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UNIDOX USE IN CONSERVATIVE GYNECOLOGY

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ABSTRACT

Unidox Solutab® investigated by Japanese company "Yamanouchi" contains doxycycline monohydrate, which does not injure the mucous membrane of the stomach and the esophagus and possesses a number of positive features beneficially differentiating it among the other doxycycline preparations. Unidox Solutab® is a semi-synthetic tetracycline, bacteriostatic wide spectrum antibiotic. It inhibits intestinal flora in a lesser degree than other antibiotics of tetracycline range and differs from them by more complete absorption and prolonged action. By its antibacterial activity doxycycline surpasses natural antibiotics.

The study involved 157 female patients at the age of 18-50 with chronic metroendometritis, bilateral chronic salpingooophoritis, chronic periparametritis, cervicitis, endocervicitis, cervical erosion, cervical dysplasia (CIN1), and sexually transmitted diseases.

All the patients were examined for viruses and infections by polymerase chain reaction (PCR) and immune-enzyme assay (IEA) methods. The following infections and viruses occurred most often: ureaplasmosis, gardenellesis, and cytomegalovirus. Mycoplasmosis also made not an insignificant percent.

The results of the vaginal smear and vaginal examination revealed long lasting relapsing vaginal candidomycoses in more than half of the patients, which are also the signs of immunodeficiency state in these patients.

The repeated PCR study carried out to reveal Ureaplasma in cervical canal (in 2 weeks following Unidox administration) revealed high efficacy of treatment by the mentioned preparation as compared to the control group. According to data of repeated ultrasound examination, positive dynamics in chronic metroendometritis and bilateral chronic salpingoaoophoritis was revealed.

Nowadays, Unidox turns to be the most highly effective, not expensive preparation with minimal side effects.

KEYWORDS: . Unidox, urogenital infections, antibiotics, conservative treatment, IEA and PCR methods.

INTRODUCTION

Sexually transmitted infectious diseases are one of the most wide spread causes making women see their gynecologists [*Mertz G., 1993; Wald A. et al., 1997; Krogh G. et al., 2000; Corey L., Spear P.G., 2002*]. Antibacterial preparations are the basic treatment of such cases [*Ford L. et al., 1986; Fischbach F. et al., 1993*; *Thorp J. et al., 2002*]. Preparations of tetracycline range are very often prescribed in cases of urogenital infections, and doxycycline, in particular. Unidox Solutab® investigated by Japanese company "Yamanouchi" contains doxycycline monohydrate, which does not injure the mucous membrane of the stomach and the esophagus and possesses a number of positive features beneficially differentiating it among the other doxycycline preparations.

The chemical name of the preparation is 6-desoxy-5 oxitetracycline or [4S-(4 alpha, 4a alpha, 5 alpha, 5a alpha, 6 alpha, 12a alpha)]-4-(dylethylamino)-1, 4, 4a, 5, 5a, 6, 11, 12a-octahydro-3, 5, 10, 12, 12a-penthahydroxi-6- methyl-1, 11-dioxo-2-naphthalene carboxamide (in the form of hydrochloride, monohydrate or giklat). Unidox Solutab® is semi-synthetic tetracycline, bacteriostatic wide spectrum antibiotic [*Shmuklarsky M. et*

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TABLE 1.

Distribution of patients according to nozology forms

Diagnosis	I group (n=114)		II group (n=43)		III group (n=15)	
	Abs.	%	Abs.	%	Abs.	%
Hypothalamic syndrome	60	52.63	14	32.56	4	26.67
Chronic metroendometritis	80	70.18	30	69.77	10	66.67
Adhesive salpingitis	13	11.4	5	11.63	1	6.67
Hydrosalpynx	2	1.75	-	-	-	-
Bilateral chronic salpingooophoritis	71	62.28	20	46.51	12	80
Chronic perimetritis	2	1.75	-	-	-	-
Chronic periparametritis	8	7.02	6	13.95	-	-
Adnextumor of inflammatory genesis	9	7.89	4	9.3	-	-
Cervicitis	19	16.67	2	4.65	-	-
Endocervicitis	55	48.25	15	34.88	4	26.67
Colpitis	8	7.02	2	4.65	2	13.33
Non-specific colpitis	1	0.88	-	-	-	-
Cervical erosion	21	18.42	3	6.98	3	20
Cervical dysplasia	-	-	-	-	-	-
- CIN 1	3	2.63	8	18.6	-	-
- CIN 2	-	-	-	-	-	-
Ovuli Nabothi	3	2.63	3	6.98	-	-
Cervical ectopy	1	0.88	-	-	-	-
Primary infertility	6	5.26	2	4.65	2	13.33
Secondary infertility	4	3.5	4	9.3	-	-
Ureaplasmosis	28	24.56	12	27.9	4	26.67
Mycoplasmosis	12	10.53	4	9.3	1	6.67
Chlamidiosis	20	17.54	9	20.93	1	6.67
Trichomonosis	8	7.02	2	4.65	2	13.33
Bacterial vaginosis	52	45.61	18	41.86	3	20
Cytomegalovirus (CMV)	47	41.23	15	34.88	4	26.67
Gonorrhea	4	3.5	1	2.33	-	-
Herpes virus mun 2	22	19.3	4	9.3	1	6.67
Human papilloma virus (HPV) 16/18	10	8.77	6	13.95	-	-
Candida albicans	62	54.39	18	41.86	4	26.67
Miscarriage	19	16.67	11	25.58	1	6.67
Adenomyosis	1	0.88	-	-	2	13.33

al., 1994; Golub L. et al., 2010; *Kang-Birken S. et al., 2010*]. It inhibits intestinal flora to a lesser degree than other antibiotics of tetracycline range and differs from them by more complete absorption and prolonged action. By its antibacterial activity doxycycline surpasses natural antibiotics. Unlike tetracycline and oxytetracycline it possesses higher therapeutic efficacy, which is manifested in treatment by 10-time lesser doses (tetracycline daily dose is 1-2 *g*, that of Unidox Solutab® makes 100-200 *mg*) and its prolonged effect, which allows to take the preparation only 1-2 times a day [*Qin J. et al., 2010*].

The goal of the present investigation was to study Unidox treatment efficacy in women with genital inflammatory diseases.

MATERIAL AND METHODS

Totally 157 patients at the age of 18-50 (the mean age was 34± 2 years) with chronic metroendometritis (n=120), bilateral chronic salpingooorphytis (n=103), chronic periparametritis (n=16), cervicitis (n=21), endocervicitis (n=74), cervical erosion (n=27), cervical dysplasia (CIN 1) (n=11), and sexually transmitted diseases: ureaplasmosis (44), mycoplasmosis (n=17), chlamidiosis (n=30), bacterial vaginosis (n=73) were studied during the period from 2007 till 2009 (Table 1).

The patients were divided into two groups depending on their age. The first group involved 114 patients at the age of 18-35; the second group was formed of 43 patients at the age of 36-50.

IEA and PCR methods were used to reveal urogenital infections. The third group involved the patients treated with antibiotics of the other group (Vilprafen, Sumamed).

All the patients underwent ultrasound examination (Voluson Expert 730 apparatus), oncocytological study, general clinical-laboratory study, bacterial inoculation from the cervical canal for antibiotic sensitivity, colposcopic examination, as well as examination for viruses and infections.

RESULTS AND DISCUSSION

Among the patients 62.8% complained of the lower abdominal dull pains. In rare cases, pain irradiation was mentioned (4.6%) (Table 2).

In 57.6% of all cases patients complained of

Table 2.

Pain symptom characteristics

Pain complaints	I group (n=114)		II group (n= 43)		III group (n= 15)	
	Abs.	%	Abs.	%	Abs.	%
Lower abdominal region	72	63.13	28	65.11	8	53.33
Iliac region	7	6.14	5	11.63	10	66.67
Lumbar region	35	30.7	16	37.2	2	13.33
Types of pain:						
Acute	-	-	-	-	-	-
Dull	28	24.56	12	27.9	8	53.33
Cutting	2	1.75	-	-	-	-
Stabbing	-	-	-	-	-	-
Aching	9	7.89	-	-	-	-
Piercing	-	-	-	-	-	-
Irradiation:	-	-	-	-	1	6.67
Left leg	3	2.63	-	-	-	-
Right leg	3	2.63	3	6.98	-	-
Lumbar region	7	6.14	-	-	-	-
Rectum	5	4,39	-	-	-	-

TABLE 3.

Ovarian disfunction by clinical groups

Ovarian disfunction complaints	I group (n=114)		II group (n=43)		III group (n=15)	
	Abs.	%	Abs.	%	Abs.	%
Algomenorrhea	28	24.56	10	23.26	2	13.33
Opsomenorrhea	15	13.16	3	6.98	3	20
Oligomenorrhea	3	2.63	2	4,65	1	6.67
Disfunctional uteral hemorrhage	3	2.63	1	2.33	-	-
Hypermenorrhea	4	3.5	4	9.3	-	-
Hypomenorrhea	5	4.39	-	-	-	-
Polymenorrhea	6	5.26	1	2.33	-	-
Proyomenorrhea	8	7.02	1	2.33	1	6.67
Amenorrhea	9	7.89	1	2.33	-	-
Hypomenstrual syndrome	7	6.14	6	13.35	1	6.67

copious discharges from the genitals, among them 37.2% had discharges with odour and 20.5% those without smell. Among the patients, 19.2% complained of itching and burning. Mean age of menarche made 13±0.5 years. Ovarian disfunction was mentioned in 77% of the patients in the first clinical group and 67% of patients in the second one. Algodysmenorrhea and opsomenorrhea were the main complaints in the first clinical group (24.6% and 13.2%, correspondingly), algodysmenorrhea and hypomenstrual syndrome in the second group made 23.3% and 13.4%, correspondingly (Table 3).

Beginning of the sexual life was mentioned at the age of 18-26, on average at 22.50.7±. The number of deliveries varied from 1 to 5 and induced abortions made from 3 up to 8. Barrier methods of contraception were not used in full volume.

It is worth paying attention to the great number (72%) of induced abortions especially in patients of the second group.

The patients with spontaneous abortions in the early terms of pregnancy made not insignificant percent (20.93% in the second group) (Table 4).

All the patients were examined for viruses and infections by PCR and IEA methods. As obvious from Table 5, the following infections and viruses

TABLE 4.

Fertility Function

Fertility function	I group (n=114)		II group (n=43)		III group (n=15)	
	Abs.	%	Abs.	%	Abs.	%
1 pregnancy	17	14.91	4	9.3	2	13.33
2 and more pregnancies	61	53.5	35	81.4	4	26.67
Delivery	67	58.77	35	81.4	4	26.67
Abortions						
- induced abortions	41	35.96	31	72.09	4	26.67
- spontaneous abortions	11	9.65	9	20.93	1	6.67
- miscarriage	8	7.02	2	4.65	-	-
Abrasio cavi uteri	30	26.32	22	51.16	1	6.67

TABLE 5.

Examination for infections and viruses by PCR and IEA methods

Infections and viruses study by IFA and PCR methods		I group (n=114)		II group (n=43)		III group (n=15)	
		Abs.	%	Abs.	%	Abs.	%
Herpes virus type 2 IgM	IEA	11	9.65	2	4.65	-	-
Herpes virus type 2 IgG	IEA	22	19.3	4	9.3	1	6.67
CMV IgM	IEA	17	14.91	2	4.65	-	-
CMV IgG	IEA	45	39.47	14	32.56	4	6.67
Mycoplasma hominis	PCR	-	-	3	6.98	-	-
Mycoplasma genitalis	PCR	12	10.53	1	2.33	-	-
Ureaplasma urealiticum	PCR	28	24.56	12	27.9	4	26.57
GN	PCR	4	3.5	1	2.33	-	-
Trichomonas vaginalis	PCR	8	7.02	2	4.65	2	13.33
Chlamidia trachomatis	PCR	2	1.75	-	-	1	6.67
Gardnerella vaginalis	PCR	38	33.33	8	18.6	3	20
HPV 16/18	PCR	10	8.77	6	13.95	-	-
HPV screening	PCR	-	-	-	-	-	-
Herpes virus type 2 in blood	PCR	1	0.88	-	-	-	-
CMV in blood	PCR	2	1.75	1	2.33	-	-

TABLE 6.

Side effects after Unidox administration

Side effects	I group (n=114)		II group (n=43)		III group (n=15)	
	Abs.	%	Abs.	%	Abs.	%
Nausea	5	4.39	2	4.65	1	6.67
Vomiting	-	-	-	-	-	-
Glossitis	15	13.16	5	11.63	2	13.33
Gastritis	-	-	-	-	-	-
Constipation	1	0.88	2	4.65	-	-
Diarrhea	4	3.5	1	2.33	1	6.67
Candidosis	-	-	-	-	-	-
Stomatitis	-	-	-	-	-	-
Glossitis	-	-	-	-	-	-
Proctitis	-	-	-	-	-	-
Vaginitis	3	2.63	4	9.3	2	13.33
Nettle rash	9	7.89	3	6.98	-	-
Photosensibilisation	-	-	-	-	-	-
Urticaria	-	-	-	-	-	-
Skin hyperemia	-	-	-	-	-	-
Loss of appetite	15	13.16	4	9.3	2	13.3
Vomiting	2	1.75	-	-	-	-
Headache	2	1.75	1	2.33	-	-
Dizziness	1	0.88	1	2.33	1	6.67

TABLE 7.

Treatment efficacy of Mycoplasmosis, Ureaplasmosis and Chlamidiosis by Unidox

Infection and virus	I group (n=114)				II group (n=43)				III group (n=15)			
	Before treatment		After treatment		Before treatment		After treatment		Before treatment		After treatment	
	Abs	%	Abs	%	Abs	%	Abs	%	Abs	%	Abs	%
Mycoplasma genitalis	12	10.5	2	1.7	1	2.3	0	0	2	13.3	1	6.6
Ureaplasma urealiticum	28	24.6	4	3.5	12	27.9	1	2.3	4	26.6	2	13.3
Chlamidia trachomatis	2	1.75	0	0	-	-	-	-	1	6.67	0	0

occurred most often: ureaplasmosis, gardenellesis, CMV. Mycoplasmosis also made not a low percent, especially in the 1st clinical group of patients.

Herpes virus type 2 was revealed in patients of the 1st clinical group (19.03%) indicating that immunodeficiency state was present in these patients.

In more than half of the patients the results of the vaginal smear and vaginal examination revealed long lasting relapsing vaginal candidomycoses, which are also the signs of immunodeficiency state in these patients.

The patients took Unidox twice a day after meal with 1 glass of water (every 12 hours), treatment course lasted on average 10-14 days making its side effects on GIT and nervous system minimal. As GIT side effects, nausea was noted in 7 patients (from 157 ones), glossitis in 20, nettle rash in 12, which disappeared after Zirtec or Diazoline intake (*per os*), loss of appetite was recorded in 50 and diarrhea in 3 patients (Table 6).

After Unidox treatment the presented complaints concerning pain in the lower abdominal, iliac and lumbar regions disappeared in 93% of the patients. Copious discharges disappeared as well in most of the patients. The repeated PCR study carried out to reveal Ureaplasma in cervical canal (in 2 weeks following Unidox administration) revealed high efficacy of the treatment by the mentioned preparation, as compared to the control group. According to data of repeated ultrasound examination, positive dynamics in chronic metroendometritis and bilateral chronic salpingooophoritis was revealed.

Good results were obtained in repeated cytological, oncocytological studies carried out 1 month following Unidox treatment.

In no patients of the 1st clinical group, as well as in 87.5% patients of the 2nd clinical group oncocytological diagnosis of CIN 1 was revealed.

CONCLUSION

As obvious from Table 7, patients with *Mycoplasma genitalis* have good results: 98.3% in patients of the first clinical group and 100% in the patients of the second clinical group after treatment by "Unidox". As for patients with *Ureaplasma urealiticum*, we revealed high efficacy of treatment with the mentioned preparation: 96.5% in first clinical group and 97.7% in second clinical group. *Chlamidia trachomatis* was revealed in 1.75% patients of the first clinical group and they had full recovery [*McGregor J., French J., 1991*; *Clad A. et al., 1993; Marra F. et al., 1997; Rastogi S. et l., 1999*].

Thus, Unidox turns to be the most highly effective, not expensive preparation with minimal side effects up-to-date.

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