

Update on treatment of varicocele: counselling as effective as occlusion of the vena spermatica

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This prospective randomized study was performed in order to investigate the effects of interventional treatment or counselling on pregnancy rates in infertile couples in whose male partners a varicocele was diagnosed. The present report extends a previous study using the same design. A total of 125 couples were included in the current study while the previous report comprised 95 couples. Couples fulfilling the inclusion criteria were allocated randomly either to interventional treatment (surgical ligation or angiographic embolization of the spermatic vein) ($n = 62$) or to counselling as the sole treatment ($n = 63$). Couples were followed over the subsequent 12 months and seen at 3-monthly intervals. At the end of the 12 month period pregnancy rates, as the main outcome measure, were 29% in the group given interventional treatment and 25.4% in the counselled group and were not significantly different. The only significant difference found, regardless of treatment modality, was the wives' age at admittance: the 34 wives achieving a pregnancy were 28.8 ± 0.6 years (mean \pm SE) old while the 91 non-pregnant wives were 31.2 ± 0.3 years old ($P < 0.05$). The study suggests that regular counselling of the infertile couples is as effective as interventional treatment of varicoceles in achieving pregnancies.

Key words: counselling/infertility/randomized study/surgery/varicocele

Introduction

In 1995 we published a study comparing the treatment of varicocele by occlusion of the vena spermatica with counselling of the couples (Nieschlag *et al.*, 1995). The study demonstrated that counselling was as effective as interventional treatment in terms of pregnancy rates. Although our study showed very similar pregnancy rates of 25.2% in the occlusion group and 27.1% in the counselling group during the 12 month observation period, it was argued that a total of 95 couples was too low to detect significant differences (Hargreave, 1997). Since the original study continued on after 1995, we would now like to present the final outcome based on 125 couples.

Materials and methods

Study design, selection and entry criteria of couples, semen and hormone analysis and statistics were the same as in the original study (Nieschlag *et al.*, 1995) and the reader is referred to that publication for details. Data on the entire study group are presented here.

Patients with varicocele (grades I–III) on the left side attending the Infertility Clinic of the Institute of Reproductive Medicine, Münster, Germany, were considered potential participants in the study. In addition to a thorough investigation of history, they underwent physical examination supplemented by ultrasonography of the scrotal contents (Behre *et al.*, 1995) and sonographic measurement of venous diameters before and under Valsalva manoeuvre, as well as Doppler sonography. Semen analysis and hormone measurements were performed twice. In order to be admitted to the study, the following criteria had to be met in addition to a Valsalva-positive varicocele: (i) infertility persisting longer than 1 year despite regular, unprotected intercourse; (ii) subnormal semen parameters as assessed by WHO guidelines (1992); (iii) no other infertility-related disease such as history of maldescended testes, infections, sperm antibodies (as detected by mixed agglutination reaction test), nor any general disease or chronic medication; (iv) no obvious causes of infertility, such as anovulation, endometriosis or tubal blockage, in the subject's partner.

Altogether 226 infertile couples fulfilled the entry criteria. Of these, 23 opted for treatment by assisted reproduction. The remaining 203 patients were randomly allocated to the treatment or counselling groups. The treatment group was again randomized to undergo either surgical ligation or angiographic embolization. The randomization scheme was established by random numbers before the first patient entered the study. A total of 125 couples completed the study. Of these, 62 were treated either by surgical ligation ($n = 30$) or angiographic embolization ($n = 32$), while 63 received no interventional treatment, but only counselling. Following treatment or allocation to the counselling-only group, patients were reinvestigated by the same procedures and counselled after 3, 6, 9 and 12 months. Patients' details are shown in Table I. The distribution of varicocele grades I–III was as follows: surgical treatment group: I = 15, II = 10, III = 5; angiographic treatment group: I = 15, II = 13, III = 4; counselling only group: I = 36, II = 20, III = 7. Of the 78 couples who failed to complete the study, 43 were lost after randomization, 14 lost after the second control examination; in 11 females infertility developed (endometriosis, tubal blockage), two developed epididymitis, two were allocated for ligation, but opted for embolization, two were allocated for counselling, but opted for embolization, one was suspected of having an intestinal tumour, two separated from their partners, and one used condoms.

Differences of pregnancy rates in different study groups were tested by the χ^2 -test with Yates' correction. Differences in testicular volume and ejaculate parameters over time and between study groups were tested by multifactor analysis of variance for repeated measures.

Results

Testicular volumes in the counselling-only group did not change during the 12 month observation period. Although in

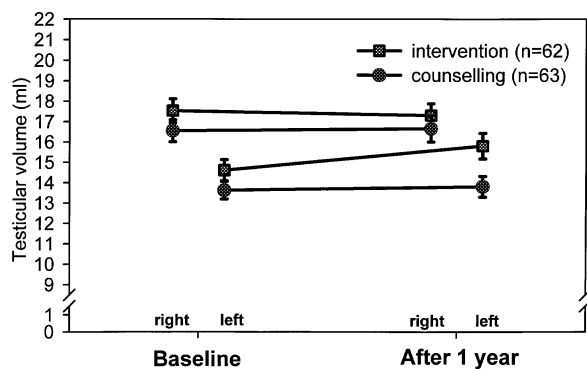


Figure 1. Testicular volumes in 125 patients participating in a clinical study comparing the effect of intervention versus counselling in right and left varicocele patients.

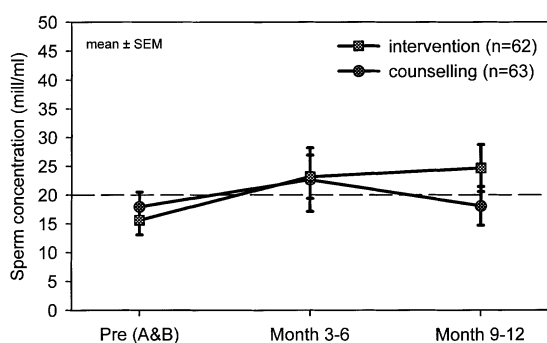


Figure 2. Sperm concentrations in a clinical study comparing the effect of intervention versus counselling in varicocele patients. Pre (A&B) = mean of the two pre-study baseline examinations; Month 3-6 and Month 9-12 = mean of the examinations at months 3 and 6 or 9 and 12.

Table I. Characteristics of the 125 couples who completed the study for the treatment of varicocele (mean ± SE)

	Counselling group (n = 63)	Intervention group (n = 62)
Patients' age (years)	32.8 ± 0.5	33.1 ± 0.4
Patients' weight (kg)	84.0 ± 1.7	85.8 ± 1.5
Patients' height (cm)	182.6 ± 0.9	183 ± 0.9
Wives' age (years)	30.5 ± 0.5	30.4 ± 0.4

the intervention group no change in volume of the right testis occurred, the left testis showed a slight, but not significant, increase from 14.6 ± 0.5 to 15.8 ± 0.6 ml after 12 months (Figure 1). Sperm concentrations in both groups tended to increase at 3-6 months, but were significantly elevated after 9-12 months only in the intervention group ($P < 0.001$) (Figure 2). All other semen or hormone (luteinizing hormone, follicle stimulating hormone, testosterone) parameters failed to show any significant intervention-related effect.

In total, 34 pregnancies (27.2% of the 125 couples) were recorded in the 12 month follow-up period, 16 of 63 (25.4%) in the counselling-only group, and 18 of 62 (29.0%) in the intervention group. The figures were not different when assessed by the χ^2 test with Yates' correction. The cumulative pregnancy rates are shown in Figure 3.

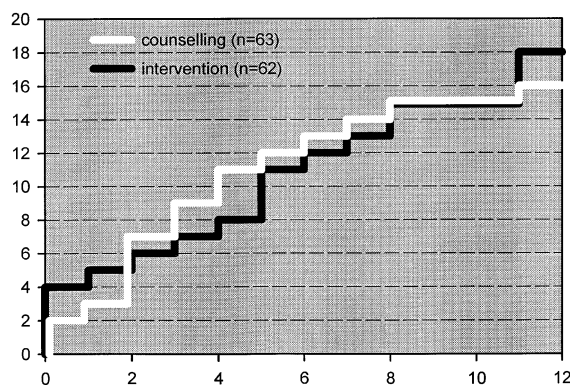


Figure 3. Cumulative pregnancy rates over 12 months in couples with varicocele treated by intervention (ligation or embolization) or counselling alone.

Discussion

A varicocele is the most frequent finding in infertile patients (Nieschlag and Behre, 1997) and dealing with this finding constitutes a considerable proportion of infertility management — all the more reason that the treatment of patients with varicoceles should be based on properly controlled studies, as required by the rules of evidence-based medicine. However, the recommendation to treat varicocele by surgical ligation dates back to the early 1950s (Tulloch, 1952) and studies since then advocating interventive treatment of varicocele have been uncontrolled or have not fulfilled the criteria of modern evidence-based medicine (reviewed in Mordel *et al.*, 1990). Considering the costs and risks of surgical or angiographic treatment, advocating these procedures should be based on strong evidence for their effectiveness.

In contrast to common practice, our original and now extended study indicates that interventive treatment of varicocele does not result in a higher pregnancy rate than counselling alone. This confirms the earlier study by Nilsson *et al.* (1979) and the conclusion other authors have drawn from their observations on varicocele treatment (Rodriguez-Rigau *et al.*, 1978; Baker *et al.*, 1985; Vermeulen *et al.*, 1986; Yamamoto *et al.*, 1996). Our study is the largest single-centre controlled study to date on the treatment of varicocele. Although we would have preferred to extend it even further to substantiate its power, it became difficult to continue because more and more patients — under the impression that there were new effective techniques of assisted reproduction — refused to participate in the study. The only larger study is sponsored by the World Health Organization and involves 238 couples. This study has found pregnancy rates of 34.8% in the surgical ligation group ($n = 129$) and 16.7% in the non-treatment group ($n = 109$). However, although presented at several meetings, this study has not yet been published as it has met with major criticism carefully expounded in a proceedings volume by Hargreave (1997). Its major problem appears to arise from the world-wide multicentre design with differing interpretations of the study protocol and serious protocol violations. The validity of that study, therefore, appears to be doubtful. Those who may still question the power of our study may view it together with results from an earlier study comparing the effects of surgical ligation and angiographic

Table II. Wives' age at admittance to trial on treatment of varicocele (mean \pm SE)

	Age (years)
Total group ($n = 125$)	30.5 \pm 0.4
Subgroup achieving pregnancy ($n = 34$)	28.8 \pm 0.6*
Subgroup not achieving pregnancy ($n = 91$)	31.2 \pm 0.3*

* $P < 0.05$.

embolization (Nieschlag *et al.*, 1993). Since patients were enrolled in this study under the same criteria as in the ensuing investigations, the results may be considered together, i.e. comprising a total of 196 couples.

We have tried to relate the results of our study to physical or laboratory findings in our patients, but could not identify any associations. For example, semen parameters, hormone concentrations and grades of varicocele were not related to the occurrence of pregnancy. It should be emphasized that our patients were carefully selected so that varicocele was the only pathological finding diagnosed. In this regard our study population may be different from those of earlier investigations. The only significant difference we found, regardless of treatment modality, was the wives' age at admittance to the study: the 34 wives of patients achieving a pregnancy had a mean age of 28.8 ± 0.6 years and were significantly younger than the 91 wives not achieving a pregnancy (31.2 ± 0.3 years, $P < 0.05$) (Table II). This underlines the well-documented importance of female age for reproduction and may lead to the recommendation that men with varicocele should start their families at the optimal reproductive age of their wives. However, such a recommendation may be as unrealistic as the general suggestion that an infertile man should search for a highly fertile woman in order to compensate for his problem. On the other hand, we did not find a relationship with the patients' age indicating that the patients' fertility may not be further aggravated by age as suggested, for example, by Bonanni *et al.* (1997).

The controversies surrounding the treatment of varicocele are perplexing for the clinician faced with making a therapeutic decision on a day-to-day basis. Several clinicians are convinced that there must be a subset of patients whose fertility would benefit from interventional treatment. However, there are no definitive diagnostic criteria that would identify these patients (Trum *et al.*, 1996). Confronted with this puzzle and considering that the pathophysiology of the varicocele and its relationship to fertility is still unclear (in the end a varicocele may be nature's attempt to heal an otherwise diseased testis rather than afflict an otherwise healthy testis), one might request a moratorium on interventional treatment until a sound and rational basis for treatment has been found. Optimization of female reproductive functions and, if needed, assisted reproduction, may be an interim solution. Meanwhile interventional treatment might be reserved for large varicoceles causing a mechanical problem or those causing pain and discomfort.

Advising against interventional treatment, however, is not the same as advising against treatment at all. Our patients were seen at 3 month intervals and underwent physical examination,

semen and hormone determinations on these occasions. In addition, a discussion between the attending physician and the patient, often also in the presence of his wife, took place, taking as much time as the patient felt necessary to deal with his problem. The results of the investigations, medical progress and matters such as timing and spacing of intercourse and female reproductive functions were covered. Often, personal and professional problems of the patient were also included. After each consultation the wife's gynaecologist was informed and requested to optimize female reproductive functions if necessary. Although formal psychological therapy was not provided, the 3-monthly sessions we had with the patients fulfilled the requirements of infertility counselling insofar as we helped the patients to assess their motivation and desire for parenting, to improve their marital relationship and to maintain or restore their feelings of self-worth and self-esteem (Mozley, 1976; Daniluk, 1991). In view of the fact that deep feelings of inadequacy arise from awareness of impaired fertility and that men often lack a confidante with whom to discuss their problem, the regular sessions at the infertility clinic provided them with a necessary outlet and, at the same time, with reassurance. Although men attending the infertility clinic in general have normal personalities and do not require psychological therapy (Deipenwisch *et al.*, 1994), the regular counselling helped them to develop strategies to cope with their fertility problem. Since counselling alone led to similar pregnancy rates as interventional treatment it may be concluded that the experience and stress of the surgical or angiographic procedures provides mainly a placebo effect which can otherwise be provided by careful medical counselling.

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E.Nieschlag et al.

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