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REVIEW ARTICLE

Interaction between Antibiotics and Oral Contraceptives: A Review for Dental Practices

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Abstract

Clinical situations sometimes require systemic antibiotic therapy. Millions of women choose oral contraceptives for birth control, there is a potential for interaction between these drugs and oral contraceptives. Until recently, dentists have been advised to warn women taking the combined oral contraceptive pill of the routine need to use additional contraceptive measures. Recent guid-ance relating to this issue has changed and dentists may not be aware of this. This paper reminds dentists of the previous guidelines and related evidence on the pharmacokinetics of hormonal contraception. (2020, Vol. 04; Issue 01: Page 23 - 28)

Keywords: Antibiotic, Contraceptives, Drug interaction, Ethinylestradiol, Progestins.

Introduction

It is estimated that 60-70 million women worldwide use birth control pills and sometimes are simultaneously receiving antibiotic drug therapy. It has been a common clinical scenario in dental prac- tices for many years that a patient requir- ing antibiotic therapy is taking oral con- traceptive pills. Several literatures have reported possible interactions between oral contraceptives and certain antibiot- ics. It is said that antibiotics supposedly reduces the blood concentrations of oral contraceptives and in this way its overall effectiveness decreases (1).

There are 3 types of oral contraceptives, as follows: (2)

1. The combined fixed-dose estrogen-pro- gesterone preparations (with high, me- dium or low estrogen content).
2. The combined sequential preparations with the doses of each steroid varied throughout the menstrual cycle.
3. The progesterone-only preparations. The estrogen component in oral contra- ceptives is usually ethinylestradiol or mes- tranol which blocks ovulation by inhibit- ing the release of follicle-stimulating hor- mone and leutinizing hormone via nega- tive feedback on the pituitary gland and hypothalamus. The progestins used can vary and include norethindrone, levonorg- estrel, drospirenone and gestodene. These

progestin components increases the vis- cosity of the cervical fluid, changes the en- dometrial lining to make it unsuitable for egg implantation and also provides some anti-ovulatory action. To be effective, oral contraceptives must have adequate circu- lating concentrations of active hormone to prevent ovulation (3, 4).

Metabolism of oral contraceptives

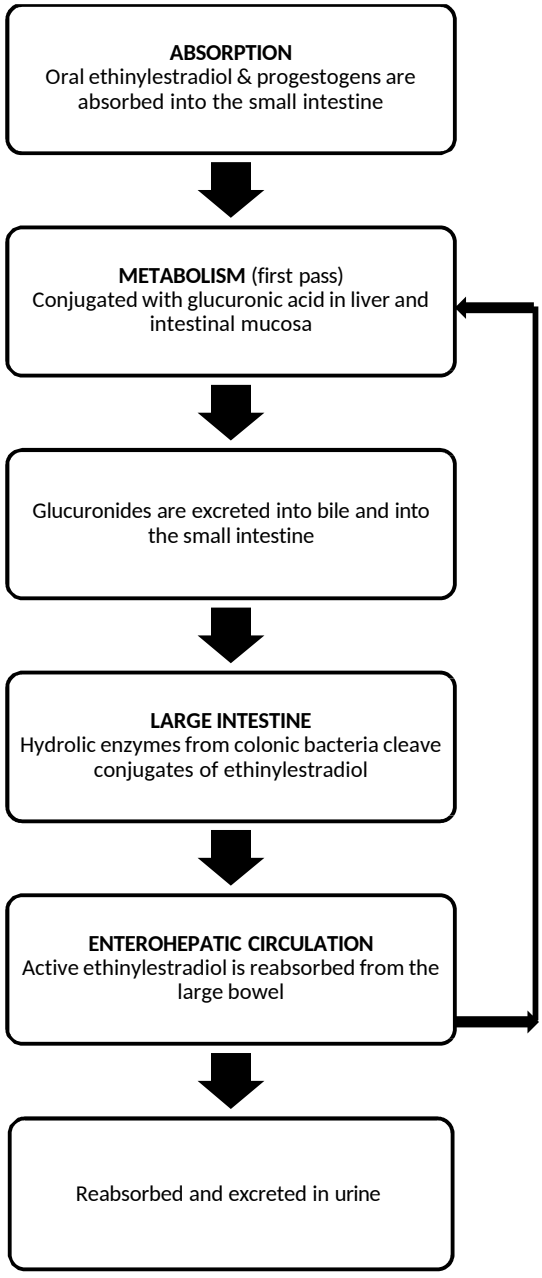

Figure: Metabolism of oral contraceptives (5)

Mechanism of interaction

The proposed mechanisms of the antibi- otic-associated interactions of oral contra- ceptives include: (2, 6)

1. Hepatic microsomal enzyme (P450 group) induction by the antibiotic (En- zyme-inducing antibiotics) thereby in- creasing the rate of metabolism of both themselves and the oral contraceptives leading to low circulating levels of estrogen and progestin preventing ovulation. E.g. Rifampin, an anti-tuberculosis agent and Griseofulvin, an antifungal agent.
2. Interference with enterohepatic circula- tion of the oral contraceptive metabolites, by killing or inhibiting the growth of co- lonic bacteria involved in deconjugation of ethinyl estradiol. E.g. Penicillins (mainly ampicillin), Cephalosporins, Macrolides, Metronidazole, antifungals, anti-tubercu- losis agents and Tetracylines.
3. Interference with oral contraceptive ab- sorption from the gastrointestinal tract by ascorbic acid.
4. Alterations in plasma protein binding of the oral contraceptive components.
5. Increased excretion of the oral contra- ceptive by urinary or fecal excretion in- cluding antibiotic-induced diarrhea.

List of different types of antibiotics which interfere with oral contraceptives (Table 1) (6)—

Table 1:

CATEGORY	DRUGS
Antibiotic that likely reduces birth control pill effectiveness	Rifampicin
Antibiotics less associated with oral contra- ceptive failure	Amoxicillin, Ampicillin, Griseofulvin, Tet- racycline, Metronidazole
Antibiotics least associated with oral contra- ceptive failure	Cephalexin, Clindamycin, Dapsone, Eryth- romycin, Isoniazid, Phenoxymethylpenicil- lin, Trimethoprim, sulphamethoxazole

Review of reported antibiotic and oral contraceptive drug interac- tions

Interaction between different types of an- tibiotics and oral contraceptives are given in table 2 (7-23).According to current rec- ommendation, the World Health Organiza- tion on Medical Eligibility Criteria for con- traceptive use in 2010 included evidence- based guidance on contraceptive use and drug interactions. In 2011, the Clinical Ef- fectiveness Unit of the Faculty of Sexual and Reproductive Healthcare (Royal Col- lege of Obstetricians and Gynaecologists) produced new clinical guidance which states that additional contraceptive pre- cautions are not required even for short courses of non-enzyme inducing antibiot- ics when taken with combined oral contra- ceptives. This new advice has been incor- porated into the guidance given in the British National Formulary. If the antibi- otics (or indeed the illness) should cause diarrhea or vomiting, then the usual addi- tional precautions should be taken (5).

Table 2:

Antibiotic class	Specific anti- biotic	Oral contracep- tive component	Mechanism of interaction
Penicillins	Ampicillin	Ethinylestra- diol/levonorg- estrel	Interruption of the enterohepatic cycling of ethinylestradiol by means of reducing the bacterial population of the small intestine, which is responsible for the hy- drolysis of the conjugated hor- mone. The inhibition of hydroly- sis can lead to an increased fecal loss of the hormone, resulting in lower circulating levels of ethi- nylestradiol
Cephalosporins			Same as above

Contd....

Contd. table 2…

Tertracyclines	Doxycycline	Ethinylestra-diol/nore- thindrone	Same as above
	Minocycline	Ethinylestra-diol/levonorg-estrel & ethinylestradiol and ethynodiol diacetate	Same as above
	Tetracycline	Ethinylestra-diol/nore- thindrone	Same as above
Sulphonamides	Co-trimoxazole		Same as above
Macrolides	Erythromycin		Same as above
Antiprotozoal agents	Metronidazole		Same as above
Antituberculosis agents	Rifampin	Ethinylestra-diol/nore- thindrone	Induction of cytochrome P450 group of hepatic microsomal en- zymes
	Isoniazid		Unknown
Antifungal agents	Griseofulvin		Induction of cytochrome P450 group of hepatic microsomal enzymes
	Fluconazole	Ethinylestra-diol/norgestrel	Unknown mechanism of interaction. Unlikely related to metabolism because these agents inhibit hepatic oxidase enzymes
	Ketoconazole		Same as above
	Intraconazole	Ethinylestra-diol/levonorg- estrel	

Conclusion

Dentists should be aware that interaction between oral contraceptives and antibiot- ics may lower the effective dosage of oral contraceptives which may fail and cause pregnancy. This may lead to future med- ico-legal problems. Hence, it is advisable for dentists prescribing antibiotics to take a thorough drug history for female pa- tients of childbearing age. Current guide- lines say that there is no need to tell pa- tients that they should use additional con- traceptive methods while prescribing non- enzyme-inducing antibiotics. Yet, it is our

duty to inform these patients to take addi- tional contraceptive measures if they suf- fer diarrhea or vomiting during the antibi- otic therapy and also of the rare possibility of contraceptive failure.

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