IMPACT OF ALTERED CONCEPTS IN THE MANAGEMENT OF INFERTILITY

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SUMMARY

This article highlight the importance of accepting and practising the modern diagnosic technologies and the refined therapeutic measures. It could be realised that these modern concepts favour maximising the fertility rate, and permit the physician to be minimally invasive in diagnostic or therapeutic approaches.

INTRODUCTION

Since 1973, when we took interest in the `super speciality' of infertility, there have been tremendous changes in and newer additions to diagnostic and therapeutic armamentarium. Ever since this period we have been continuously evolving our management protocol in par with the modern technological developments. These evolutionary changes in the investigation and management of infertility over a period of 17 years, ending with early 1989 have been summarised in our earlier communications (Rajan, 1989, and 1990).

Over the last 2 years, ending with March, 1991, we have had the following changed concepts in the management of infertility, which were not practised in my earlier series. They include : (i) Endovaginal sonography as an integral part of female evaluation, (ii) Intensified monitoring of ovulation induction cycles and evolution of the ideal treatment schedule within 3 cycles, (iii) Liberal application of serum prolactin studies even for subjects with slightest menstrual alterations, and other biological markers, and those with `unexplained infertility'. (iv) critical approach to laparoscopies, with an idea to minimise the `purely' diagnostic laparoscopies and maximise the operative laparoscopies. (v) more aggressive approach at `paradoxical' adnexal removal in subjects with unilateral adnexal pathology (either endometriosis or PID); (vi) greater reliance on medical treatment (danazol) of endometriosis; (vii) preference for endoscopic ovarian follicular puncutre and diathermy for the `CC-failed' PCOD subjects; (viii) optimise the diagnosis of uterine pathology by endovaginal sonography in preference to hysteroscopy, and hysteroscopy preferred only if luminal pathology is suspected at sonography; (ix) greater care in management of oligospermic males which

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include advice on hygenic measures (avoid smoking and other addictions), good food, antibiotics and liberal use of hCG.

The purpose of this communication is to review the results of these changed concepts and to discuss the merits and advantages :

ENDOVAGINAL (TRANSVAGINAL) SONOGRAPHY (TVS) : It has been made that all infertile subjects will have a thorough sonographic study. TVS has been employed as a routine screening procedure to recruit the subjects for other more invasive diagnotic procedures. Among the 1233 infertile couples registered over the 2 year period, there have been 332 couples with predominant male factor (26.93%). Among the remaining 901 couples a definite female factor could be diagnosed in 443. (49.17%)

Focusing on the promising role of TVS, we observe that among the 443 subjects in whom a female factor has been identified, a pelvic factor was exclusively diagnosed by TVS in 301 subjects (69.52%), and suspicion of pelvic factor necessitating endoscopic confirmation was raised in 67 subjects (15.12%). Thus, altogether in 368 subjects (83.06%) a cause for female infertility could be identified or suspected at endovaginal scan.

Etiology for infertility in the 433 infertile females, and the nature of female factors diagnosed at TVS are given in Table I. Accordingly we find that conditions such as ovarian endometriosis particularly with endometrial cysts,

TABLE I

Etiology of Infertility
(April, 1989 to March 1991)

Total Couple : 1233 ::	Female Factor : 443 :: (35.93%)	Male Factor : 332 (26.93%)

Etiology of female factor confirmed at all investigation			Etiology of female factor diagnosed exclusively at endosonography			
Endometriosis	:	95	Endometriosis	:	70	(73.68%)
Anovulation	:	121	Anovulation	:	81	(66.94%)
Fibroids	:	85	Fibroids	:	85	(100.00%)
P.I.D.	:	40	P.I.D.	:	20	(50.00%)
Uterine anomalies	:	10	Uterine anomaly	:	10	(100.00%)
Ovarian Mass	:	10	Ovarian Mass	:	10	(100.00%)
Asharman Syndrome	:	5	Asharman Syndrome	:	5	(100.00%)
Cornual block	:	10	Cornual block	:	Nil	

Pelvic disorder suspected by TVS at 67 and confirmed in 90% at laparoscopy

Normal TVS finding in 71, confirmed at laparoscopy in 90.14% (excluding stage I endometriosis and tubal block)

uterine anomalies, fibroids, hydro-salpinx, ovarian enlargements and ovulatory disorders such as PCOD remain optimally diagnosed at TVS and do not need further confirmation at laparoscopy. Thus 69.52% of female factors are diagnosed with reasonable precision at TVS.

In another 15.12% (67 subjects) a pelvic factor has been suspected at scan, which needs confirmation at laparoscopy (i) for real presence of a pelvic factor, and (ii) if so, the nature of the disorder. Among these scan suspected cases 90% were confirmed to have a pelvic factor at diagnostic laparoscopy.

However, the negative predictive value of TVS could only be 62.75% normal pelvic findings being confirmed in 64 of the 102 subjects, obviously because proximal tubal block and minimal to mild endometriosis (Stage I) is not expected to be diagnosed by TVS. When tubal blocks have been picked up by HSG, the negative predictive value is enhanced to 71.11%, and if stage I endometriosis is not considered (atleast for young subjects) the negative predictive accuracy of TVS will be 64 for 71 subjects (90.14%). Thus we find TVS could be employed as pelvic screening test, and its negative predictive value depended for excluding a pelvic pathology in subjects at low risk for a pelvic disorder such as : (i) young subjects less than 25 years and married less than 3 years : (ii) those with anovulatory infertility, (iii) those with a predominating male factor. In young subjects we would prefer to have TVS complemented by HSG.

Disorders of ovulation : Amenorrhoeic subjects with hypoestrogenis (unstimulated) endometrium identified at scan are divided into two categories : (i) those in whom the ovaries could be properly imaged with atleast small follicles identified; these subjects are considered to have secondary gonadal failure; and (ii) those in whom the ovaries could not be imaged clearly, and hence considered to be primary gonadal failures. We could prove this by confirming the diagnosis at gonadotropin study in 13 subjects with secondary gonadal failure, and 14 subjects with primary gonadal failure. Among the former hyperprolactinemia was located as the cause of secondary gonadal failure. Along with the clinical features the typical polycystic nature of the ovaries could be discerned in 51 subjects with PCOD. Thus we find a preliminary endosonographic survey means a lot for evaluation of endocrine infertility.

Intrauterine adhesions have been diagnosed in 5 subjects by the typical endometrial echodensity, the velementous pattern or the relative nonresponse to ovarian cyclicity.

In this study follicular monitoring and endometrial dating have be made mandatory for all subjects undergoing ovulation induction. Subjects being treated by CC were administered hCG at the time of optimal follicular maturation. Pregnancy rate for CC along was 11 for 26 (42.31%), whereas with hCG conception rate was 15 for 28 (53.57%). Moreover, 10 of the 15 pregnancies (66.67%) were achieved by the first cycle of treatment.

In the first cycle of CC regimen if folliculogenesis and or endometrial maturation was suboptimal, or if TVS evidence of endometrial luteal lag was detected, the regimen was altered in the next cycle in favour of CC and Brom or CC and Dex. Thus, within 3 cycles the most optimal regimen will be selected. Subjects with borderline hyperprolactinemia and/or galactorrhoea will have CC and Brom, or CC and Dex. Thus, within 3 cycles the most optimal regimen will be selected. Subjects with borderline hyperprolactinemia and/or galactorrhoea will have CC and Brom, and those `mildly androgenised' thin subjects, particularly if the DHEA (S) level is high, will be treated with CC and Dex. If these three cycles fail to evidence optimal follicular and endometrial response, higher dosage regimen for CC (100 mg / day) or extended CC regimen (50 to 100 mg or 10 to 15 days) will be considered, for couple of cycles. If within 6 cycles altogether the desired results have not been achieved we prefer ovarian diathermy and multiple follicular puncture at

laparoscopy. We have found that the CC-Brom combination has resulted in 23.68% success rate (9 for 38), and CC-Dex in 25% (2 for 8 subjects). CC failed PCOD subjects treated by laparoscopic ovarian diathermy achieved 44.44% conception rate (4 pregnancies for 9 subjects treated). Over the last 2 years 20 subject with `typical' hyperprolactinemia have been treated with Brom with 60% success rate, and 4 subjects with seconday gonadal failure treated with hMG/hCG regimen with 50% success rate. The overall success rate for ovulation induction over the 2 years is 41.35%. (Table II).

Best results have been achieved for operative laparoscopy for stage II endometriosis, involving ovarian adhesiolysis and fulguration following by danazol (83.33 % fertility rate), and next best results for pre-operative danazol and conservative surgery for stage III endometriosis (62.50% conception rate). Three of the 7 subjects with stage III endometriosis, treated exclusively with danazol also achieved a conception without any surgical intervention.

General trend in treatment results for endometriosis favour best outcome for ovarian surgeries (with no tubal involvement) or for

TABLE II

Induction of Ovulation

Ovulation induction regimen	No. treated.	No. conceived	Preg. rate %
All anovulatory subjects	133	55	41.35
CC alone	26	11	42.31
CC & hCG or CC, Brom and hCG	28	15	53.57
Brom alone	20	12	60.00
Brom and CC (cc nonresponders)	38	9	23.68
CC and Dex (CC nonresponders)	8	2	25.00
hMG and hCG (Second, Gonad. Failure)	4	2	50.00
Operative laparoscopy (Refractory PCOD) Follicular puncture and diathermy	9	4	44.44%

Endometriosis and Infertility : There has been a substantial improvement in the conception rate following treatment of endometriosis over the past 2 years, as against the previous period. The overall conception rate has risen to 48.28% from the earlier rate of 44.00%.This improvement has been achieved exclusively at treatment of stage II and III endometriosis, and the results for stage I endometriosis continues to be poor (16.67%) eventhough danazol has been employed liberally for all stages of endometriosis. unilateral adnexal removal (if tubal involvement is present) complemented by pre-or-post-operative danazol, and this is irrespective of the degree of endometriosis. However, the results are quite disappointing for endoscopic fulguration of stage I endometriosis, followed by danazol. Hence we speculate that infertility caused by endometriosis-induced altered pelvic anatomy alone optimally responds to surgical treatment complemented by danazol; with pregnancy resulting in 22 of the 33 subjects treated (66.67%). Whereas endometriosis

diagnosed at laparoscopy and not contributing to pelvic adhesions and not compromising the tubo-ovarian anatomy (Stage I) reveal poor response to either form of treatment (16.67%). This observation questions the wisdom of over-enthusiastic endoscopic diagnosis of pelvic endometriotic implants in infertile subject by a very liberal approach to diagnostic laparoscopy; this is particularly true with respect to younger subjects who have a very high prospect for spontaneous conceptions following any form of infertility evaluation such as HSG. (Table III).

Unilateral or `paradoxical' adnexal removal : Whenever one adnexum is more than damaged, either by endometriosis or PID, total extirpation of the diseased adnexum equates the woman to a normal fertile subject, with one ovary functioning every month the tube performing the function of optimal ovum pick-up. Even if both adnexa are diseased, but asymmetrically, the patient stands much more benefited by extirpation of the severely affected side, and repair of the contralateral adnexum.

Among the 15 conceptions reported following conservative surgery (and preoperative danazol) for stage III endometriosis, atleast 10 were following unilateral adnexal removal (66.67%). Similarly among subjects conceiving following surgical treatment of endometriosis, among the 4 conceptions 3 were following unilateral adnexal removal (75.00%). All of them were subjects with unilateral hydrosalpinx, where we had preferred tubectomy over salpingostomy.

Management of oligospermia : Fresh Seminal samples showing 8 to 10 sperms, with 80-90% evidencing grade II or II + motility at high power field are considered fertile, particularly if PCT in estrogenised cervical mucus is positive

TABLE III

Endometriosis and Infertility

Treatment of endometriosis	No. treated	No. Conceived	Preg. rate %
Total patients treated	58	28	48.28
Stage III ; Conservative surgery/ and pre-operative danazol	24	15	62.50
Stage III : Operative laparoscopy and post - operative danazol	3	2	66.67%
Stage III : Danazol alone	7	3	42.86
Stage II : Operative laparoscopy and post operative danazol	6	5	83.33
Stage I : Operative laparoscopy and post operative danazol	18	3	16.67
Combined surgery and Danazol for endometriosis excluding stage I	33	22	66.67

(atleast 1 to 2 actively motile sperms per field). If these criteria are not satisfied at repeated studies the male partner is considered for treatment. The treatment includes specific remedies such as varicocele ligation, and non-specific remedies such as abstinance from smoking and other addictions, use of antibiotics as a routine (doxycyclin), and administration of hCG in a dose of 5000 units twice a week for 10 weeks.

There have been 20 conceptions for the 64 oligospermic subjects treated (31.25%), and 9 pregnancies following varicocelectomy and post-surgery hCG therapy in 25 subjects (36.00%).

CONCLUSION :

Need for a particular investigation and the role of a specific therapeutic approach in infertility practice must be assessed by the overall fertility rate that is achieved. This study proves that a careful clinical assessment complimented by routine applicationof TVS evaluation could improve the diagnostic precision, and limit the role of endosocpies more as therapeutic measures. Liberal and critical approach to follicular monitoring increases the fertility rate, decreases the treatment cycles, and identifies the resistant group without much delay. Operative laparoscopy for ovarian endometriosis, aggressive approach at extirpation of diseased adnexum and wider application of danazol should optimise the results for endometriosis. However, the significance of diagnosis of stage I disease (endometrial implants) and its therapeutic outcome remain a real dilemma. Unilateral hydrosalpinx is best treated by salpingectomy than salpingostomy as proved in this study. A careful evaluation of oligospermia and institution of optimal treatment should brighten the prospects for couples with male fertility disorder.

REFERENCES :

1. *Rajan, R : 'postgraduate Reproductive Endocrinology' II Edn, 1989, p. 593.*
2. *Rajan, R, J., Obst. Gynec. Indian, 4) : 6, 1990*