

Oral contraceptive use and prevalence of infection with *Chlamydia trachomatis* in women

G R KINGHORN AND M A WAUGH

From the Department of Genitourinary Medicine, Leeds General Infirmary, Leeds

SUMMARY One thousand and eighty non-pregnant women aged 16-34 years, presenting for the first time at a clinic for sexually transmitted diseases (STD), were examined and screened for infection with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, and *Candida* species. The respective prevalence rates were 21.1%, 20.7%, 13.4%, and 27.8%. Isolation rates for *C trachomatis*, either occurring alone or in association with other genital infections, were significantly greater in women using oral contraceptive agents. This was not because oral contraceptive users were more promiscuous.

The findings strengthen the case for providing a routine chlamydial culture service for women attending STD clinics. They also indicate that the likelihood of chlamydial infection in women taking oral contraceptives is increased.

Introduction

Infection with *Chlamydia trachomatis* is now recognised as a major cause of genital tract infection. In contrast to infections in men, who usually present with nongonococcal urethritis, those in women often have no specific symptoms or signs.¹ Unless routine cultures for this organism are undertaken, such infection is easily overlooked. Several recent studies have suggested that chlamydial infection is promoted by the use of oral contraceptive agents,²⁻⁴ although this is disputed by others.⁵⁻⁹ If such an effect does exist, it is not clear whether this is secondary to differences in the sexual behaviour of oral contraceptive users and non-users leading to increased exposure to *C trachomatis* or due to a specific hormonal effect causing increased susceptibility to the organism.

Since 1975 women with new complaints attending the department of genitourinary medicine at Leeds General Infirmary have had specimens taken routinely for the culture of *C trachomatis* at their first attendance. The aims of the present study were: (1) to compare the isolation rate for *C trachomatis* with that for other major genital pathogens and to compare the rate in 1979 with that found in a previous study¹⁰; and (2) to examine more closely the possible association between chlamydial infection and the use of oral contraceptive agents.

Address for reprints: Dr G R Kinghorn, Department of Genitourinary Medicine, Special Clinic, Royal Infirmary, Sheffield S6 3DA

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Patients and methods

The study population consisted of 1080 consecutive non-pregnant women aged between 16 and 34 years presenting for the first time to the department of genitourinary medicine, Leeds General Infirmary, Leeds, between 1 January and 30 September 1979.

SPECIMEN COLLECTION

After a full history had been taken, patients were examined in the lithotomy position. Specimens for immediate microscopy and the appropriate culture were taken from the urethra and cervix for the identification of *N gonorrhoeae* and from the posterior forniceal pool for *T vaginalis* and *Candida* species. The methods of specimen collection, cultural techniques, and diagnostic criteria have been described.¹¹

Specimens for culture for *C trachomatis* were collected by rotating a cottonwool swab in the cervical canal and on any exposed ectopic columnar epithelium. The swabs were then placed in transport medium (McCoy cell growth medium with 0.5% glucose and 10% sorbitol) and stored at 4°C before being transferred to the virology laboratory. The method used for isolating *C trachomatis* in untreated McCoy cells has been described.¹²

DATA ANALYSIS

For analysis of the results patients were divided into two groups, those who used oral contraceptives and those who used other methods or no contraception at all. Demographic and clinical data on the two groups

infected with *C trachomatis* were compared. In this study the presence of cervicitis was defined as the presence of mucopurulent or purulent cervical secretion showing >5 white cells per high-power field ($\times 100$ magnification) associated with one or more of the following: hyperaemia of the ectocervix, hypertrophic ectopy of the columnar epithelium, and contact bleeding from the endocervical canal. Statistical analysis was made by the χ^2 test with Yates's correction.

Results

ISOLATION RATES

The isolation rates for *C trachomatis*, *N gonorrhoeae*, *T vaginalis*, and *Candida* species in the 1080 women studied are given in table I. *C trachomatis* was found in 160 (26.6%) of all 601 oral contraceptive users compared with only 72 (15%) of all 479 non-users ($P < 0.001$). *T vaginalis* was found significantly less frequently in oral contraceptive users (11%) than in non-users (16.5%) ($P < 0.02$). There were no significant differences between oral contraceptive users and non-users in the incidences of *N gonorrhoeae*, *Candida* species, or of women uninfected with any of these four pathogens.

TABLE I Isolation rates in relation to use of oral contraceptives

Pathogens	Oral contraception					
	All women		Users		Non-users	
	No	%	No	%	No	%
<i>Chlamydia trachomatis</i>	232	21.5	160	26.6*	72	15.0
<i>Neisseria gonorrhoeae</i>	224	20.7	125	20.8	99	20.7
<i>Trichomonas vaginalis</i>	145	13.4	66	11.0†	79	16.5
<i>Candida</i> species	300	27.8	180	30.0	120	25.1
No pathogen isolated	360	33.3	187	31.1	173	36.1
Total No of patients	1080		601		479	

* $\chi^2 = 20.6$; $P < 0.001$

† $\chi^2 = 6.5$; $P < 0.02$

Single infections

Use of oral contraceptives in women with single infections is shown in table II. The number of oral contraceptive users in women infected with *C trachomatis* alone was significantly increased compared with those infected with each of the other three pathogens alone and with those uninfected with any of these organisms ($P < 0.002$). The incidence of infection with *C trachomatis* alone was 10.8% of all oral contraceptive users in the study population compared with 5.2% of all non-users ($\chi^2 = 10.2$; $P < 0.002$).

TABLE II Use of oral contraceptive agents in women with single infections

Pathogens	Total No of women	Users*		Statistical difference†	
		No	%	χ^2 test	Probability
<i>C trachomatis</i> alone	90	65	72.2		
<i>T vaginalis</i> alone	43	16	37.2	13.5	<0.001
<i>N gonorrhoeae</i> alone	68	36	52.9	5.4	<0.05
<i>Candida</i> species alone	113	64	56.6	4.6	<0.05
No pathogen isolated	360	187	51.9	11.2	<0.002

*Of oral contraceptive agents

†In use of oral contraceptives compared with isolation of *C trachomatis* alone

Concomitant infections

The incidences of concomitant infection with *C trachomatis* in all women infected with *N gonorrhoeae*, *T vaginalis*, and *Candida* species were 37.5%, 29.0%, and 16.0% respectively (table III). In each of these groups, the incidence of concomitant infection with *C trachomatis* was significantly increased in oral contraceptive users compared with non-users.

Thus, whether occurring as the sole pathogen or in association with another genital pathogen, infection with *C trachomatis* was significantly more common in oral contraceptive users than in non-users.

TABLE III Isolation rates of *Chlamydia trachomatis* in women with mixed infections

Pathogens	Total No of women	With concomitant chlamydial infection					
		All		Users*		Non-users*	
		No	%	No	%†	No	%†
<i>N gonorrhoeae</i>	224	84	37.5	59	47.2‡	25	25.3
<i>T vaginalis</i>	145	42	29.0	28	42.4§	14	17.7
<i>Candida</i> species	300	48	16.0	38	21.1¶	10	8.3

*Of oral contraceptive agent

†Based on numbers of users and non-users of oral contraceptives with each condition given in table I

‡ $\chi^2 = 10.4$; $P < 0.01$

§ $\chi^2 = 9.5$; $P < 0.01$

¶ $\chi^2 = 7.8$; $P < 0.01$

DEMOGRAPHIC DATA

Demographic and social data on all women infected with *C trachomatis* are shown in table IV, together with a comparison of results in oral contraceptive users and non-users. There was a predominance of young, single, nulliparous, Caucasian women. One hundred and fifty-seven (63.4%) of all the 232 infected women presented to the clinic for reasons other than being known contacts of men with nongonococcal urethritis. There was no difference between oral contraceptive users and non-users in

TABLE IV Demographic data on women with chlamydial infection

Data	All	Users*	Non-users*
No of patients	232	160	72
Age			
% less than 25 years	72.8	74.4	69.9
Marital state			
% Single	69.4	71.9	63.9
% Married	10.8	7.5†	18.1
% Divorced/separated	19.8	20.6	18.1
Ethnic group			
% Caucasian	90.5	91.3	88.9
Job status			
% Employed	54.3	60.6‡	40.3
% Student	15.1	16.3	12.5
Reason for attendance			
% Known contacts of NSU	36.6	36.3	37.5
% Known contacts of gonorrhoea	34.5	34.3	34.7
% Other	28.9	29.3	27.8
No of sexual partners in previous 3 months			
% 0	0.4		1.4
% 1	68.5	70.0	65.3
% 2	23.3	25.0	19.4
% 3 or more	7.8	5.0§	13.9
No of pregnancies			
% 0	59.8	66.3	45.8
% 1	20.7	20.0	22.2
% 2 or more	19.4	13.8¶	31.9

*Of oral contraceptive agents

† $\chi^2 = 4.7$; $P < 0.05$ ‡ $\chi^2 = 7.5$; $P < 0.01$ § $\chi^2 = 4.3$; $P < 0.05$ ¶ $\chi^2 = 9.4$; $P < 0.01$

age, ethnic group, or reason for attendance. Non-users infected with *C trachomatis* differed from their counterparts using oral contraceptives; more were likely to be married ($P < 0.05$), to be unemployed ($P < 0.01$), to admit to three or more sexual partners in the preceding three months ($P < 0.05$), and to have had multiple pregnancies ($P < 0.01$). No significant differences were shown in the proportions in each group admitting to multiple sexual partners in the three months before attendance at the clinic between oral contraceptive users and non-users in the groups of women with gonorrhoea alone, trichomoniasis alone, candidosis alone, or with no infection.

CONCOMITANT INFECTIONS

In women with chlamydial and concomitant infections there were no significant differences between oral contraceptive users and non-users in the incidence of gonorrhoea, trichomoniasis, candidosis, or infection with other STDs (table V).

CLINICAL FEATURES

The clinical details of women infected with *C trachomatis* alone are shown in table VI. Of the 90

TABLE V Concomitant infections in women infected with *C trachomatis*

Pathogens	All	Users*	Non-users*
No of patients	232	160	72
% With no other infection	38.8	40.6	34.7
% With <i>N gonorrhoeae</i>	36.2	36.9	34.7
% With <i>T vaginalis</i>	18.1	17.5	19.4
% With <i>Candida</i> species	20.7	23.8	13.9
% With other STD	10.3	9.4	12.5

*Of oral contraceptive agents

TABLE VI Clinical features in women infected with *C trachomatis* alone

	Total No	Users %*	Non-users %*
Symptoms			
None	60	67.6	64.0
Excessive vaginal discharge	27	29.2	32.0
Frequency/dysuria	5	6.2	4.0
Abdominal pain	4	4.6	4.0
Signs			
No clinical abnormality	23	16.9†	48.0
Cervicitis	66	81.5‡	52.0
Vaginitis	13	15.4	12.0
No of women infected with <i>C trachomatis</i> alone	90	65	25

*Of oral contraceptive agents

† $\chi^2 = 6.6$; $P < 0.01$ ‡ $\chi^2 = 7.6$; $P < 0.01$

women 60 (66.7%) were asymptomatic; there were no differences in the presence and type of symptoms between oral contraceptive users and non-users. However, oral contraceptive users infected with *C trachomatis* alone had cervicitis significantly more often than non-users ($P < 0.01$).

Discussion

The isolation of *C trachomatis* from 21% of women aged between 16 and 34 years attending the Leeds clinic is comparable with the isolation rates found in a smaller previous study¹⁰ in the same department and in recent studies elsewhere in England.^{2,6,8,13,14} It is noteworthy that only 75 (37%) of all 232 infections with *C trachomatis* occurred in women who were known contacts of men with nongonococcal urethritis and who would therefore routinely have received antichlamydial therapy. This finding supports the view of those who consider that a service for culture of *C trachomatis* is essential¹⁵ and as important as that for culture of *N gonorrhoeae* in women attending STD clinics. We have found that infected women are usually asymptomatic and that there are no reliable clinical indicators of infection. Seventy-three per cent of women infected with *C trachomatis* alone had some degree of cervicitis,

although this was usually minor. The most frequent clinical abnormality was cervical mucopus associated with contact bleeding from the endocervical canal. We also noted that a small percentage of women in whom no pathogen other than *C trachomatis* could be isolated also had a vulvovaginitis with a frothy mucopurulent vaginal discharge with or without cervical abnormalities.

The finding of a reduced incidence of trichomoniasis in oral contraceptive users in this study, in which the diagnosis was made by both microscopy and culture, confirms an earlier report, in which the diagnosis was made by microscopy alone.¹⁶ The present study suggests a clear association between *C trachomatis* infection, whether occurring alone or with concomitant gonorrhoea, trichomoniasis, or candidosis, and the use of oral contraceptive agents. It confirms previous studies of both selected³ and non-selected² groups of women attending STD clinics and a gynaecological clinic,⁴ which showed a similar increased incidence of chlamydial infection in oral contraceptive users. We found no evidence that this effect was related to increased promiscuity in such women. Indeed non-users of oral contraceptives with chlamydial infection had multiple sexual partners significantly more often. It is still not clear, however, whether the increased isolation rate is due to a greater infectivity in oral contraceptive users—perhaps because of increased exposed susceptible columnar epithelium—or to easier detection of *C trachomatis* by present cultural methods, possibly as a result of a stimulative effect of steroids on the growth of *C trachomatis*¹⁷ within the cervical epithelium.

This study clearly emphasises the importance of a routine chlamydial culture service in women attending STD clinics, particularly as the number of young women using oral contraceptive agents is increasing and may well serve to increase the potential reservoir for chlamydial infection within the community.

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