast feeding
Acid inhibitory drugs					
H2 antagonists	*No risk shown*	*Possible increased risk for asthma*	No	*Possible increased risk for asthma*[1]	*Possible compatible – low concentrations present in milk*
Proton pump inhibitors	No risk shown	Not shown	No	*PPI preferred*	Compatible - low concentration in milk
Prokinetics					
Metoclopramide	*No increased risk shown*[2]	*Monitor extrapyramidal syndrome in neonates in third trimester*	*Unknown*[3]	*Probably safe – first choice is meclozine second choice is metoclopramide*[5]	*Possible compatible*[4] *– passes blood-brain-barrier, short term use possible*
Domperidon	*Limited human data*	*Limited human data*	*No*	*Probably safe – meclozine preferred during pregnancy*	*Low dose present – does not cross Blood-Brain-Barrier, monitor QT-interval*
Constipation					
PEG +/− electrolytes Macrogol	*No data – systemic exposure neglible*[6]	*No data – systemic exposure negligible*	*No*	*No absorption is taking place – probably safe*	*Compatible – no oral absorption*
Lubiprostone	*Adverse effects in animals (fetal loss) – limited human data*[7]	*Adverse effects in animals (fetal loss) – limited human data*	*Unknown*	*Limited human data – avoid during pregnancy, Macrogol preferred*	*Avoid – no data*
Contact laxative					
Senna	*Limited human data shown no adverse effects*[8]	*Limited human data shown no adverse effects*[8]	*No*	*Short term use only*	*Possible compatible – low concentration in milk*[9]
Bisacodyl	*Animal studies show no adverse effects – limited human data*[10]	*Animal studies show no adverse effects – limited human data*	*No*	*Short term use only*[11]	*Compatible – no GI absorption*
Antibacterial drugs					
Aminoglycosides					
Gentamycin Tobramycin (i.v., inhal.)	Associated with fetal nephro- and ototoxicity	Associated with eighth cranial nerve damage in fetus but not in CF literature	No	Reserve for life threatening infections – inhaled causes minimal risk due to limited systemic absorption	Probably compatible[12] – monitor infant on GI flora effects i.e. diarrhea, candidiasis, beware of hypersensitivity
Cephalosporins					
Ceftazidim (and other cephalosporins)	*No risk shown*	No risk shown	No	Probably safe – only on strict indication	Compatible - excreted in low concentrations[13]
Fluoroquinolones					
Ciprofloxacin (and other fluorquinolones)	*Unknown*	Cartilage damage and arthropathy shown in animals[14]	No	Avoid during pregnancy, if needed ciprofloxacin drug of choice	Avoid - high concentration *Ciprofloxacin - probably compatible*[12]
Lincomycins					
Clindamycin	*No risk shown*	No risk shown	No	Probably safe – use in absence of safer alternative	*Possible Compatible – cases of bloody stool, monitor infant GI flora*[12,15]
Macrolides					
Erythromycin	*No risk shown*[16]	No risk shown	No	Use as first choice	Possible Compatible[12]
Azithromycin	*Probably no risk*	No risk shown	No	Erythromycin first choice	*Probably compatible*[12]
Roxithromycin	*No risk shown*[16]	Probably no risk	No	Erythromycin first choice	*Possible compatible*
Clarithromycin	*No risk shown*	No risk shown	No	Erythromycin first choice	*Possible compatible* – low concentration in milk, monitor infant
Penicillins					
Amoxicillin (and other penicillins + clavulanate or tazobactam)	*No risk shown*	No risk shown	No	Probably safe	Compatible – trace in milk, beware hypersensitivity
Polymyxins					
Colistin (i.v., inhal.)	*Limited human data*	*Limited human data*	No	IV avoid if possible - Inhalation probably safe	Inhaled -possible compatible IV – caution (poorly absorbed from gut)