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Pelvic inflammatory disease associated with Chlamydia trachomatis infection after therapeutic abortion

A prospective study

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SUMMARY *Chlamydia trachomatis* was cultured from the cervix of 70 of 557 (12·6%) patients admitted for therapeutic abortion. Postoperatively, 22 (3·9%) developed acute pelvic inflammatory disease (PID); of these women, 14 (63·6%) had harboured *C trachomatis* in the cervix before the abortion. Thus of 70 patients with chlamydial infection, 14 (20%) developed PID postoperatively. Of the chlamydia-positive patients, six of the 15 (40%) aged <20 years and eight of the 53 (15%) patients aged 20-30 years developed PID. Twelve of the 70 women with chlamydial infections showed a significant increase in serum chlamydial IgG antibody titres over a four week period; four of these women developed PID. *Neisseria gonorrhoeae* was recovered from only four patients, one of whom developed PID after the abortion. Treatment with a single dose of intravenous doxycycline (200 mg) was given before and during surgery to about half of the patients. In our study, this regimen had no protective effect against the development of PID associated with *C trachomatis*.

Introduction

Pelvic inflammatory disease (PID) is the most important complication of therapeutic abortion, occurring in 1-9% of all cases.[1-3] One episode of PID may result in tubal dysfunction, and tubal patency may be impaired with recurrent infections causing subsequent infertility.[4] In addition to infertility the tubal infection may cause chronic abdominal pain and increased risk of extrauterine pregnancy.[5] The presence of *Chlamydia trachomatis* in the cervix is a frequent causal factor in the epidemiology of PID in Scandinavia.[6-8] In addition to *C trachomatis, Neisseria gonorrhoeae, Mycoplasma hominis,* and anaerobes are known to be causative agents of acute PID.[7]

The aim of the present study was to determine the incidence of *C trachomatis* infection in women admitted for therapeutic abortion, its association with postoperative PID, and the prophylactic effect of a single dose of doxycycline before and during the operation.

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Patients and methods

STUDY POPULATION

A total of 557 women admitted consecutively to hospital for termination of pregnancy from December 1980 to June 1981 was studied. The surgical procedure was dilatation and vacuum aspiration. About half of the patients (268/557) were given a single intravenous dose of 200 mg doxycycline before and during the operation. With this regimen therapeutic serum concentrations are maintained for at least 24 hours and in most cases for 48 hours.[9] The other patients did not receive antibiotic treatment.

The mean age of the patients was 25·6 (range 16-44) years. Two hundred and ninety five (53%) women were pregnant for the first time whereas 153 (27·5%) had had one or more therapeutic abortions previously; 151 (27·1%) women had had at least one full-term delivery.

The diagnosis of PID was based on the clinical criteria of pelvic pain, tender adnexal masses, increased erythrocyte sedimentation rate, and usually fever. The patients who developed acute salpingitis were treated with doxycycline for 10-14 days (an initial dose of 200 mg followed by a daily dose of 100

mg). All patients were advised to return for a follow-up examination four weeks after the abortion. Altogether, 541 (97%) patients attended for follow-up or sent some information postoperatively.

ISOLATION OF *C TRACHOMATIS* AND *N GONORRHOEAE*

Before surgery specimens for culture for *C trachomatis* and *N gonorrhoeae* were collected from the cervix. Cotton-tipped swabs were used to collect cervical material and were transported to the laboratory in a sucrose phosphate buffer (2SP). All the specimens were cultured within 24 hours. Specimens for culture for *N gonorrhoeae* were collected with charcoal-treated cotton-tipped swabs, which were transported to the laboratory in a modified Stuart medium. *C trachomatis* was cultured in cycloheximide-treated McCoy cells[10] and *N gonorrhoeae* on a modified Thayer-Martin medium and identified by sugar fermentation tests.

SEROLOGY

Before the abortion and at the follow-up visit serum specimens were examined for chlamydial IgG antibodies by an enzyme-linked immunosorbent assay (ELISA).[11] The ELISA was performed on flat-bottomed microtitre plates coated with a suspension of partially purified cell-cultured *C trachomatis* subtype LGV-2 particles. LGV-2 was used as antigen throughout this study, since about 95% of sera containing antibodies to *C trachomatis* may be detected solely using the strain LGV-2.[12] Antibody titres were expressed as the reciprocal of the highest sample dilution showing at least twice the mean absorbance value of a group of negative serum specimens. A titre of >8 was defined as a positive result. A fourfold or greater rise in titre and a positive culture result were regarded as evidence of active chlamydial infection. In the patients with cervical gonorrhoea antibodies against *N gonorrhoeae* were examined by the complement fixation test.

STATISTICAL ANALYSIS

The χ^2 test and the binominal statistic (z)[13] were used to analyse the difference between the two groups.

Results

C trachomatis was isolated from the cervix in 70 of the 557 (12·6%) patients, more often in the younger patients (table I). *N gonorrhoeae* was cultured in four (0·7%) patients, and one patient harboured both microorganisms in the cervix.

Before abortion chlamydial IgG antibodies were detected in 336 (60%) women. Among the 70 women with cervical *C trachomatis* infection, chlamydial IgG antibodies were detected in 66 (94%) whereas 270 (55%) patients from whose cervices *C trachomatis* was not isolated had chlamydial antibodies (table II). Thus, chlamydial IgG antibodies were detected more frequently ($p \leqslant 0{\cdot}001$) in the chlamydia-positive group than in the chlamydia-negative group.

PID developed postoperatively in 22 of the 557 (4%) women (table III), in six of whom it was severe and in 16 more moderate. All infections occurred within three weeks of surgery. Before the abortion, 14 (64%) of the 22 patients with PID harboured chlamydiae in the cervix and one (5%) had cervical gonorrhoea. Thus, 14 of the 70 (20%) patients from whose cervices *C trachomatis* was isolated developed PID postoperatively. The highest incidence of PID occurred among teenagers with cervical chlamydiae (table III). Fifteen of the 22 (68·2%) patients who

TABLE I *Results of cervical culture and serological tests for C trachomatis in patients before therapeutic abortion in relation to age*

Age group (years)	No (%) of patients		
	Total	Culture-positive	With ELISA titre >8
⩽19	96	15 (15·6)	40 (41·7)
20-24	212	38 (17·9)	139 (65·6)
25-29	142	15 (10·6)	99 (69·7)
⩾30	107	2 (1·9)	58 (54·2)
Total (16-44)	557	70 (12·6)	336 (60·3)

TABLE II *Results of culture for C trachomatis and of serological tests in 557 patients admitted for therapeutic abortion*

Results of chlamydial culture	No (%) of patients	
	Total	With chlamydial antibodies
Preoperatively:		
Negative	487	270 (55·4)
Positive	70	66 (94·3)
At follow up:		
Positive	60	57 (95·0)

TABLE III *Number of patients with PID after therapeutic abortion in relation to age and chlamydial culture results*

Age group (years)	No (%) of patients:		No (%) culture-positive	
	Total	With PID	Total	With PID
⩽19	96	7 (7)	15	6 (40)
20-24	212	9 (4)	38	6 (16)
25-29	142	5 (4)	15	2 (13)
⩾30	107	1 (1)	2	0
Total	557	22 (4)	70	14 (20)

developed PID were primigravidae. There was no significant difference in the incidence of PID between primigravidae and multigravidae.

A fourfold or greater rise in ELISA IgG titre was detected in 12 of the chlamydia-positive patients who attended for follow-up examination; four of these 12 patients developed PID. The patient who was infected with *N gonorrhoeae* and who developed PID postoperatively had gonococcal antibodies which were detected by the complement fixation test.

Before and during surgery a single intravenous dose of doxycycline was given to 268 patients; the other 289 patients were not given antibiotics. Of the 22 patients who developed PID, seven of the 15 women had been given doxycycline. Among the 70 patients who were infected with *C trachomatis,* 32 of the 38 received doxycycline. In each group five and nine patients developed PID.

Discussion

The presence of pathogenic microorganisms in the cervix before therapeutic abortion seems to be of crucial importance in the development of ascending infection. The incidence of chlamydial infection of the cervix in women undergoing termination of pregnancy has ranged from 5% to 13%, whereas the incidence of gonorrhoea has been as low as 1-3%.[14 15] The high incidence of *C trachomatis* infections and the fact that about 20% of the patients with cervical chlamydiae develop PID postoperatively[14 15] underline the importance of these infections. The small number of cases of gonococcal PID reflects the low incidence of gonorrhoea, however; similar results were found in the present study in which 20% of patients from whose cervices *C trachomatis* was isolated developed PID postoperatively. Only one case of PID was probably caused by *N gonorrhoeae.* Moreover, this study has shown that abortions in patients under 30 years are more likely to be complicated by PID than those performed on older women.

Almost every woman with genital chlamydial infection developed chlamydial serum IgG antibodies detectable by immunofluorescence.[16] Similar results have been obtained by the ELISA test,[11] and in this study 66 of the 70 (94%) patients with a positive culture result for *C trachomatis* had detectable chlamydial IgG antibodies. Twelve women showed a significant rise in chlamydial IgG antibody titres when sera were examined several weeks later. After the abortion four of these patients developed PID. Previous studies have, however, shown that PID associated with *C trachomatis* may occur without symptoms.[6] Thus the 14 cases of PID associated with *C trachomatis* were probably an underestimate.

In the present study, though the incidence of cervical chlamydiae was about the same, serum chlamydial antibodies were found more frequently in women in their 20s than in teenagers. On the other hand, of the patients with cervical chlamydial cultures, six of the 15 patients under 20 years and eight of the 53 patients in their 20s developed PID after surgery. Thus PID associated with *C trachomatis* developed significantly more frequently ($z = 2 \cdot 11$; $p \leqslant 0 \cdot 05$) among the teenagers than among the older patients. Thus earlier *C trachomatis* infections may to some extent prevent ascending chlamydial infection and PID after therapeutic abortion in women with cervical chlamydial infections. The human host is capable of producing both humoral and cellular immune responses, but the relative importance of these in controlling chlamydial infections is not entirely clear.

A single oral dose of 500 mg doxycycline reduces the incidence of pelvic infections after abortion.[17] In the present study a single intravenous dose of 200 mg doxycycline was given to about half of the patients before and during surgery. Of the patients with PID harbouring cervical chlamydiae, five out of 32 had received doxycycline and nine of 38 no antibiotics. In our study this regimen of doxycycline was ineffective in preventing chlamydia-associated PID after therapeutic abortion. Recent studies have shown, however, that longer treatment of women with chlamydial infection with doxycycline during and after abortion significantly reduced the incidence of PID.[14]

Our results indicate that patients with *C trachomatis* of the cervix at the time of termination of pregnancy are at risk of developing PID postoperatively. Cultures for *C trachomatis* should therefore be performed before abortion and appropriate treatment against *C trachomatis* given.

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References

1. Nathanson BN. Ambulatory abortion: experience with 26 000 cases. *N Engl J Med* 1972;**286**:403-7.
2. Moberg P, Sjöberg B, Wiqvist N. The hazards of vacuum aspiration in late first trimester abortions. *Acta Obstet Gynecol Scand* 1975;**54**:113-8.
3. Jerve F, Fylling P. Therapeutic abortion. *Acta Obstet Gynecol Scand* 1978;**57**:237-40.
4. Weström L. Effect of acute pelvic inflammatory disease on fertility. *Am J Obstet Gynecol* 1975;**121**:707-13.
5. Weström L. Diagnosis, aetiology and prognosis of acute salpingitis. *Thesis.* Sweden: University of Lund, 1976.

6. Punnonen R, Terho P, Nikkanen V, Meurman O. Chlamydial serology in infertile women by immunofluorescence. *Fertil Steril* 1979;**31**:656-9.
7. Mårdh P-A. An overview of infectious agents of salpingitis, their biology, and recent advances in methods of detection. *Am J Obstet Gynecol* 1980;**138**:933-51.
8. Vik ISS, Skaug K, Qvigstad E, Ulstrup JC, Jerve F. Isolation and serological diagnosis of *Chlamydia trachomatis* in acute salpingitis. *Tidsskr Nor Laegefor* 1982;**102**:315-7.
9. Gnarpe H, Dornbusch K, Hagg O. Doxycycline concentration levels in bone, soft tissue and serum after intravenous infusion of doxycycline. *Scand J Infect Dis* 1976; **9** suppl: 54-7.
10. Ripa T, Mårdh P-A. New simplified culture technique for *Chlamydia trachomatis*. In: Hobson D, Holmes KK, eds. *Non-gonococcal urethritis and related infections*. Washington DC: American Society for Microbiology, 1977:323-7.
11. Skaug K, Vik ISS, Qvigstad E, Ulstrup JC, Jerve F. Chlamydial serum IgG antibodies in patients with acute salpingitis measured by an enzyme-linked immunosorbent assay. *Acta Pathol Microbiol Scand (C)* 1982;**90**:67-71.
12. Thomas BJ, Reeve P, Oriel JD. Simplified serological test for antibodies to *Chlamydia trachomatis*. *J Clin Microbiol* 1976;**4**:6-10.
13. Dunn OJ. *Basic statistics: a primer for the biomedical sciences*. New York: John Wiley & Sons, 1964: 106-8.
14. Möller BR, Ahrons S, Laurin J, Mårdh P-A. Pelvic infection after elective abortion associated with *Chlamydia trachomatis*. *Obstet Gynecol* 1982;**59**:210-3.
15. Qvigstad E, Skaug K, Jerve F, Vik ISS, Ulstrup J. Therapeutic abortion and *Chlamydia trachomatis* infection. *Br J Vener Dis* 1982;**58**:182-3.
16. Wang S-P, Grayston JT, Kuo C-C, Alexander ER, Holmes KK. Serodiagnosis of *Chlamydia trachomatis* infection with the micro-immunofluorescence test. In: Hobson D, Holmes KK eds. *Non-gonococcal urethritis and related infections*. Washington DC: American Society for Microbiology, 1977:237-48.
17. Brewer C. Prevention of infection after abortion with a supervised single dose of oral doxycycline. *Br Med J* 1980;**281**:780-1.