20

The results of *Chlamydia trachomatis* antibody should not influence patient/doctor decision on performing tubal studies

J. Zohn, J.H. Check, K. Nowroozi and A. Nazari

INTRODUCTION

Many investigators have suggested that there is a higher prevalence of positive *Chlamydia trachomatis* antibody (CTA) in infertile women compared with fertile controls and also a higher prevalence of positive CTA tests in infertile women with tubal disease than in infertile women with normal tubes[1–5].

The possibility exists, however, that since many chlamydial infections are subclinical and that the damage inflicted may be mild, that chlamydial infection *per se* may not substantially decrease fertility. The finding of mild adhesions may lure the treating physician into complacency and the erroneous belief that lysis of adhesions alone may be adequate to treat the fertility problem when in fact more aggressive evaluation and treatment of other factors should be undertaken. This, in turn, could result in an apparently lower frequency of pregnancies in the antibody-positive group.

A study was initiated in which all new infertility patients registering in a private infertility practice were meticulously evaluated and treated for all factors that could contribute to their infertility problem. The choice of a laparoscopy was completely optional. Serum was obtained for determination of CTA levels in all patients, but the results were not presented to the clinician or discussed with the patients until 6 months after the initial visit. The pregnancy rates in patients with positive and negative CTA titers were compared.

MATERIALS AND METHODS

A total of 165 consecutive patients with infertility and who had not had previous tubal studies or tests for CTA were included in this study.

Ovulatory disorders were diagnosed in patients with apparently regular ovarian cycles by late luteal phase endometrial biopsies employing the Pipelle endometrial suction device. Patients in whom endometrial samples were more than 2 days out of phase were diagnosed as having luteal phase defects (LPD). Normal follicular maturation was accepted if the lead ovarian follicle attained an average diameter of at least 18 mm as determined by pelvic sonography at the same time that the serum estradiol concentration (E_2) was at least 200 pg/ml. Patients with LPD but a mature follicle (as defined above) were diagnosed as having pure LPD. These patients were treated with progesterone vaginal suppositories (PVS) starting at 25 mg twice daily beginning 3 days after ovulation. The dose was increased in each subsequent cycle until the endometrial biopsy was corrected. Patients with LPD but in whom the follicle was immature were treated with luteal phase PVS in a manner similar to patients with pure LPD, and, in addition, either clomiphene citrate or bromocriptine mesylate, if hyperprolactinemia was detected (serum PRL > 25 ng/ml).

Patients who were anovulatory on the basis of maximum serum prolactin levels < 25 ng/ml were treated with clomiphene citrate or bromocriptine mesylate as above or human menopausal gonadotropins (hMG) if hypogonadotropic hypogonadism was present.

A spermiogram with a count $\geq 20 \times 10^6$ sperm per ml, motility greater than 50%, or the presence of less than 50% abnormal morphology was considered normal.

Patients admitted to this study were offered the option of either laparoscopy or hysterosalpingogram as an initial part of the evaluation or deferring these procedures for 6 months in an attempt to conceive. If laparoscopy was performed, coagulation of endometriotic implants or lysis of adhesions was performed as appropriate.

The CTA test was performed at the time of the patient's initial office visit. The results were kept in the laboratory and were not disclosed to the patients or treating physician. Thus, the results of the CTA tests did not influence decisions concerning laparoscopy. The CTA test was performed by an enzyme-linked immunosorbent assay (ELISA) utilizing the 'Chlamydia Stat' Test Kit (Whittaker M.A. Bioproducts, Inc., Walkersville, MD).

RESULTS

There were 169 women evaluated. Four patients had equivocal tests for CTA and were eliminated from the study. 62% of the patients evaluated were found to be positive for CTA and 38% were negative. The pregnancy rate as a function of the result is presented in Table 1. There was no statistical difference between the 35% pregnancy rate in patients with negative CTA levels versus the 47% pregnancy rate observed with positive tests.

Only 8.4% of patients with negative CTA had bilateral tubal occlusion compared to 15.3% of patients with positive CTA, but these results were not statistically significant (see Table 2). Although 25% of patients with positive CTA were found to have adhesions compared to only 7% with

Table 1 Pregnancy rate as a function of the result of *Chlamydia trachomatis* antibody (CTA) test. The pregnancy rate in patients with a positive CTA titer was not statistically different from patients with a negative titer

Antibody group	*+ Pregnant*	*− Pregnant*	*Total*
Negative	22	41	63
Positive	48	54	102

$\chi^2 = 1.878$; $p = 0.17$

Table 2 Tubal patency (hysterosalpingography or laparoscopy) as a function of the result of *Chlamydia trachomatis* antibody (CTA) test. No difference in incidence of tubal occlusion with positive or negative antibody titer

Antibody group	*Patent*	*Not patent*	*Not studied*	*Total*
Negative	33	3	27	63
Positive	55	10	37	102

$\chi^2 = 0.495$; $p = 0.17$

negative levels; again this difference was not statistically significant.

Interestingly, there were five ectopic pregnancies out of 48 pregnancies in patients with positive CTA (10%) compared to only one in 22 pregnancies with negative CTA (5%). While the number of patients evaluated was too small to show statistical significance ($p = 0.34$ using Fisher's Exact Test), the possibility exists that positive for CTA is associated with an increased likelihood of intratubal disease.

These data are not supportive of the concept that positivity for CTA in women is associated with a decrease in the fecundity rate. Adhesions (27%) were more likely than tubal occlusion (15.3%) in patients positive for CTA.

DISCUSSION

The objective of this study was to determine if the CTA test should be performed on all infertility patients and if a positive CTA should direct them toward having laparoscopy early in the infertility evaluation. The data from this study does not support the theory that having an earlier laparoscopy on a patient with positive CTA would yield a higher pregnancy rate. Nevertheless, the patient would still be advised that there is a minority group of patients in which clinically significant adhesions may be present and that the subsequent lysis of these adhesions may improve fertility success.

The prevalence of *C. trachomatis* antibodies as measured by ELISA in this study was higher than in some studies previously reported in which an immunofluorescent test was employed[6–9]. This may be due to a difference in the populations studied, but it is also possible that the ELISA system utilized in these studies is more sensitive and can detect lower antibody titers.

Only 15.3% of patients with positive CTA had bilateral tubal occlusion compared to 8.4% of patients with negative CTA. However, 90% of those

with adhesions had positive CTA compared to the 68% rate in the entire population. Since pregnancy rates did not differ, one has to consider the possibility that the adhesions reported are mild and do not have a strong bearing on the infertility. Even some earlier studies by Conway *et al.*[10] showed a high prevalence of positive CTA levels in fertile women seeking sterilization (47.5%) or termination of pregnancy (46%) and in 31% of infertile women with normal Fallopian tubes. Hawes *et al.*[11] showed CTA levels to be positive in 85% of patients with tubal disease, but also in 56% of women who were infertile for other reasons.

Different patient populations might explain to some degree differences in interpretation of antibodies to *C. trachomatis*. The possibility exists that infection with *Chlamydia* is generally mild and is not associated with significant tubal damage. However, the more sexually active the woman has been in the past, the more likely she is to acquire a host of different infections. If certain populations that are sexually active are more prone to acquire *Neisseria gonorrhoeae* infection than others, then it is possible that negative CTA is reflective of a merely diminished prior sexual activity and thus less chance of a damaging gonorrhea infection in these susceptible populations. The patients in this study were predominantly middle class private patients. Some of the other studies suggestive of a correlation between the presence of CTA and tubal damage may have been composed predominantly of populations that were at higher risk for gonorrhea infections. Our data are not supportive of the concept that a positive CTA test should prompt consideration for early tubal studies. The sexual history of the patient and prevalence in the population being studied of risk of tubal disease may be more important in making this decision.

ACKNOWLEDGEMENTS

The authors wish to acknowledge Matthew L. Check for his help in compiling the data, Richard Epstein, MD for his help in statistical analysis, and Carolyn Lauer, MT for her technical assistance.

REFERENCES

1. Jones, R.B., Ardery, B.R., Hui, S.L. and Cleary, R.E. (1982). Correlation between serum antichlamydial antibodies and tubal factor as a cause of infertility. *Fertil. Steril.*, **38**, 553
2. Kosseim, M. and Brunham, R.C. (1986). Fallopian tube obstruction as a sequela to Chlamydia trachomatic infection. *Eur. J. Clin. Microbiol.*, **5**, 584
3. Sarov, I., Kleinman, D., Holcberg, G., Potashnik, G., Insler, V., Cevenini, R. and Sarvov, B. (1986). Specific IgG and IgA antibodies to *Chlamydia trachomatis* in infertile women. *Int. J. Fertil.*, **31**, 193
4. Anestad, G., Lunde, O., Moen, M. and Dalaker, K. (1987). Infertility and chlamydial infection. *Fertil. Steril.*, **48**, 787
5. Robertson, J.N., Ward, M.E., Conway, D. and Caul, E.O. (1987). Chlamydial and gonococcal antibodies in sera of infertile women with tubal obstruction. *J. Clin. Pathol.*, **40**, 377
6. Kane, J.L., Woodland, R.M., Forsey, T., Darousar, S. and Elder, M.G. (1984). Evidence of chlamydial infection in infertile women with and without fallopian tube obstruction. *Fertil. Steril.*, **42**, 843

7. Miller, B.R., Taylor-Robinson, D., Furr, P.M., Toft, B. and Allen, J. (1985). Serological evidence that Chlamydiae and Mycoplasmas are involved in infertility of women. *J. Reprod. Fertil.*, **73**, 237
8. Tjiam, K.H., Zeilmaker, G.H., Alberda, A.T., van Heijst, B.Y., de Roo, J.C., Polak-Vogelzang, A.A., can Joost, T., Stolz, E. and Michel, M.F. (1985). Prevalence of antibodies to *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Mycoplasma hominis* in infertile women. *Genitourin. Med.*, **61**, 175
9. Brunham, R.C., Maclean, I.W., Binnis, B. and Peeling, R.W. (1985). *Chlamydia trachomatis*: its role in tubal infertility. *J. Infect. Dis.*, **152**, 1275
10. Conway, D., Glazener, C., Caul, E.O., Hodgson, J., Hull, M.G., Clarke, S.K. and Stirrat, G.M. (1984). Chlamydial serology in fertile and infertile women. *Lancet*, **I**, 191
11. Hawes, L.A. and Gilbert, G.L. (1986). Seroepidemiology of *Chlamydia trachomatis* infection in infertile women in Melbourne. *Med. J. Aust.*, **154**, 497