

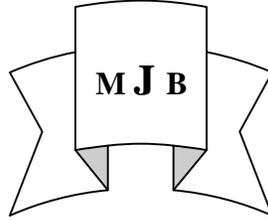
## Treatment Options for Negative Postcoital Test in Cervical Factor Infertility

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### Abstract

Thirty two infertile couples who have cervical factor as a cause for their infertility were investigated in Al-Amal clinic for infertility management. Causes of negative postcoital test were listed and treatment was stated. Significant improvement ( $p < 0.05$ ) of postcoital score after treatment noticed and total pregnancy rate (PR) was 37.5%. Intrauterine insemination achieved only 10% PR, for the patients who didn't respond to medical treatment. Cervical factor infertility needs special care and patience from the clinician, because it's easily treatable and can achieve good results after treatment.

### الخلاصة

تمت دراسة 32 حالة من حالات العقم التي كان عامل عنق الرحم سببا في عدم حدوث الحمل في عيادة الامل للعناية بالعقم. بينت الدراسة اسباب الحالات السلبية لفحص ما بعد الجماع و كذلك طرق و نوعية العلاج لكل سبب من هذه الاسباب. وجد تحسن معنوي ( $p < 0.05$ ) في نتيجة فحص ما بعد الجماع بعد العلاج، ونسبة الحمل المتحققة كانت 37.5%. تمت عملية التلقيح الاصطناعي للحالات التي لم تستجب للعلاج الدوائي، وكانت نسبة الحمل 10%. ان عامل عنق الرحم كسبب في حالات العقم تحتاج الى عناية و تروي من قبل الطبيب المعالج لان طريقة العلاج بسيطة و يمكن ان تحقق نتائج جيدة.

### Introduction

To manage infertile couples effectively the clinicians need a realistic and practical prediction of their chance of conception without treatment. If this is poor, the couples should proceed to definitive treatment immediately, otherwise they can be advised to continue trying to achieve a natural conception [1]. The Post Coital Test (PCT) of cervical mucus (CM) for detection of the presence of progressively motile sperm has become an important part of infertility investigation. It is used

routinely in nearly half of infertility clinic in Britain and 2\3 of such clinic across Europe [2]. A PCT can suggest problems regarding the quality of the sperm or CM or the presence of antisperm antibodies. A negative test is only meaningful if it's repeatedly negative under perfect condition [3] The PCT has been the subject of controversy since it was first advocated by Sim's in 1866 [4]. Opinions are still divided as the value of the test in infertility investigation. From our opinion the PCT is useful monitor of sexual function, an

indicator of sperm function, a barometer of periouvlatory hormonal status and a possible basic screen for the detection of cervical factor. Antagonists feel it's prognostic significance almost valueless [5-7]. The PCT is one of the most important tests in predicting the probability of spontaneous conception that lead to postponing of sometime harmful investigation and treatment [8-10]. This study is undertaken to examine clinically the many therapeutic potentialities provided to the physician in case of negative PCT, in an effort to determine it's role in infertility treatment.

### **Materials and Methods**

Thirty two infertile couples were studied in Al-Amal Clinic for Infertility Investigation and Management, from April 2007 to May 2008; the selection criterions of the couples were:

1. Couples with primary infertility for more than twelve months at first presentation
2. Semen quality compatible with conception.
3. Regular ovulatory cycle by Ultra Sound (U\S), and normal hormonal profile ..
4. Normal tubes provided by hysterosalpingiography or laparoscopy.
5. Repeated negative PCTt.
6. Normal coital performance and frequency.

Preovulatory phase PCT was done 6-8 hours after coitus. Non-lubricated speculum introduced into the vagina gently. Mucus was aspirated with a standard narrow 1 ml, 10 cm long disposable syringe without needle. Ductility (spinnbarkeit) was assessed, CM parameters were noted and

judged according to criteria suggested by Insler,et,al; [12] A sample of mucus is then transferred onto a glass slide and examined under the microscope. The sperm were counted and their degree of activity was assessed . The sperm must be normal in appearance and moving across the slide and not shaking on the spot. Results are considered valid only, if mucus was in a good condition or if the test had been repeated and timed by (U\S) measurement of the follicle. The pct was classified as follows: positive: if at least one forward progressing spermatozoon per field in most (at least 5) high power field (HPF). Negative: less than one forward progressing spermatozoon in most (HPF). [13-15] Negative results need conformation in a second cycle. Treatment was given according to the result of the test, and the PCT was performed before and after treatment and the CM score as well. If leukocytes were present, this indicate an infection in either partner, treatment with antibiotic was given according to culture and sensitivity of the CM, and we may prescribe an antibiotic even the culture came back negative [16]. Both partner have been treated to ensure that they are not passing the disease back and forth . To avoid exposing an early pregnancy to antibiotic, the female take the drug during the fallowing mense [17]. If immunological cause is suspected by presence of immotile spermatozoa or shaking sperm on the spot, while the original semen sample is normal; we started the intermittent graduated dose of prednisolon, together with condom therapy for at least 3-6 months [18,19]. Poor cervical mucus quality and volume abnormality have been

supplemented with a low dose oral estrogen of 0.1-0.2 mg of diethylstilbestrol from 5th through the thirteenth day of the cycle [20]. Acidic pH of CM was treated with bicarbonate vaginal douches [21]. Unexplained poor pct or failed trial of treatment was shifted to a series of intrauterine insemination (IUI) with the aid of ovarian stimulation program with 100 mg clomiphene citrate [22] from CD3-CD7 followed by injection of 10,000 IU of human chorionic gonadotropin. This is followed 36 h later by artificial insemination by husband sperm after semen collection and preparation with simple layer technique. Pregnancy was based on positive pregnancy test in urine.

### **Results**

Antibiotic therapy was given according to culture and sensitivity results of CM; thirteen couples of our study group (40.6%) received such treatment and six couples show improvement of PCT and achieve pregnancy as well (PR: 46.5 %). The other seven couples, who didn't turn positive, underwent IUI courses. Short intermittent course prednisolone therapy was given to 12 couples (37.5%) who have been suspected to have immunological cause of their negative PCT. Four couples passed to negative PCT in the following 3-6 months and PR was 33%. The remaining 8 couples have shifted to IUI program. Poor ferning, small volume CM was treated with estrogen therapy. Two pct scored proven to be better after treatment, (PR: 5%). Bicarbonate ( $\text{NaHCO}_3$ ) vaginal douches have been advised to acidic PH CM (n=3), pct score proved

to be improved after  $\text{NaHCO}_3$  douching PR: 6%. So total PR was (37.5%) 12\32 with treating the cause. Twenty couples underwent IUI courses: only two become pregnant (PR 10%) the success rate of treatment show no significant difference ( $p>0.05$ ) between treatment option offered according to Fischer exact test Table 1

### **Discussion**

This study highlighted some treatment options for negative PCT in cervical factor infertility. Infection in either partner proved to be the cause in 40.6% of our study group, it was successfully treated and pregnancy rate after treatment was 46.5%. Inflammatory process and cell mediated immunological reaction in the cervix and vagina have been implicated as a causal factor in some causes of infertility, so routine cervical smear in causes of abnormal pct are useful in detecting couples with infertility, which maybe due to simple undetectable asymptomatic bacterial infection [16]. Infectious organism in either partner may kill or maim sperm. Specific microorganism can be identified by performing culture of CM. Also we prescribe anti-biotic even if the culture came back negative [17] A poor PCT turned favorable after treatment with antibiotic (CM score were better after treatment than before treatment). The unexplained poor PCT is almost always due to presence of anti sperm antibodies in the CM or semen [23]. In immunological infertile patient, a PCT maybe negative even when no abnormality is observed in general semen test of the husband [23]. For unknown reasons 30% of all women

produces anti bodies against sperm in CM. If a fairly recent semen analysis showed that unexposed sperm have normal forward motility, but the PCT shows them shaking or clumping, it'll suspect that the women is producing antibodies [18,24]. Steroid treatment is effective in treating sub fertile couples with antisperm antibodies, it suppress certain isotope in different lactation and improves sperm motility. Many steroid regimen have been advocated: long term low dose prednisolon; Intermitted high dose methyl prednisolon and intermittent graduated dose prednisolon [25,19], which was effective in treating our sub fertile couples. (PCT scores before treatment were <5, pct scores after were treatment >10). The 33% PR after short course intermitted prednisolon therapy was in accordance with that if Hendry and Sharma [25,19]. Mucus viscosity and volume abnormality maybe caused by surgical procedures performed on the cervix or by the use of clomiphene citrate used for ovulation induction. Twelve and half percent of our study group have this problem and have been treated satisfactorily with diethylstilbestrol of 0.1 - 0.2 mg from 5<sup>th</sup>-13<sup>th</sup> day of the cycle. One female have improved CM quality and have positive pregnancy test (PR :3%), the other failed to respond, and have been shifted to IUI program. Many researchers agreed that CM with good degree of ferning during the ovulatory period permits a better sperm penetration, and increase their possibility of conception [26]. Gibor, et,al; [27] and Everhardt, et,al; [21] , notice a great improvement of CM score after sodium bicarbonate vaginal douching (NaHCO<sub>3</sub>) . This

was applied to 9.37 % who have negative pct. Acidic PH is unfavorable to sperm mucus penetration and is associated with infertility. PH measurement should be performed immediately after mucus collection to avoid misinterpretation of the result [28]. Glazener, et ,al ; [22], Friedman, et, al; [29] and Cohen, et, al; [30] , recommended IUI in case of negative PCT , while Oui, et, al; [31] advocate that IUI appeared of new benefit in case if infertility which was due to failure of sperm mucus penetration or defined by negative PCT . Twenty couples who attend our study underwent series of IUI for at least 3 cycles, only 2 (PR 10%) achieved pregnancy. These two couples were conclusively from the immunological case of negative PCT . This proves that washing the sperm from the antibodies by our preparation method, avoiding exposure to antibodies in semen and mucus. If IUI failed we can go IVF or ICSI [31]. On the basic of our study, pct will both prevent couples with good sperm function from having assisted reproductive technology unnecessarily and will also ensure that poor CM should proceed to necessary treatment without delay.

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**Table 1** Demonstrats causes of negative postcoital test, treatment options offered

	Cause of neg. pct	No. of patients (%)	CM score before treatment	Treatment offered	CM score* after treatment	No. of pregnancy (%)
1.	Infection	13(40.6)	<5	Antibiotic according to culture& sensitivity	>10	6(46.2)
2.	Immunological	12(37.5)	<5	Prednislon therapy	>10	4(33)
3.	Small volume neg. ferning	4(12.5)	<5	Ethylstilbistrol therapy	>10	1(5)
4.	Acidic PH	3(9.37)	<5	Bicarbonate douches.	>10	(6)1
	Total					37.5%

\* Significant improvement of CM score after treatment than before treatment , (p<0.05).