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SUCCESSFUL PREGNANCY OUTCOME WITH IUI IN PATIENTS WITH UNEXPLAINED RECURRENT MISCARRIAGE, WHOSE MALE PARTNERS HAVE LOW SCORE HYPO-OSMOTIC SWELLING TEST

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ABSTRACT

In order to determine outcome of pregnancy with IUI in patients with unexplained recurrent miscarriage whose husbands have low hypo-osmotic swelling test scores, a prospective clinical intervention was performed at a university referral clinic of recurrent abortion.

Out of 56 patients whose husbands had abnormal hypo-osmotic swelling tests, 43 patients underwent IUI, from which only 14 patients became pregnant (treatment group) and 13 patients became spontaneously pregnant without IUI as control group.

Our main outcome measure was successful pregnancy (continuation of pregnancy after 20 weeks).

Among the 14 patients who became pregnant, 3 patients aborted below 20 weeks (21.4%), and 11 patients continued pregnancy after 20 weeks of gestation (78.6%). In the control group among the 13 patients with spontaneous pregnancy, 8 patients aborted below 20 weeks (61.5%) and 5 patients continued pregnancy over 20 weeks (36.4%), success rate ratio was 2.04% and the difference was statistically significant (c^2= 4.49, p<0.05).

Treating the unexplained recurrent aborter whose male partner has a low hypo-osmotic swelling test score with IUI could be effective. This is the first study to present an ideal way for selection of recurrent aborters who benefit from IUI. The probable mechanism for this effect may be selection of the best quality sperms which will be discussed in detail.

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Keywords: Recurrent miscarriage, Hypo-osmotic swelling test, IUI.

INTRODUCTION

Spontaneous miscarriage is the most important complication of pregnancy, affecting 15% to 20% of pregnancies. The prevalence of recurrent miscarriage, defined as three consecutive pregnancy losses, may be as high as 0.3%, but in most of the patients the etiology remains unexplained.[1]

The contribution of abnormalities in male partners of couples with recurrent miscarriages is unexplored, although abnormal sperm morphology has been associated with increased miscarriage rates in patients undergoing IVF-ET.[2,4]

The hypo-osmotic swelling test assesses the functional

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integrity of the sperm membrane and the hypo-osmotic swelling score is the proportion of sperms with functionally intact membranes. It has been reported that a score <60% is suboptimal.[1,4]

Recent studies have indicated that a low hypo-osmotic swelling score correlates with recurrent miscarriage.[1]

On the other hand some investigators also showed that sperm washing by centrifugation altered the hypo-osmotic swelling test result, whereas the swim-up method selected a population of spermatozoa with intact head and tail membranes.[3] The purpose of this study was to see whether washing of spermatozoa and intrauterine insemination in patients with recurrent miscarriage and low score hypo-osmotic swelling tests in male partners could improve the outcome of pregnancy.

MATERIAL AND METHODS

Between February 1998 and September 2000, all patients who were referred to our clinic of recurrent abortion were studied.

A diagnosis of unexplained recurrent abortion was made when no abnormality was detected in:

1- Peripheral blood karyotype of both partners

2- Hysterosalpingogram

3- Female serum TSH, T4, prolactin

4- Anticardiolipin Ab titer and lupus anticoagulant (measured by PTT).

A total number of 56 patients who met the above criteria, and their ages ranged from 22-35 years and with 3-9 previous abortions were included in the study.

Semen samples from male partners were taken for analysis and also for hypo-osmotic swelling test, performed by mixing 0.1 mL aliquots of semen and 1 mL of a 150 mos/kg hypo-osmotic solution prepared by mixing 7.35 mg of sodium citrate and 13.5g of fructose in 1000 mL of distilled water. The mixture was incubated for 60 minutes at 37°C in 5% CO_2 and 95% air. Then 0.2 mL of the mixture was placed on a slide and mounted with a coverslip and examined immediately at a magnification of 400 under a phase-contrast microscope.

The percentages of hypo-osmotic swelling reacted sperms (with curled and swollen tails) and non-reacted sperms (with straight tails) were assessed by counting multiples of 100 sperm. All of the tests were performed by a single person.

Then the 43 patients who had low hypo-osmotic swelling test scores underwent superovulation with colomiphene+HMG and after maturation of follicles which were monitored by ultrasound, HCG 10000 was injected and after 34 hours sperm washing was performed by hams-f10 and the selected swim-up spermatozoa used for intrauterine insemination.

This procedure was repeated for 1-6 cycles until the patient became pregnant and she was under follow-up without any other medical or sugical intervention thereafter.

Among the patients in the control group with abnormal husband tests, 13 patients became pregnant without IUI. The age of the patients and number of previous abortions were matched in both groups. None of the patients in IUI and control groups had infertility problems and they were primary aborters (no live birth in the past). Continuing of pregnancy after 20 weeks of gestation was considered as a successful outcome because the risk of abortion ended at this time.

RESULTS

Out of 43 patients who underwent IUI, 14 patients became pregnant. The outcome of the pregnancies were as follows: 11 patients continued pregnancy after 20 weeks (78.6%) [8 terminated with fullterm fetuses, 2 between 28-37 weeks of gestation as premature, and one in the first trimester (21.4%) (Table II, III).

In the control group, of the patients who became pregnant without IUI, 5 patients continued pregnancy after 20 weeks (38.4%) [4 terminated with fullterm fetuses and 1 terminated at 35 weeks], and 8 patients aborted (61.5%).

Success rate in the treatment group was 78.6%, while in the control group this was 38.4% with a success rate ratio of 2.04% and the difference was statistically significant ($\chi^2 = 4.49$, $p<0.05$).

DISCUSSION

A routine semen analysis has long been the standard laboratory test of male fertility potential. Although a routine semen analysis quantitates sperm concentration, motility and morphologic features, it can not ascertain the functional capacity of a given semen sample.[6]

Hypo-osmotic swelling test can evaluate the functional integrity of the sperm membrane and a score of

Table I. Obstetric history of patients with recurrent abortion in both groups.

	No. of patients	Early abortion	Late abortion	Total
IUI Group	14	39 (81.2%)	9 (18.7%)	48
Control Group	13	40 (90%)	4 (10%)	44

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Table II. Outcome of pregnancy among the treated and control groups.

	Total	Abortion	Continued pregnancy
Patient	14	3 (21.4%)	11 (78.6%)
Control	13	8 (61.5%)	5 (38.4%)

Table III. Outcome of fetuses in patients who continued pregnancy after 20 weeks.

	Total	20-27 weeks	28-37 weeks	>37 weeks	Live birth
IUI Group	11	1 (9%)	2 (18%)	8 (72.7%)	10 (91%)
Control Group	5	__	1 (20%)	4 (80%)	5 (100%)

<60% hypo-osmotic reacted sperm usually is regarded as suboptimal.[1,4]

Esteves et al. studied semen parameters and their relationship to hypo-osmotic swelling test and concluded that abnormal routine semen parameters have a lower degree of sperm swelling as compared to those with normal parameters. Other studies have shown that low hypo-osmotic swelling test scores in couples undergoing IVF do not affect rates of fertilization or pregnancy, but are associated with higher rates of spontaneous miscarriage.[4]

Bouckett et al. in their study showed a low hypo-osmotic swelling score among patients with recurrent miscarriage.[1]

On the other hand some investigators concluded that sperm washing by centrifugation altered the hypo-osmotic swelling test result, whereas the swim-up method selected a population of spermatozoa with intact head and tail membranes.[5]

Out study originates from these studies and is based on the theory that if we can separate the best qualified sperms for fertilization, therefore miscarriage should occur less frequently. This is the first study to present an ideal way for selection of recurrent aborters who would benefit from IUI.

Although the patients who underwent this method of pregnancy have had better outcomes till present, further studies with larger populations should be considered to confirm the effectiveness of this approach.

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