Seminal *Helicobacter pylori* Treatment Improves Sperm Motility in Infertile Asthenozoospermic Men

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OBJECTIVE To assess the effect of treatment of seminal *Helicobacter pylori* in infertile asthenozoospermic men.

METHODS In all, 223 infertile asthenozoospermic men were consecutively selected. They were subjected to history taking, clinical examination, semen analysis, and estimation of *H pylori* IgA antibodies in their seminal fluid. Infertile men with high seminal *H pylori* IgA were subjected to triple drug treatment, omeprazole, 20 mg; tinidazole, 500 mg; and clarithromycin, 250 mg twice a day for 2 weeks. Semen analysis as well as *H pylori* IgA antibodies was estimated after 3 months.

RESULTS In all, 22 of 223 men (9.87%) demonstrated *H pylori* IgA antibodies in their seminal plasma. After treatment, mean seminal *H pylori* IgA levels demonstrated significant decrease (1.55 ± 0.4 vs 0.52 ± 0.26; 95% confidence interval, 0.83-1.21; $P = .001$) concomitant with improved progressive as well as nonprogressive sperm motility. *H pylori* IgA antibodies demonstrated significant negative correlation with progressive sperm motility, nonprogressive sperm motility, normal sperm morphology, and significant positive correlation with immotile sperm motility.

CONCLUSION *H pylori* treatment significantly improves sperm motility in infertile asthenozoospermic men with elevated seminal *H pylori* IgA. UROLOGY 84: 1347–1350, 2014. © 2014 Elsevier Inc.

Infertility is one of the traditional concerns among a considerable percentage of married couples. Different factors are known to contribute for this problem, including congenital, endocrinologic, and infectious factors.[1-4] Infections by *Ureaplasma urealyticum* and *Chlamydia trachomatis* were demonstrated to cause epididymitis, provoking luminal scarring as well as obstruction. Also, *Herpesvirus hominis*, papilloma virus, hepatitis B virus, hepatitis C virus, and human immunodeficiency virus type 1 were demonstrated to damage spermatozoa.[5-8]

Helicobacter pylori, a gram-negative curved bacillus that colonizes the stomach was previously described since the finding by Marshall and Warren.[9] The prevalence of *H pylori* infection ranges from >70% in the developing countries to <40% in the developed world.[10] A strong link had been established between *H pylori* (especially the cytotoxin-associated gene A protein [CagA], a product of cytotoxin-associated gene A positive strains) and a diverse spectrum of diseases as acute or chronic gastritis, peptic ulcer, gastric cancer, and mucosa-associated lymphoid tissue lymphoma.[11]

It has been reported that *H pylori* infection may be associated with some extra-gastrointestinal diseases such as cholelithiasis; coronary heart disease; childhood asthma; autoimmune, skin, vascular, and platelet disorders; and so forth.[12-14] Proposed mechanisms underlying that extra-gastric pathogenicity included direct effect of the bacterium, activation of inflammatory processes with cytokines release, flogistic mediators, and the mimicry between bacterial and host antigens.[15,16]

The possibility of involvement of *H pylori* as a factor in male infertility is intriguing. Ambrosini et al[17] pointed that the infection is significantly more common in both men and women with fertility problems; in semen, follicular fluid, and vaginal secretions of infected individuals. They detected specific *H pylori* Ab's antibodies, which cross-reacted in vitro with spermatozoa, suggesting existence of an autoimmune phenomenon. *H pylori* infection, particularly when caused by strains expressing CagA, had been proposed as a possible concomitant cause of reduced male fertility and sperm alterations associated with reduced sperm motility and increased unviable spermatozoa.[18]

This study aimed to assess the effect of treatment of seminal *H pylori* in infertile asthenozoospermic men.

METHODS

In this study, 223 asthenozoospermic infertile men (progressive and nonprogressive sperm motility <40%) were recruited consecutively from the university hospital, starting from Aug

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Table 1. Comparison between different semen variables before and after treatment (n = 22)

Variables	Before Treatment	After Treatment	95% CI of the Difference	*P* Value
Sperm count (10^6/mL)	33.9 ± 18.4	34.2 ± 14.8	4.04-4.69	.879
Sperm normal forms, %	35.2 ± 17.6	65.7 ± 13.8	21.4-39.6	.001*
Progressive sperm motility, %	4.8 ± 3.4	21.0 ± 7.7	13.2-19.4	.001*
Nonprogressive sperm motility, %	2.8 ± 8.6	49.9 ± 8.1	17.3-26.8	.001*
Immotile sperms, %	69.7 ± 14.3	33.6 ± 14.1	28.0-34.8	.001*
Seminal *H pylori* IgA	1.55 ± 0.4	0.52 ± 0.26	0.83-1.21	.001*

CI, confidence interval.
* Significant difference.

2011 (mean age, 29.3 ± 1.4 years; range, 24-34 years). The study was approved by the Research Ethical Committee, Faculty of Medicine with an informed consent. Exclusion criteria were varicocele, smoking, leucocytospermia, hormonal therapy, malignancy, chemotherapy, radiation, previous infections, vasectomy reversal, and trauma.

The patients were subjected to history taking, clinical examination, semen analysis by computer-assisted semen analysis, and estimation of seminal *H pylori* IgA. Cases with elevated seminal IgA were scheduled to receive anti-Helicobacter triple therapy (omeprazole, 20 mg; tinidazole, 500 mg; and clarithromycin, 250 mg) twice a day for 2 weeks followed up by repeated semen analysis and seminal *H pylori* Ig A level after 3 months.

Semen samples were obtained in the laboratory after 4 days of sexual abstinence in sterile containers and analyzed within 1 hour of collection. Semen analysis was carried out by Sperm Class Analyzer (Microptic, Barcelona, Spain) automated system. World Health Organization[19] criteria were followed regarding sperm motility types:

- Progressive sperm motility: sperms moving actively, either linearly or in a large circle, regardless of speed.
- Nonprogressive sperm motility: all patterns of sperm motility with absence of progression.
- Sperm immotility: no movement.

Seminal plasma was used for determination of *H pylori* IgA using the enzyme-linked immunosorbent assay (Adaltis, Rome, Italy). The cut-off value for the test was set at 0.178 according to the manufacturer's criteria with sensitivity and specificity of the test 79.31% and 63.64%, respectively. The test was performed in duplicate and the mean absorbance was recorded. Values above the cut-off value were considered infected with *H pylori*.

Statistical Analysis

Statistical analysis was carried out using SPSS program, version 18 (SPSS Inc., Chicago, IL). The Mann-Whitney *U* test was used as a test of significance for comparison of 2 groups. The Spearman rank correlation coefficient was used to study the relation between variables. $P < .05$ was set as significant.

RESULTS

Elevated seminal *H pylori* IgA antibody testing was demonstrated in 22 of 223 men (9.87%). After treatment of these cases, there was significant decrease in the mean level of seminal *H pylori* IgA antibodies (1.55 ± 0.40 vs 0.52 ± 0.26; $P = .001$). Concomitantly, there was significant increase in the progressive sperm motility and nonprogressive sperm motility and significant decrease in immotile sperm motility as well (Table 1).

Seminal *H pylori* IgA demonstrated a significant negative correlation with progressive sperm motility ($r = -0.796$; $P = .001$), nonprogressive sperm motility ($r = -0.776$; $P = .001$), and normal sperm morphology ($r = -0.707$; $P = .001$); a significant positive correlation with immotile sperm motility ($r = 0.759$; $P = .001$); and a nonsignificant correlation with sperm count ($r = -0.097$; $P = .532$; Fig. 1).

COMMENT

The capability of the male gamete to fertilize the ovum is compromised by the presence of anti-sperm autoantibodies. Prevalence of such autoantibodies in the general population ranges from 0% to 2%, but it is greatly increased in infertile men, ranging from 7% to 26%.[20] In the present study, seminal *H pylori* IgA levels were detected in 22 infertile men (9.87%) of the investigated infertile men with weak sperm motility. This shed a light on that *H pylori* could be to some extent a cause of weak sperm motility in these exposed cases.

In the present study, *H pylori* IgA antibodies demonstrated significant decrease after treatment concomitant with improved progressive as well as nonprogressive sperm motility. Previously, Collodel et al[18] demonstrated that the effect of *H pylori* infection on spermatozoa could occur through an immune mechanism due to the presence of mimicry between *H pylori* antigens and tail proteins of spermatozoa. Mimicry has been demonstrated between human ß-tubulin protein (present in spermatozoa) and *H pylori* flagellin, CagA, and VacA where antibodies to these antigens cross-reacted with human spermatozoa.[18] In coordination, it was demonstrated that antibodies in the vaginal secretion and follicular fluid of *H pylori*–affected women could affect spermatozoa through an immunologic reaction.[21-23]

In addition, *H pylori* infection has various adverse effects on the humans. The infection increases the inflammatory process where many vasoactive substances and cellular mediators such as tumor necrosis factor-α may be transported in the blood stream promoting an inflammatory response in distant organs from the stomach.[24] *H pylori* infection was demonstrated also to stimulate the production of reactive oxygen species that has a sperm damaging effect.[25,26] These agents altogether are damaging agents to the spermatozoa, and it can reduce the capacity of sperm-oocyte interaction.[27,28] In addition, it is known that infections may expose a sperm's antigens