The value of Chlamydia trachomatis–specific IgG antibody testing and hysterosalpingography for predicting tubal pathology and occurrence of pregnancy

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Abstract

We assessed two diagnostic methods, *Chlamydia trachomatis*–specific IgG and hysterosalpingography (HSG), as a screening test for the likelihood of tubal damage or occurrence of pregnancy before laparoscopy in 178 subfertile women who were randomly assigned to HSG followed by laparoscopy or immediate laparoscopy. The diagnostic accuracy and prognostic value of both *C. trachomatis*–specific IgG antibody testing and HSG are comparable but show poor performance.

Introduction

Tubal pathology accounts for approximately 14% of the causes of subfertility\(^1\). Therefore, assessment of the tubal status has become a routine part of the fertility work-up. Several diagnostic tests can be used to assess tubal status, of which *Chlamydia* antibody testing (CAT) and hysterosalpingography (HSG) comprise the first-line approach. These tests are usually followed by the gold standard laparoscopy and dye\(^2\). The CAT and HSG tests provide risk estimates of tubal pathology before laparoscopy, but the diagnosis of tubal pathology can only be made with laparoscopy and dye. The diagnostic accuracy of CAT and HSG compared with laparoscopy and dye is well established\(^3\)\(^–\)\(^7\). Most studies have shown that CAT performs just as well or better than HSG. However, the prognostic value of both tests in predicting occurrence of pregnancy is not well known. Idahl *et al*.\(^8\) showed that there were no differences in achieving pregnancy between *C. trachomatis* IgG negative or positive women. Moreover, as shown by several studies, the prognostic value of HSG also is low\(^9\)\(^–\)\(^13\).

Material and methods

The aim of the present study was twofold. First, we assessed the diagnostic accuracy of *C. trachomatis*–specific IgG (CtsIgG) and HSG compared with laparoscopy and dye in a large group of subfertile women. Second, we used both tests as prognostic indicator to assess occurrence of pregnancy.

All women in this study participated in a multicenter, randomized controlled trial with or without the performance of HSG to assess the usefulness of HSG as routine investigation in the fertility work-up before laparoscopy and dye. Recruitment strategy, description of subjects, and the main results of this study have been
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published elsewhere\textsuperscript{14}. The present part of the trial took place only at the Division of Reproductive Medicine, Department of Gynecology, Leiden University Medical Center. The institutional review board of the hospital approved all stages of the study.

As part of the fertility work-up, blood was drawn at the patient’s first visit. All spare serum was cryopreserved. For the present study, the spare serum of the participating women was thawed to perform a species-specific peptide-based serologic assay for the presence of IgG antibodies to \textit{C. trachomatis} (SeroCT; Savyon Diagnostics, Ashdod, Israel). The results of CtsIgG antibody testing were compared with the findings of HSG in the diagnosis of tubal pathology using laparoscopy and dye as the reference standard. The results of both tests were also compared with occurrence of pregnancy within 18 months after randomisation as the clinical end point in terms of cumulative pregnancy rate. The diagnosis of clinical ongoing pregnancy was based on positive urine or serum pregnancy test in association with an intact intrauterine gestation sac on ultrasound scans.

The HSG was performed with a water-soluble contrast medium (Omnipaque 300, Nycomed Ltd, Birmingham, UK). An HSG was considered abnormal if there was occlusion of one or both tubes or peritubal adhesions without tubal occlusion. Laparoscopy and tubal testing was performed with methylene blue dye. Laparoscopic findings of tubal factor subfertility were defined as extensive periadnexal adhesions and/or distal occlusion of one or both tubes\textsuperscript{15}. Endometriosis was not included.

The SeroCT IgG assay and calculation were performed according to the manufacturer’s instructions. The qualitative outcome of the assay (cut-off index) was categorized as negative (< 1.0) or positive (> 1.10). Values in the equivocal zone (optical densities between the values for negativity and positivity) were considered as negative results in the calculations when a second sample was also borderline or negative.

The diagnostic accuracy of CtsIgG and HSG compared with laparoscopy were assessed by calculating sensitivity, specificity, and likelihood ratios. The prognostic value of CtsIgG and HSG in predicting occurrence of pregnancies was assessed with Kaplan-Meier survival analysis and Cox proportional hazard models. \textit{P} values of .05 were considered to be statistically significant.
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Results

A total of 178 subfertile women participated in the present study. Sixty-five women underwent both HSG and laparoscopy, 25 women only HSG, and 88 women only laparoscopy. Therefore, the CtsIgG results could be compared with laparoscopy in 153 women, whereas the HSG results could be compared with laparoscopy in 65

Figure 1. Cumulative pregnancy rates between CtsIgG result and HSG findings.
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women. Out of all 153 women, 9 (6%) showed unilateral occlusion, 14 (9%) showed bilateral occlusion, and 8 (5%) showed peritubal adhesions without tubal occlusion at laparoscopy.

In 35 out of 153 women studied (23%), CtsIgG was positive; 14 of these seropositive women (40%) had tubal pathology according to laparoscopy. Out of the 118 CtsIgG-negative women, 17 had tubal pathology (14%). The sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio for CtsIgG in predicting tubal pathology were 45%, 83%, 2.6, and 0.7, respectively.

In 65 out of 153 women, an HSG and laparoscopy were performed. A total of 41 women had a normal HSG, and 24 had an abnormal HSG. Fifteen women (23%) showed unilateral occlusion, eight (12%) showed bilateral occlusion, and one (2%) showed peritubal adhesions without tubal occlusion. In 11 out of 24 women with abnormal HSG (46%), tubal pathology was found at laparoscopy. Out of the 41 women with normal HSG, 5 had tubal pathology at laparoscopy (12%). The sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio for HSG were 69%, 73%, 2.6, and 0.4, respectively.

For women who achieved pregnancy during the trial period, whether spontaneous or treatment related, there were no statistically significant differences found in cumulative pregnancy rate between CtsIgG-negative and CtsIgG-positive results (hazard ratio 0.73, 95% confidence interval [CI] 0.42–1.25; \( P = 0.25 \)) (Fig. 1A). Pregnancy rates at given times throughout the study were also not significantly different. There was also no significant difference in cumulative pregnancy rate between normal and abnormal findings at HSG (hazard ratio 1.33, 95% CI 0.73–2.41; \( P = 0.35 \)) (Fig. 1B).

Discussion

The main strength of the present study is the prospective design. All women included had a diagnostic laparoscopy for evaluation of tubal status. An allocation concealment was applied with 0% loss to follow-up. The shortcoming of the study is that the diagnostic or prognostic value of CAT and HSG can be determined separately, but the total sample size is too small for the combination of diagnostic and prognostic value.

We showed that \( C. \) trachomatis IgG antibodies have comparable diagnostic accuracy with HSG in detecting tubal pathology. These findings have been shown
by other studies that also compared CAT with HSG and used laparoscopy as reference standard\(^3\)–\(^7\). Those authors’ measured \textit{C. trachomatis} IgG antibodies by microimmunofluorescence (MIF) assay, but we used a species-specific (peptide-based) immunoassay (EIA) as predictor of tubal pathology. These new EIA tests are well standardized, less laborious, less expensive, and easier to perform than the MIF test\(^16\). The disadvantage of using CAT is that there is yet no uniformity in assays and cut-off levels. In addition, \textit{Chlamydia} antibody testing cannot predict tubal factor subfertility due to other causes (previous surgery or endometriosis), and the laboratory procedure has its limitations (e.g., cross-reactivity with other \textit{Chlamydia} species such as \textit{C. pneumoniae}). The greatest advantage of \textit{Chlamydia} antibody testing is its simplicity, limited inconvenience, and no complications.

We demonstrated that \textit{Chlamydia} antibody testing and HSG have comparable limited value in predicting pregnancy rates. No significant differences were found in cumulative pregnancy rate between CtsIgG-negative and CtsIgG-positive results. Idahl \textit{et al.}\(^8\) also showed that there were no differences between \textit{C. trachomatis} IgG–negative or –positive women concerning pregnancy rates. There was also no difference in cumulative pregnancy rates between normal and abnormal findings at HSG. This low prognostic value of HSG was also found in other studies\(^8\)–\(^12\). Only one recent prospective study showed results on the diagnostic and prognostic role of \textit{Chlamydia} serology compared with HSG and laparoscopy and supported our findings\(^13\). That study did not record the definition of tubal pathology found at HSG or laparoscopy.

In conclusion, we assessed two diagnostic methods, CtsIgG and HSG, as a screening test for the likelihood of tubal damage or occurrence of pregnancy in subfertile women before laparoscopy. The diagnostic accuracy of \textit{C. trachomatis}–specific IgG antibody testing is comparable with HSG, but both show poor performance. The prognostic value of occurrence of pregnancy of both tests is also poor. \textit{Chlamydia} antibody testing as screening test to estimate the risk of tubal pathology before laparoscopy is preferable to HSG owing to its simplicity and limited inconvenience.
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References

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