

Insight into Male Infertility in Bahrain

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ABSTRACT

170 male patients attending the Urology clinic at Bahrain Defence Force Hospital were investigated for infertility. In all, 61 cases (36%) had azospermia, most commonly caused by idiopathic hyperprolactinaemia.

Serum antisperm antibodies were detected in 7 cases, 5 of whom were treated with Prednisolone with moderate success.

A testicular biopsy was performed on 30 infertile men with azospermia who exhibited normal hormonal profiles. Histological examination revealed normal spermatogenesis in 4 cases indicating a possible extra-testicular seminal pathway obstruction, subsequently confirmed on scrotal exploration.

Various medications including Clomiphene citrate, androgens and steroids were used in treating various forms of infertility with encouraging results.

39 infertile males whose wives were pronounced gynaecologically normal were referred to the newly established assisted fertility programme which utilises the gamete intra-fallopian tube transfer (GIFT) technique. The results are eagerly awaited.

Errectile impotence was diagnosed in 11 cases (5%) with variable aetiology, and treatment was instituted accordingly.

Male infertility and errectile impotence are problems which only recently have come to light in the Arabian Gulf region, and people are becoming increasingly aware of the possibility of treatment.

This is particularly significant in a society where until recently infertility in the male was never recognised as a

serious possibility and where a childless marriage was invariably blamed on the wife, resulting in martial breakdown or the man seeking a second or even third or fourth wife with similar outcome, before it was realised that the male and not the female partner was initially to blame.

At the Bahrain Defence Force Hospital, an infertility service was previously run as part of the general urological outpatient clinic, and only during June 1988–June 1989 a separate infertility clinic was established.

METHODS

Male infertility could be defined as the inability of the male to initiate pregnancy in a fertile female following a reasonable period of unprotected sexual intercourse. Over a one-year period, 170 male patients (age range 18-51 years) were reviewed in the clinic. Of these, the majority (64%) were Bahraini nationals, the remainder were from the Middle East and Far East (Table 1).

Table 1
Ethnic Composition of Patients

| <i>Total number of patients 170</i> | | |
|-------------------------------------|-----------|----------|
| <i>Age range 18-51 years</i> | | |
| <i>Nationality</i> | <i>No</i> | <i>%</i> |
| Bahraini | 110 | 64 |
| Pakistani | 16 | 9 |
| Jordanian | 15 | 9 |
| Indian | 10 | 6 |
| Syrian | 9 | 6 |
| Yemeni | 6 | 4 |
| Egyptian | 2 | 1 |
| Sudanese | 1 | 0.5 |
| Kuwaiti | 1 | 0.5 |
| Total | 170 | 100 |

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All patients were subjected to an extensive history taking based on a detailed questionnaire and a physical examination including a detailed examination of the genitalia. Semen analysis (Semenogram) was performed on all patients at least on two occasions with a minimum interval of 3 weeks following a 3 day abstinence from ejaculation on each occasion.

All patients underwent a serum hormonal profile assessment which included serum levels of FSH, LH, Testosterone, Prolactin, T3/T4 and TSH, as well as assessment of serum fasting blood sugar and a urine biochemical and bacteriological assay.

A skull x-ray was performed on all cases that exhibited an elevated serum Prolactin level to exclude a pituitary tumour. Screening for antisperm antibodies was performed on these cases where there was persistent azoospermia or severe oligozoospermia in spite of all other parameters being normal.

Testicular biopsies were performed on all cases with azoospermia or oligozoospermia with normal hormonal profiles, normal testicular size on clinical examination, and negative screening for serum antibodies, to study the state of spermatogenesis within the seminiferous tubules. This also assisted in indicating suspected cases of seminal pathway obstruction when the biopsy revealed normal spermatogenesis.

Several cases with secondary impotence, after excluding other possible causes such as Diabetes mellitus, neurogenic and psychogenic factors, were investigated for the possibility of penile venous incompetence. Penile cavernosography performed on those patients proved very effective in demonstrating the site and extent of the leakage. It was repeated post-operatively on cases whose erection did not improve or only slightly improved following venous ligation to confirm there were no further incompetent veins to account for the persistent impotence. Cavernosography was performed in the BDF hospital utilising direct manual injection on contrast into the cavernosa through a 23 gauge butterfly needle. A constant flow infusion pump was not available but manual injection was found to produce satisfactory results with minimal discomfort to the patient.

RESULTS

61 of the 124 patients presenting with primary infertility (Table 2) had azoospermia. This was found to be due to a variety of causes, the commonest-surprisingly being idiopathic hyperprolactinaemia, where serum levels exceeded the regional high-normal value

Table 2
Aetiology of Male Infertility in Bahrain

| <i>Primary Infertility 124 cases (73%)</i> | | |
|---|----|-----|
| Causes: | No | % |
| - Complete testicular atrophy | 8 | 6.5 |
| - Partial testicular atrophy | 4 | 3.5 |
| - Idiopathic Hyperprolactinaemia | 39 | 32 |
| - Seminal pathway obstruction | 4 | 2 |
| - Varicocele | 6 | 5 |
| - Bilateral undescended testis in childhood | 1 | 0.9 |
| - Autoimmune infertility (antisperm antibodies) | 3 | 2.4 |
| - Bilateral tuberculous epididymitis | 1 | 0.9 |
| - Reduced spermatogenesis (on biopsy) | 1 | 0.9 |
| - Hypogonadism and poor spermatogenesis | 2 | 1.8 |
| - Diabetes mellitus | 1 | 0.9 |
| - Cause unknown | 48 | 37 |
| <i>Secondary Infertility 46 cases (27%)</i> | | |
| Causes: | No | % |
| - Complete testicular atrophy | 1 | 2 |
| - Partial testicular atrophy | 3 | 6.5 |
| - Varicocele | 11 | 24 |
| - Idiopathic hyperprolactinaemia | 13 | 28 |
| - Autoimmune infertility (antisperm antibodies) | 4 | 8 |
| - Depressed spermatogenesis (on biopsy) | 1 | 2 |

(ie 10 ngm/ml). Similar findings were seen in patients with secondary infertility.

Although the majority of patients with Hyperprolactinaemia exhibited azoospermia, another 25 had oligozoospermia with sperm counts below 60 million/ml and another 21 had normal sperm counts exceeding 60 million and sometimes as high as 160 million/ml despite persistently raised serum prolactin levels.

This high proportion of infertile males with Hyperprolactinaemia is unusual and would be due to the

unusually low regionally adopted normal serum prolactin value (10 ngm/ml)¹. This is further supported by the fact that only 18 cases (11 of the entire group in the study) showed serum prolactin values exceeding 20 ngm/ml. This particular group were all treated with Bromocriptine in progressively increasing doses to a maximum daily dose of 3.5 gms, and 10 of them responded well and their serum prolactin levels returned to normal values (less than 4 ngm/ml) within 4 months of commencing treatment.

The presence of serum antisperm antibodies accounted for infertility in 7 (8%) of all cases submitted for investi-

Table 3
Testicular Biopsy

| <i>Findings and further management</i> | <i>Cases</i> | |
|--|--------------|----------|
| | <i>No.</i> | <i>%</i> |
| Complete testicular atrophy | 8 | 26 |
| - leave alone | 7 | |
| - lost to follow-up | 1 | |
| Partial testicular atrophy | 8 | 26 |
| - leave alone | 6 | |
| - lost to follow-up | 1 | |
| - low sperm count, referred to GIFT | 1 | |
| Bilateral normal spermatogenesis | 3 | 10 |
| - epididymal obstruction - repaired | 1 | |
| - obstruction at rete testis - leave alone | 1 | |
| - scrotal exploration requires - patient reluctant | 1 | |
| Maturation arrest | 3 | 10 |
| - leave alone | 2 | |
| - lost to follow-up | 1 | |
| Bilateral hypoplastic testes | 2 | 7 |
| - lost to follow-up | 2 | |
| Hypoplastic testes and arrested spermatogenesis | 3 | 10 |
| - leave alone due to complete azoospermia | 1 | |
| - low sperm count, referred to GIFT | 1 | |
| - lost to follow-up | 1 | |
| Reduced spermatogenesis - cause unknown | 2 | 7 |
| - wife pregnant | 1 | |
| - lost to follow-up | 1 | |
| Hypercurvaturism - leave alone | 1 | 3.5 |

gation. Of these 5 were treated with oral Prednisolone 5 mgs daily resulting in complete clearance of antibodies from the circulation in 2 cases, the rest were unfortunately lost to follow-up.

Bilateral testicular biopsies were performed on 30 cases with persistant azoospermia or oligozoospermia with normal hormonal profiles and no evidence of serum antisperm antibodies. Histological examination revealed the presence of partial or complete testicular atrophy in 26 cases (87%), the remaining 4 exhibited normal spermatogenesis inspite of persistent azoospermia thus raising the suspicion of possible seminal pathways obstruction, which was subsequently confirmed on scrotal exploration in 2 cases (Table 3); a third case revealed no evidence of obstruction but when testicular biopsy was repeated, closer inspection revealed a rare entity, namely Hypercurvaturism, where due to excessive tortuosity of the seminepherous tubules sperm flow is impeded and reduced to a virtual stand still, resulting in expiration of the sperms before they leave the testis.

In the 2 cases where seminal pathway obstruction was confirmed on scrotal exploration, this was found to be at the rete testis in 1 case, therefore it is not surgically correctable, while in the other case, the obstruction was at the caudal end of the epididymas and was readily corrected by Epididymo-vasostomy resulting in a sperm count of 8 millions/ml two months post-operatively.

92 oligozoospermic patients with normal hormonal profiles were treated with Clomiphen citrate (50 mgs orally on alternate days) for a period of 1-48 months. In 25 cases, sperm counts rose to levels exceeding 60 millions/ml and subsequently 11 pregnancies were reported. In another 41 cases, the results were less encouraging and treatment with Clomiphen for 4-6 months achieved minimal or no improvement in sperm counts. In 17 of these cases, the sperms were of good quality although of low count and these patients were referred with their wives to the IVF unit at our hospital provided that the wives were confirmed to be gynaecologically normal. No pregnancies were, however, reported up to the conclusion of this study.

Androgen supplements (Proveron 20-25 mgs daily) were given to 26 oligozoospermic patients who either showed no improvement in sperm parameters after adequate Clomiphen therapy for at least 4 months, or who had adequate sperm counts (more than 40 millions/ml) with low sperm motility. This therapy managed to improve sperm motility in 6 patients resulting in 2 pregnancies while it failed in the rest, although 3 of these were considered to have reasonably adequate sperm counts and motility to justify their inclusion in the IVF programme (Table 4).

Table 4
Gamete Intra-Fallopian Transfer Programme
GIFT

39 cases (21%) referred or being considered for referral

| Reasons for referral: | No | % |
|--|----|-----|
| - Low sperm count | 7 | 14 |
| - Low sperm motility | 8 | 19 |
| - Low sperm count and motility | 7 | 14 |
| - Low sperm count and low normal morphology | 4 | 11 |
| - Normal sperm count with persistent low morphology after adequate treatment | 1 | 3 |
| - No pregnancy inspite of improved sperm count and quality | 3 | 8.5 |
| - Weak ejaculation with normal semen parameters | 1 | 3 |
| - No pregnancy although both partners are fertile | 5 | 14 |
| - Persistent low sperm count, motility and morphology inspite of adequate medication | 3 | 8.5 |

All patients with serum prolactin values between 10 and 20 ngm/ml were not started on Bromocriptine, but were followed up periodically with serum prolactin assessment and semen analysis, provided that the raised prolactin levels were truly idiopathic and a pituitary tumour has been safely excluded. The wisdom or otherwise of this policy will have to be borne by future assessment of the patients.

Out of 88 cases screened for serum antisperm antibodies, only 7 (8%) proved positive. Only 5 of these patients received steroid therapy (Prednisolone 5 mgs orally daily) and of these only 2 gave satisfactory results; the others were unfortunately lost to follow-up.

DISCUSSION

A lack of commitment on the part of many patients included in this study and their poor attendance of the infertility clinic as well as the high drop-out rate reflected on the accuracy of the results of the study. A greater effort must be exerted by all primary health care workers, particularly general practitioners, to emphasise upon their patients the importance of regular attendance of the infertility clinic thus insuring an accurate follow-up⁵. This was made very clear to all referring physicians.

An unusually high proportion (31%) of patients in this study were reported to have idiopathic hyperprolactinaemia. This was due to adopting a relatively low serum prolactin level (10 ngms/ml) as normal at the BDF hospital. A higher value (30 ngms/ml) would appear more realistic.

There is a general belief that patients with serum prolactin values lower than five-fold the regionally adopted high-normal value should not be treated with Bromocriptine. This would exclude the majority of our group of patients but seems a more realistic approach.

Although we were unable to report any pregnancies following successful improvement in semen parameters, particularly in semen counts, and we believe that justifies the use of this medication in infertile males with truly idiopathic hyperprolactinaemia.

Screening for antisperm antibodies in this study was performed entirely on patients serum and not on seminal plasma. Besides being less accurate, serum antibody assays were more costly and time-consuming as all samples had to be dispatched to the UK since such assays were not available in the Gulf region. To improve accuracy, antisperm antibody screening should be performed on seminal plasma since this is more relevant to infertility than serum antisperm antibodies³ and assays for performing seminal fluid antibody screening should be made available locally.

Furthermore, the incorporation of screening tests, such as the mucosal agglutination reaction (MAR) test and the tray agglutination test (TAT), within the routine seminal analysis to detect seminal antisperm antibodies, and likewise, performing the post-coital cervical mucus penetration test to detect antisperm antibody activity in cervical mucus², would have been helpful - had they been available locally - in reducing the number of patients subjected to the time-consuming, costly and less accurate serum antibody screening.

In the management of male infertility caused by antisperm antibodies, we adopted an admittedly low steroid dose in comparison to other studies where much higher doses (ex. Prednisolone 40-80 mgs daily) were used intermittently or in relation to certain days in the wife's menstrual cycle, hence our results were not so encouraging and this was made worse by the lack of patient commitment to attend follow-up sessions.

In our defence, I can only point out that attempting to use an intermittent or cyclic regime rather than the regular -

and easy to remember – daily dose in a community like ours with a relatively high illiteracy rate and limited education would have undoubtedly resulted in failure of the patients to take their medication promptly or in abandoning it altogether.

Finally, the adoption of assisted conception techniques, such as IVF and GIFT points the way to improving conception rates in childless couples when improvement in semen parameters following medication is not sufficient to achieve a pregnancy following sexual intercourse. In the Middle East, such programmes are entirely dependent on husband sperm which has to be of sufficient quality to ensure successful fertilisation.

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A lack of commitment on the part of many patients included in this study and their poor attendance at the infertility clinic as well as the high drop-out rate reflected on the accuracy of the results of the study. A greater effort must be exerted by all primary health care workers, particularly general practitioners, to emphasise upon their patients the importance of regular attendance at the infertility clinic this involving an active follow-up. This was made very clear to all returning patients.