Microbial And Clinical Associations Of Vaginal Mycoplasma Carriage

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Abstract

Probable clinical and microbial associations of genital mycoplasmas were investigated. Archive records of 290 female patients with Mycoplasma hominis and Ureaplasma urealyticum were reviewed. A strong association was present between Mycoplasma hominis and bacterial vaginosis (BV) (OR: 4.8; 95% CI: 2.65-8.69) and absence of normal vaginal flora (NVF) (OR: 3.08; 95% CI: 1.76-5.39). Ureaplasma urealyticum was associated with BV (OR: 4.419; 95% CI: 2.43-8.03, p<0.010), weakly associated with candida growth (OR: 1.84; 95% CI: 1.02-3.33), leukocyte presence in smear (leukocyte/epithelial cells>1) (p=0.045) and contraceptive methods used (p=0.043). Detection of the two agents together was rather associated with BV (OR: 3.32; 95% CI: 1.82-6.04) and weakly with absence of NVF (OR: 2.15; 95% CI: 1.19-3.89). In conclusion, although causative agent of BV is still unclear, Mycoplasma hominis and Ureaplasma urealyticum alone or together have a significant co-incidence with BV and absence of normal vaginal flora.

INTRODUCTION

Causative role of genital mycoplasmas in pathogenesis of some female upper genital system infections is clearly known ([1]). However their roles in lower genital system infections is highly controversial, except for bacterial vaginosis (BV). Despite opposing issues ([2], [3]) there is a strong consideration of an association between BV and Mycoplasma hominis alone or together with Ureaplasma urealyticum. However, the nature of this association and whether it is causative is still unclear ([1]). In this retrospective study we investigated the probable associations between Mycoplasma hominis and Ureaplasma urealyticum existence in vaginal samples with various microbial and clinical parameters.

MATERIAL AND METHODS

Patients and data screening. The March 1999-March 2003 digital laboratory records of Fatih University hospital were screened and it was observed that in this interval a total of 2579 women (aged: 16-56; 31.84 ± 8.4, Median: 31) vaginal mycoplasma (Mycoplasma hominis and Ureaplasma urealyticum) testing were performed. From these patients 290 were randomly selected and their clinical and microbiological records were retrospectively investigated in detail from patient files in hospital archive and digital laboratory records.

Screened parameters. Clinical parameters: Age, sexual activity, marrige, menstrual irregularity, menstrual retard, dysmenorrhea, contraceptive method, vaginal discharge, vaginal pruritus, lower abdominal pain, inguinal pain, dysparonea, postcoital pain, postcoital bleeding. Microbial parameters: Normal vaginal flora status, Trichomonas vaginalis by direct microscopy or culture, Candida growth, leukocytes in smear (leukocyte/epithel ratio) and bacterial vaginosis.

Routine culture and microscopic examination. Vaginal swabs collected and transported with standard methods were subjected to routine vaginal culture and wet and stained microscopic examinations beside the mycoplasma research. Gram-stained smears were scored for bacterial vaginosis according to Nugent criteria ([4]). Trichomonas vaginalis detection was performed by direct microscopy and, in case of its failure, by cultivation in Diamond medium.

Mycoplasma detection. Mycoplasma IST2 (BioMérieux, France) kits were used for cultivation of Mycoplasma hominis and Ureaplasma urealyticum. All of the processes were performed according to the manufacturer instructions.

Statistical analysis. Statistical analyses were performed in SPSS 11.5 for Windows software program by using X^2 and Fisher's Exact tests. The p values lower than 0.05 were

considered significant. For some parameters seemed significant, odds ratios and 95% confidence interval limits were also calculated.

RESULTS

Totally 2027 (78.6 %) samples were negative for both mycoplasmas. Of 552 (21.4 %) positive samples, 110 (4.3 %) had M.hominis, 525 (% 20.4) had Ureaplasma urealyticum, 83 (% 3.2) had Mycoplasma hominis and Ureaplasma urealyticum together. Mycoplasma detection profile of the screened patients can be seen in the Table 1.

The data obtained from screening the patient files and the laboratory records are summarized in the Table 2. X^2 analyses results of associations between mycoplasma positivity and the screened parameters are also presented in that table.

Figure 1

Table 1: and profile of the patients included in the study.

	Ureaplasma urealyticum +	Ureaplasma urealyticum -	Total
Mycoplasma hominis +	80	26	106
Mycoplasma hominis -	84	100	184
Total	164	126	290

Figure 2

Table 2: Statistical analyses of associations between , and some clinical and microbiological parameters

Parameter	Valid cases n.	Positive cases n.	M.hominis Pos. n.	Ureaplasma urealyticum Pos.n.	Association with M.hominis	Association with Ureoplasma urealyticum	Association with M+U*
					P	P	P
Age	286	-	-	-	0.642	0.123	0.172
Sexually active	191	181	70	99	0.528	0.280	0.456
Married	286	260	93	147	0.129	0.939	0.467
Menstrual irregula	203	50	14	29	0.076	0.324	0.460
Menstrual retard	203	51	17	29	0.299	0.390	0.423
Contraceptive use	178	132	44	66	0.262	**0.043**	0.626
Vaginal discharge	217	151	60	84	0.277	0.854	0.278
Vaginal pruritus	216	94	32	55	0.494	0.074	0.788
Lower abdo. pain	209	92	28	49	0.075	0.491	0.149
Inguinal pain	210	91	29	45	0.132	0.234	0.145
Dysmenorrhea	203	55	20	35	0.561	0.057	0.374
Dyspareunia	195	36	15	16	0.345	0.101	0.172
Postcoital pain	195	26	12	16	0.565	0.788	0.490
Postcoital bleeding	195	9	1	4	**0.021**	0.741	0.056
NVF missing	272	157	71	91	**0.000**	0.054	**0.000**
T.vaginalis	272	8	7	4	**0.003**	0.494	0.126
Candida growth	272	67	24	45	0.803	**0.045**	0.396
Leukocy. in smear	272	20	10	6	0.112	**0.045**	0.364
Bacterial vaginosis	272	69	43	48	**0.000**	**0.010**	**0.000**

*Mycoplasma hominis with Ureaplasma urealyticum

As it can be seen in the Table 2, Mycoplasma hominis alone was strongly associated with normal flora missing (OR: 3.08; 95% CI: 1.76-5.39), BV (OR: 4.8; 95% CI: 2.65-8.69) (p<0.0001), post-coital bleeding (p=0.021) and Trichomonas vaginalis (p=0.003). Ureaplasma urealyticum alone was strongly associated with BV (OR: 4.419; CI: 2.43-8.03, p<0.010), weakly associated with Candida growth (OR: 1.84; 95% CI: 1.02-3.33) leukocyte presence in smear (leukocyte/epithel>1) (p=0.045) and contraceptive method used (p=0.043). Detection of the two agents together was rather associated with BV (OR: 3.32; 95% CI: 1.82-6.04) and weakly with NVF missing (OR: 2.15; 95% CI: 1.19-3.89) (p<0.0001).

Ureaplasma urealyticum detection rate was significantly lower in women applying any contraceptive method (intrauterine device: n.60, 33.7 %; coitus interruptus: n.29, 16.3 %; condom: n.32, 18 %; calendar method: n.9, 5 %; vaginal lavage: n.2, 1.1 %; or oral contraceptive: n.2, 1.1 %) than the others (50 versus 67.4 per cent respectively; p=0.03). A more detailed analysis revealed that the significant difference was arisen from merely intrauterine device use (p=0.017); that is, women using this method had lower Ureaplasma urealyticum isolation rate (42.2 versus 60.5 per cent).

DISCUSSION

Our mycoplasma isolation rates (4.3 % for Mycoplasma hominis, 20.4 % for Ureaplasma urealyticum) were very low compared to the current knowledge in the textbooks (about 20 and 60 per cent respectively) ([1,5]). This may be arisen from probable failure in sample collection and transport, sensitivity of the isolation method used or some unknown factors. However, it should be noted that there is not enough data about genital mycoplasma colonization rates in Turkish women. Like to finding in another study ([6]) we more frequently isolated Ureaplasma urealyticum from Mycoplasma hominis positive samples than the negative ones (75 % and 18 % respectively).

Our findings of BV and Mycoplasma hominis/ Ureaplasma urealyticum association are similar to many of previous reports. This clear association was supported by both X^2 test results and high OR values. Although they are among the normal vaginal flora members of sexually active women, Mycoplasma hominis and Ureaplasma urealyticum play fairly well documented roles in pathogenesis of some infectious disorders. While Mycoplasma hominis is associated with pyelonephritis, pelvic inflammatory diseases (PID), postabortal fever and postpartum fever; Ureaplasma urealyticum is among the etiologic agents of nongonococcic urethritis, Reiter disease, urinary calculi, postpartum fever,

infertility, spontaneous abortion, premature birth and corioamnionitis. All of the disorders above develop following the invasion of these mycoplasmas to the certain extravaginal sites ([1,5]). On the other hand, whether these microorganisms have any role in the lower genital tract disorders is controversial. One important exception of that widely accepted truth is BV. In spite of some opposite reports ([2, 3]) there are many studies implying to an association between Mycoplasma hominis, alone ([7,8,9,10,11,12,13,14]) or together with Ureaplasma urealyticum ([11]), and BV. Moreover, in a study it was asserted that Mycoplasma hominis is more associated with BV than Gardnerella vaginalis ([2]). However the nature of that association is not clear yet. Do the mycoplasmas play a causative role in BV or they are merely cofactors proliferating due to the environmental changes of lower genital tract? In an interesting study of this context, inoculating M.hominis, Skharupeta et al accomplished to develop inflammation in BALB/c mice vaginal mucosa, experimentally ([15]). All the same, more and comprehensive experimental studies are needed to explore the nature of the mycoplasma-BV association.

A significant coexistence of Mycoplasma hominis and Trichomonas vaginalis was mentioned in some previous studies ([7, 16]). Although our findings also support such coexistence, this association should be evaluated cautiously, because the number of positive cases was too low (only 8 cases). A similar interpretation can be made for the association between Mycoplasma hominis and post-coital bleeding (only 9 cases).

The association between Candida growth and Ureaplasma urealyticum was very weak; indeed the lower limit of CI was equal to almost 1.00. While there is some report implying that Mycoplasma hominis isolation has a lower rate in Candida positive women probably due to acid pH of vagina ([17]) we could not reached to any published data about Ureaplasma urealyticum-candida relations.

IUDs had been accused of causing PID by allowing microbial contaminants in the lower genital tract such as Chlamydia trachomatis, Ureaplasma urealyticum, and Neisseria gonorrhoeae to invade the pelvic tissues moving upward on them ([18]). Our finding is apparently paradoxical, that is, on the contrary of a previous report ([19]) our Ureaplasma urealyticum isolation rate was lower in IUD users. This may be due to the antibacterial effects of some IUDs ([20]). But, lower isolation rate may be not implying a lower PID rate.

Considering the fact that Mycoplasma hominis is among the core microorganisms of BV ([12]), some gynecologists (at least in our country) request sometimes mycoplasma culture/detection for BV diagnosis. However, in our opinion, this approach neither really contributes to the diagnosis nor is cost-effective. Keeping in mind that Mycoplasma hominis and Ureaplasma spp harmlessly colonize lower genital tract of about 20-60 % healthy women, it is very difficult to interpret the meaning of detection of these agents in a vaginal sample. Although some quantitative approaches of mycoplasma cultures are exist, they are valid only for urine samples. Besides, mycoplasma culture is a labor-intensive process either by using conventional methods or by using commercial kits. Whereas, some cheaper, easier to carry out and more effective methods such as gram stain and BV scoring are available for the BV diagnosis. There is no justification to prefer the mycoplasma culture instead of these methods, even to confirm them by it. Indeed, since 2002 we achieved a significant decrease in the requests for vaginal mycoplasma culture, by interviewing with and persuading our hospital gynecologists.

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