

Outcome of Treatable Causes of Male Infertility

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النتائج المستقبلية لعلاج الأسباب القابلة للعلاج لعقم الرجال

الخلاصة:

تم دراسة ثلاثمائة وستة وخمسين مريضاً مصاباً بعقم الرجال أعمارهم تتراوح بين ٢١-٤٠ سنة (معدل الأعمار ٣٢.٢) سنة دراسة استعادية ومستقبلية في مركز الخصوبة والعقم في مدينة الصدر الطبية في النجف من كانون الثاني ٢٠٠٨ إلى أيلول ٢٠١٠. أوضحت هذه الدراسة أن الأسباب القابلة للعلاج لعقم الرجال الأكثر شيوعاً أو الأسباب المحتملة القابلة للعلاج كانت ٤٩.٤٣ % مجهولة ، ٢٦.١٢ % الالتهابات التناسلية و ٢٤.٤٣ % دوالي الخصية ، وقد تم استثناء الأسباب النادرة وغير القابلة للعلاج.

أوضحت النتائج أن هناك تحسناً مهماً في قيم تحليل السائل المنوي عند مرضى دوالي الخصية ومرضى الالتهابات التناسلية ومرضى ذوي الأسباب المجهولة (٥٨.٦٢ % و ٣٩.٠٧ % و ١٠.٦١ %) وحسب الترتيب، ولكن ليس هناك اختلاف مهم بين العلاج الهرموني لمدة ثلاثة أشهر والعلاج الهرموني لمدة ستة أشهر. أوضحت النتائج أيضاً أن هناك تحسناً مهماً في معدل الحمل عند مرضى دوالي الخصية ومرضى الالتهابات التناسلية (٣٧.٩٣ % و ٢٦.٨٨ %) حسب الترتيب.

Abstract :

Three hundred and fifty six infertile male patients, their age ranged from 21 – 40 years (mean 32.2 years), were studied prospectively and retrospectively in infertility center in Al-Sader teaching hospital from January 2008 to september 2010.

This study showed that the most common treatable causes were idiopathic group 49.43%, leukospermic group 26.12 % and varicocelic group 24.43%. Rare and untreatable causes were excluded. Our results showed significant improvement ($p < 0.05$), in semen parameters for varicocelic, leukospermic and idiopathic groups (58.62%, 39.075%, and 17.61%) respectively. There was no significant difference between 3 months and six months hormonal therapy. ($p > 0.05$). There was significant increase in pregnancy rate in varicocelic and leukospermic group.

Introduction:

Infertility is the inability of a sexually active, non-contracepting couple to achieve pregnancy in one year. ⁽¹⁾

Sterility is the term that can be correctly applied only to an individual who has some absolute factor preventing conception. ⁽²⁾ In 50% of childless couples a male infertility associated factor is found together with abnormal semen parameters. The cumulative pregnancy rate in infertile couples with 2 years of follow-up and oligozoospermia as the primary cause of infertility is 27% . ⁽³⁾ Female age is an important variable influencing outcome in assisted reproduction . ⁽⁴⁾ The process of sperm production and maturation is started and completed by hormonal mechanism. ⁽⁵⁻⁸⁾

Treatable causes of male infertility:

- | | |
|---|---------------------------|
| -Varicocele | - Infection |
| -obstructed vas (acquired , congenital) | - Ejaculatory dysfunction |
| -Hypogonadotropic hypogonadism | -Sexual dysfunction |
| -Immunological problem | -Hyper prolactinemia |

The most common causes of infertility that included in this study:

Varicocele :

It is abnormal tortuosity and dilatation of testicular veins within the spermatic Cord. The following classification of varicocele ⁽⁹⁾ is useful in clinical practice:

- Subclinical: not palpable or visible at rest or during Valsalva manoeuvre, but demonstrable by special tests (Doppler ultrasound studies). ⁽¹⁰⁾
- Grade 1: palpable during Valsalva manoeuvre.
- Grade 2: palpable at rest, but not visible.
- Grade 3: Visible and palpable at rest.

Varicocele is a physical abnormality present in 11% of adult males ^(11,12) and in 25% of those with abnormal semen analysis. ⁽¹³⁾ The exact relation between male infertility and varicocele is not well known, but WHO data clearly indicates that varicocele is related to semen abnormalities, decreased testicular volume and decline in Leydig cell function. ^(14,15,16)

Leukocytospermia:

Presence of greater than 1 million WBCs/ml is considered abnormal and raises the possibility of genital tract infection or inflammation. ⁽¹⁷⁾

Management of pyospermia in the absence of genital tract infection is by anti-inflammatory medication, antibiotics, frequent ejaculation and prostatic massage. Management with ARTs (assisted reproductive techniques) that include processing to remove the WBCs should be considered in these cases.

Idiopathic infertility :

This term is referred to patients who have abnormal semen analysis for which no etiology can be found ⁽⁸⁾. Treatment of the idiopathic infertility is either by empirical medical therapy or assisted reproductive technique (ART).

Empirical medical therapy include:-

A- Hormonal therapy : attempted to alter the HPG axis to enhance sperm production, this include:-

1- Gonadotropin – releasing Hormone (GnRH) :- Given to increase gonadotropins production and potentially spermatogenesis. ⁽¹⁸⁾

2- Gonadotropins: include hCG as Pregnyl, human menopausal gonadotropin (HMG) as Pergonal and Metrodin and recombinant FSH as gonaf. ⁽¹⁹⁾

3- Low dose androgens.

4- Testosterone rebound therapy :- Increase sperm count and improved spermatogenesis occur after withdrawal of high dose androgens usually after 4 months. It is not longer used as an empiric therapy. ⁽²⁰⁾

5- Antiestrogen therapy: It inhibits negative feedback inhibition of estrogens on pituitary. So increase FSH and LH. This therapy include:

* clomiphene citrate: It has mild estrogenic effect, It competitively bind to estrogen receptors in the hypothalamus and pituitary thereby blocking the inhibitory effect of estrogen normally circulating in the male. ⁽²¹⁾

* Tamoxifen citrate: Its action is similar to that of clomiphene citrate with less estrogenic effect. It is given orally in a dose of 10-15 mg twice daily for 3-6 months. ⁽²²⁾

* Aromatase inhibitors: These agents inhibit conversion of testosterone to estrogen. ⁽²³⁾

B- Non – Hormonal therapy :-

Include carnitine that play role in intracellular metabolism and spermatozoa membrane stabilization, so it improves sperm motility. Also include kinin-kallikrin system.

Patients and methods:

From a total number of 560 infertile males, 356 patients with treatable or potentially treatable causes included in this study. Studied from Jaun. 2008 to September 2010 in infertility center in Al-Sader teaching hospital .

The patients subjected to full history, clinical examination and investigation, which included GUE, CBP and ESR, several seminal fluid analyses, hormonal profile, Doppler U/S for testes and culture test for those with infection.

Patients were classified into the following groups:

1. Those with varicocele who were diagnosed by clinical examination ,Doppler u/s and treated by varicocelectomy by inguinal and subinguinal approach .
2. Those with infection (leukospermia) who were treated according to culture and sensitivity tests and those with negative culture treated by Trimethoprim-Sulfamethaxazole and Doxycycline on the basis of the proposed most common causes of genital tract infection which was Chlamydia or Urea plasma urealyticum, which is difficult to be cultured here.
3. The idiopathic group: includes undetectable causes and hormonal imbalance because they underwent the same line of treatment, they were given humegon (75 units FSH and 75 units LH) and pregnyl (human chorionic gonadotrophin 5000 units). For some patients with high prolactin level, parlodil (bromocriptin 2.5mg) was given. These patients were subdivided into 2 groups according to the duration of hormonal therapy, for three and six months.

Each group was subdivided according to the sperm count; azoospermia, oligospermia and normal count with asthenospermia. Each patient did seminal fluid analysis and hormonal profile before and after treatment.

Results:

Three hundred fifty six infertile male patients classified into 3 groups: Idiopathic 176 (49-43%), leukocytospermia 93 (26.12%), and varicocele 87 (24.43%).

The improvement in spermigram and pregnancy rate from the total number 356 (3 groups) 33.70% and 21.34% respectively as shown in table (1).

The best results obtained in this study was in varicocele group, who were treated by varicocelecomy, the improvement rate was 58-62% and pregnancy rate 37-93%, which was significant results ($P<0.05$). In this group the improvement rate in normal sperm count with asthenospermia and oligospermia was 71.42%, 63.01% and the pregnancy rate 57.14% , 39.72% respectively and there was no improvement, nor pregnancy in azoospermic patients as shown in table (2).

In the leukocytospermic group the improvement rate in seminal fluid analysis was 39.78% and the pregnancy rate was 26.88%, which was significant results ($P<0.05$). The improvement rate with normal sperm count with asthenospermia, oligospermia and azoospermia was 80% ,41.49% and 6.25% respectively and pregnancy rate was 60% and 28.35% in normal sperm count with asthenospermia and oligospermia respectively and there was no pregnancy with azoospermia patients as shown in table (3).

In the idiopathic group the improvement rate was 17.61% and pregnancy rate 10.22% which was significant results ($P<0.05$). The improvement rate in the normal sperm count with asthenospermia, oligospermia and azoospermia was 22.22%, 19.76% and 5.55% respectively, and the pregnancy rate was 16.66% and 10.46% in normal sperm count with asthenospermia and oligospermia respectively and there was no pregnancy in azoospermic patients as shown in table (4).

In the azoospermic patients there was no significant changes ($p>0.05$) in all groups (varicocele, leukocytospermia and idiopathic) as shown in table (5).

In the oligospermic patients there was significant changes ($p<0.05$) in the improvement rate and pregnancy rate in varicocele, leukospermia and idiopathic groups as shown in table (6).

In the normal sperm count infertile patients with asthenospermia there was highly significant changes ($p < 0.05$) in the improvement rate in varicocele, leukospermic and idiopathic groups as shown in table (7).

Table (1) : Improvement and pregnancy rate from the total number

Total	Improvement		Pregnancy	
	N	%	N	%
356	120	33.70	76	21.34

($p<0.05$)

Table (2) Varicocele Group

VARICOCELE	N	IMPROVEMENT		PREGNANCY RATE	
		N	%	N	%
Azoosprmia	7	0	0	0	0
oligospermia	73	46	*63.01	29	39.72
Normospermia	7	5	*71.42	4	57.14
Total	87	51	*58.62	33	37.93

P(<0.05)

Table (3) Leukospermic Group

LEUKOSPEMIA	N	IMPROVEMENT		PREGNANCY RATE	
		N	%	N	%
Azoosprmia	16	1	6.25	0	0
Oligospermia	67	28	41.49	19	28.35
Normospermia	10	8	80	6	60.0
Total	93	37	39.78	25	26.88

$X^2=13.5, P<0.05$

TABLE (4) Idiopathic group

IDIOPATHIC	N	IMPROVEMENT		PREGNANCY RATE	
		N	%	N	%
Azoospermia	36	2	5.55	0	0
Oligospermia	86	17	19.76	9	10.46
Normospermia	54	12	22.22	9	16.66
Total	176	31	17.61	18	10.22

$X^2=10.3, P<0.05$

Table (5) Azoospermic Group

AZOOSPERMIA	N	IMPROVEMENT		PREGNANCY RATE	
		N	%	N	%
Varicocele	7	0	0	0	0
Leukospermia	16	1	6.25	0	0
Idiopathic	36	3	8.33	0	0
Total	59	4	6.77	0	0

$P<0.05$

Table (6) Oligospermic Group

Oligospermic	N	IMPROVEMENT		PREGNANCY RATE	
		N	%	N	%
Varicocele	73	46	63.01	29	39.72
Leukospermia	67	28	41.49	19	28.35
Idiopathic	86	17	19.76	9	10.46
Total	226	91	34.21	57	21.42

$P<0.05$

TABLE (7) Normal Count Sperm With Asthenospemia .

Asthenospermia	N	IMPROVEMENT		PREGNANCY RATE	
		N	%	N	%
Varicocele	7	5	71.42	4	57.14
Leukospermia	10	8	80.0	6	60
Idiopathic	54	12	22.22	9	16.66
Total	71	25	35.21	19	26.76

$P<0.05$

Discussion:

About (40%) of cases of infertility results from pathological factors in the man , (40%) from factors in women and (20%) from contributing factors in both (male and female) therefore male factors is at least partly responsible in about 50% of infertile couples ⁽¹⁷⁾.

1. The mean age of varicocele in our study was 31 years , while mean age of varicocele in other studies was 26 years like in G. Mustafa Arain et al. ⁽²⁴⁾

The improvement rate in our study in patients with varicocele who were treated by varicocelectomy was 58.62% and pregnancy rate was 37.93% were low if compared with other studies like "Dubin and Amalar 1977, and Cockett et al.1979 and Marks et al. 1988⁽²⁵⁾ Nieschlag et al. 1998" which had improvement rate 70% and conception rate 40.50% and this is probably due to delay presentation of our patients as shown with the difference in mean age .

2. In the leukospermic group , the improvement rate in our study was 39.78% and pregnancy rate 26.88% which was significant results ($P<0.05$) and goes with most studies which suggest detrimental effect of leukospemia on sperm function ." Berger et al. 1982, Negy et al.1989⁽²⁶⁾and Yanush – Polsky et al., 1996". Infertile couple has been found had greater concentration of WBC than did fertile populaton " walf and Anderson 1988⁽²⁷⁾

3. In the idiopathic group , the improvement rate was 17.61% and pregnancy rate was 10.22 % which was low if compared with other studies like "Chevaland and Mehan study 1979⁽²⁴⁾ which showed improvement rate of 69% and pregnancy rate of 36% .This relative low rates probably due to lack of sophisticated investigation , which add more patients to idiopathic group, like immunological problems , immotile cilia syndrome and inaccurate hormonal profile or may be due to irregular hormonal therapy (treatment according to availability of drugs) or probably due to pollution secondary to other factors related to wars .

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