Improvement of semen quality by nocturnal scrotal cooling and moderate behavioural change to reduce genital heat stress in men with oligoasthenoteratozoospermia

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A questionnaire assessing factors that might cause an increase in scrotal temperature was completed by patients with reproducible oligoasthenoteratozoospermia of idiopathic nature or caused by varicocele. Evaluation by means of a grading scale revealed increased scrotal heat stress in oligoasthenoteratozoospermic patients compared with normozoospermic men (P < 0.01). In addition, long-term determination of 24 h scrotal temperature profiles showed that compared with semen donors, oligoasthenoteratozoospermic patients frequently had scrotal temperatures above 35.5°C despite the same environmental temperatures (P < 0.05). In 88% of cases, maximum scrotal temperatures were measured during rest or sleep phases, whereas minimum values were recorded during physical activity or frequent change of position.

Nocturnal scrotal cooling by means of an air stream resulted in a decrease in scrotal temperature of approximately 1°C. Furthermore, a highly significant increase in sperm concentration (P < 0.0001) and total sperm output (P < 0.0001) was achieved after nocturnal scrotal cooling for 12 weeks together with a moderate decrease in factors leading to genital heat stress. A significant improvement in sperm motility (P < 0.05) and sperm morphology (P < 0.05) was also observed, but this improvement was markedly less pronounced than the changes in sperm concentration. This study shows the importance of genital heat stress as a cofactor in fertility impairment in men and indicates nocturnal scrotal cooling as a therapeutic option.

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over 24 h. Scrotal temperature profiles were also determined during physical activity compared with those during physical rest, for example, in the sitting or lying position (Brindley, 1982; Lerchl et al., 1993). The dynamic factors influencing testicular temperature have been discussed in several review articles (Mieusset, 1998; Thoneau et al., 1998; Morgentaler et al., 1999).

The present study was performed to determine whether semen quality could be improved by lowering scrotal temperatures by using a simple cooling device (continuous air stream) at night in men with oligoasthenoteratozoospermia of idiopathic nature or caused by varicocele. In addition, a questionnaire was developed to determine and evaluate scrotal heat stress factors (Brindley, 1982), focusing mainly on increased scrotal temperature during sleep (Lerchl et al., 1993) and physical inactivity (Mieusset, 1998). Scrotal temperature profiles were also determined over 24 h.

Selection of patients for cooling treatment

Between September 1998 and September 1999, patients with oligoasthenoteratozoospermia of idiopathic nature or caused by varicocele (assumed pathogenetic role of increased genital heat stress) attending the andrological outpatient department were invited to participate in a therapeutic study for improvement of semen quality using nocturnal scrotal cooling for 12 weeks. Approval to perform the study was obtained from the Ethic Commission at the Faculty of Human Medicine, Justus Liebig University Gießen (application 35/98) with an amendment on September 1998. All patients gave written informed consent to participate in the study. The patients showed no signs of testicular damage (normal gonadotrophin concentration, testicular volume of at least 12 ml on both sides, no retractile testis or history of maldescendent testis), and infection or chronic inflammation of the seminal tract was excluded. Varicocele was diagnosed clinically and by using Doppler sonography. During the 3 months before the study, no therapy had been performed to improve semen quality. A recruitment period of 1 year was chosen to avoid seasonal influences on semen quality (Levine, 1996). Of the 25 patients (‘potential patients undergoing cooling treatment’) who were initially interested, 20 participated in the study (‘patients undergoing cooling treatment’). The remaining five men withdrew from the trial during preliminary examinations.

The influence of scrotal cooling on semen quality and serum hormone status was assessed in the 20 patients undergoing cooling treatment. At least one previous spermogram with oligoasthenoteratozoospermia was followed by an initial spermogram at the beginning of the trial (oligoasthenoteratozoospermia as inclusion criterion) according to the World Health Organization (1992) and

Materials and Methods

Equipment

The cooling device used to reduce scrotal temperature (Fig. 1) was made using an 8 mm drill. Twenty holes were drilled into one flat side of each of two polyvinyl chloride (PVC) receptacles (30 ml sample bottles, 64 mm × 40 mm × 17 mm³). Contralaterally, the receptacles were fixed on an elastic band 30 mm in width, one side of which was sewn on to an abdominal belt. The distance between the receptacle and the upper border of the belt was 60 mm. The distance between the inner borders of the elastic bands at the belt was 90 mm. The elastic bands were placed around the thighs and were fixed at the belt, and the receptacles were situated in the groin with the openings facing the scrotum. A continuous air stream was supplied through a plastic tube (approximately 6 m in length, inner diameter 4 mm, outer diameter 6 mm) connected to a membrane pump (Schego optimal, 5 W, 250 l h⁻¹; Schemel & Goetz GmbH & Co. KG, Offenbach/Main). Owing to the mild but still perceivable noise of the pump it was recommended that the pump be placed outside the bedroom. The duration of use of the cooling device was recorded each day by the patients.

For continuous measurement of scrotal temperature over two nights (comparison between cooling and non-cooling) and determination of a 24 h temperature profile (Jockenhövel et al., 1990), temperature sensors (YSI model 409BD; Yellow Springs Instrument Co., Yellow Springs, OH; accuracy of measurement ± 0.1°C) were fixed on either side of the scrotum using Fixomull® stretch (30 mm × 30 mm; Beiiersdorf AG, Hamburg) throughout the monitoring period. Values were registered every 2 min via a portable data recorder AGF-Thermoport 2 (Funkelektronik Gräwe, Münster). In parallel with measurement of scrotal temperatures, patients and volunteers recorded the type of activity they were undertaking, including bed rest, sitting, standing and physical activity as well as a mixture of all these types of activity.

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serum concentrations of FSH, LH and total testosterone were determined. Follow-up spermograms were analysed after 4, 8 and 12 weeks (deviation of ± 1 week was allowed). The serum hormone status was redetermined at the end of the trial after 12 weeks.

Questionnaire assessing scrotal heat exposure and description of control group 1

Factors that might have a negative influence on scrotal temperature were assessed by means of a questionnaire to clarify whether all 25 potential patients undergoing cooling treatment had increased genital heat stress. Both the questionnaire and evaluation by means of a grading scale (Table 1) were designed to record the influence of physical inactivity (high scrotal temperature during sleep or when sitting) through a time-dependent multiplier. Clothing habits and coincidental increases in temperature as a result of fever or lifestyle habits were also considered. The questions referred to mean values from the previous 3 months and included the last spermatogenesis cycle.

The results from the questionnaires of the 25 potential patients undergoing cooling treatment were compared with data from 26 normozoospermic men with sperm concentrations > 10^8 ml^-1 (control group 1; infertile wife) who had been interviewed during the same period. At the end of the study, the questionnaire was repeated by the 20 patients undergoing cooling treatment to determine the influence of behavioural change in addition to nocturnal scrotal cooling.

Table 1. Questionnaire for scoring individual scrotal heat exposure during 3 months

<table>
<thead>
<tr>
<th>Question</th>
<th>Points</th>
<th>Yes</th>
<th>Partly</th>
<th>No</th>
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<tbody>
<tr>
<td>How many hours per day do you sleep?</td>
<td>2 per h</td>
<td>4</td>
<td>2</td>
<td>0</td>
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<tr>
<td>How many hours per day (apart from sleep) do you spend at physical rest</td>
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<td>(sitting, standing, lying) while eating, working, watching TV, driving</td>
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<td>or travelling by train?</td>
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<tr>
<td>During the day do you wear: tight underpants (for example, jockey)?</td>
<td>2 per h</td>
<td>4</td>
<td>2</td>
<td>0</td>
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<tr>
<td>tight trousers (for example, jeans)?</td>
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<tr>
<td>At night do you wear: underpants?</td>
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<td>pyjamas?</td>
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<tr>
<td>Do you use a down-filled duvet?</td>
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<td>Do you use saunas?</td>
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<td>Do you take hot baths?</td>
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<td>Do you use a heated blanket?</td>
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<td>Do you use a heated seat in your car?</td>
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<td>Are you exposed to heat at work?</td>
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<td>Have you had a fever in the past 3 months?</td>
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<td>Do you use a solarium?</td>
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</table>

Score value: Total points

Scrotal temperature profiles and description of control group 2

Because of the limitations of the questionnaire, the 24 h scrotal temperature profiles of the patients undergoing cooling treatment were compared with those of ten semen donors (fertile or normozoospermic, control group 2). Long phases of sleeping, sitting or moving were noted. In addition, the outdoor temperatures measured each hour by the Gießen weather station (Deutscher Wetterdienst, Offenbach) were considered to exclude all environmental influences of temperature. After the 24 h scrotal temperature profile was recorded, the patients undergoing cooling treatment continued to measure scrotal temperature during the subsequent night. The cooling device was used to evaluate the individual cooling effect compared with the first night without cooling.

Patients with oligoasthenoteratozoospermia without cooling as control group 3

As deviating semen parameters were unavoidable and it was impossible to perform a prospective double-blind randomized trial on the effect of scrotal cooling, the spermograms of another 20 patients with oligoasthenoteratozoospermia of idiopathic nature or caused by varicocele (normal gonadotrophin concentrations, testicular size at least 12 ml on both sides, no retractile testis or history of maldescendent testis; control group 3) were evaluated at the same time, during which no therapy was performed because of current diagnostic examination. The first semen
analyses of control group 3 were performed as close as possible to week 0 of analysis of a cooling patient (longest interval was 2 weeks). The second semen analyses of control group 3 were evaluated at intervals between weeks 7 and 16. This range was chosen because it represents the minimum duration for the 8 week analysis of patients undergoing cooling treatment (deviation of ± 1 week was allowed) and the maximum duration of the 12 week analysis of patients undergoing cooling treatment.

Statistical analysis

Tests for non-parametrically distributed values only were used. The P values were calculated two-sided. The Mann–Whitney U test was used for comparison of the scores for heat stress among patients undergoing cooling treatment and control group 1. The scores before and after cooling were compared using Wilcoxon paired sample test. The Mann–Whitney U test was applied for comparison of temperature frequencies above 35.5°C in patients undergoing cooling treatment and control group 2. Comparison of the median values of the nocturnal scrotal temperatures in patients undergoing cooling treatment, with and without cooling, was made using Wilcoxon paired sample test. Basic spermiogram parameters (concentration, motility, morphology) and serum hormone concentrations of the patients undergoing cooling treatment were analysed using Wilcoxon paired sample test and together using Friedman’s test for repeated measurements. Changes in the semen analyses of control group 3 were compared using Wilcoxon paired sample test.

Results

The questionnaires (Table 1) assessing the possible influence of heat on spermatogenesis in patients with oligoasthenoteratozoospermia of idiopathic nature or caused by varicocele (including the five patients who did not participate in the cooling treatment study) and in normozoospermic men with sperm concentrations > 10⁸ ml⁻¹ (control group 1) revealed significant genital heat stress in patients with impaired semen quality (P < 0.01; score values for median and 10–90% percentile, respectively: 46 versus 36; 34–52 versus 28–48). The higher values were primarily due to longer periods of physical rest (sitting, standing or lying; median: 10 h versus 8 h) independent of night rest (median: 7 h in both groups). Increased periods of physical rest showed statistical significance (P < 0.05). In addition, tight-fitting underwear was worn significantly more frequently (P < 0.02).

Long-term monitoring of scrotal temperatures in patients undergoing cooling treatment and semen donors (control group 2) again showed that physical activity is an important factor, which steadily improves scrotal heat dissipation (Brindley, 1982; Lerchl et al., 1993); a representative example of a profile from a cooling patient is shown (Fig. 2). Physical inactivity during desk work or night rest was associated with scrotal temperatures of > 36°C, whereas
temperatures between 34°C and 35°C or lower were measured during housework or gardening.

The 24 h scrotal temperature profiles of the 20 patients undergoing cooling treatment and the ten semen donors (control group 2) differed significantly in that scrotal temperatures > 35.5°C were predominant in patients before nocturnal cooling (P < 0.002). Median values for scrotal temperatures during sleep were higher than those for the total 24 h profiles (patients undergoing cooling treatment at sleep: 35.92°C on the right, 35.73°C on the left; 24 h profile: 35.50°C on the right, 35.54°C on the left; control group 2 at sleep: 35.76°C on the right, 35.57°C on the left; 24 h profile: 34.99°C on the right, 35.29°C on the left). The 24 h profiles of control group 2 were compared with those of the ten patients undergoing cooling treatment who had been exposed to the same outdoor temperatures during the period of monitoring to exclude a possible influence by environmental temperature. Mean outdoor temperature was 5.47°C in the patients undergoing cooling treatment and 5.50°C in control group 2 (Fig. 3). High scrotal temperatures were significantly more frequent in patients before they received nocturnal cooling treatment (P < 0.05).

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Statements from control group 2 and the patients undergoing cooling treatment regarding the activity undertaken at the time of maximum and minimum values of scrotal temperature profiles revealed that maximum values occurred during sleeping (40.0% in control group 2 and 37.5% in patients undergoing cooling treatment) and sitting (50.0% in control group 2 and 42.5% in patients undergoing cooling treatment), particularly by the end of a period of such activity. However, minimum values occurred during periods of movement (60% in control group 2 and 30% in patients undergoing cooling treatment) or during alternation between moving, lying, sitting or standing (25% in control group 2 and 40% in patients undergoing cooling treatment). Minimum values of scrotal temperature were accompanied by fewer statements on activity and repeatedly occurred between 06:00 and 09:00 h.

A comparison of the nocturnal scrotal temperatures in patients undergoing cooling treatment, with and without cooling, showed a reduction in the median value of scrotal temperature from 35.8°C (range 34.6–36.3°C) to 34.9°C (range 32.8–35.5°C). The frequency distribution of scrotal temperatures is shown (Fig. 4). Comparison of the median values using the Wilcoxon paired sample test revealed a highly significant difference.

The following diagnoses were established among the 20 patients undergoing cooling treatment who participated in the study: primary infertility (17), secondary infertility (2) and an unfulfilled wish to father a child for 8 months (1),
previously treated for varicocelectomy or sclerotherapy (5, 1 with persisting varicocele), varicocele or subclinical varicocele (4), previously treated for seminal tract infection or inflammation (6), previous anabolic abuse (1) and small prostatic cyst (1). Other relevant parameters of the patients undergoing cooling treatment are summarized (Table 2).

One patient deviated widely from the study design (130 days, including 73 nights without cooling) because of poor compliance due to the noise of the membrane pump, which prevented use during overnight accommodation with parents or friends. Other compliance problems with the cooling device were not reported. One patient had a follow-up semen examination after 8 weeks of therapy, which was performed in another andrological centre.

The semen parameters of the patients undergoing cooling treatment revealed a highly significant improvement in sperm concentration (Fig. 5) and total sperm output (median: 1.99 × 10^7 before the study, 1.81 × 10^7 at week 0, 3.7 × 10^7 at week 4, 6.86 × 10^7 at week 8, 6.66 × 10^7 at week 12) (Friedman’s test for repeated non-parametric measurements: P < 0.0001). In addition, sperm motility (Fig. 6) and sperm morphology (Fig. 7) showed a small, but significant improvement (P < 0.05).

The semen parameters of men in control group 3 who did not receive cooling treatment revealed no significant changes in sperm concentration (Fig. 5), motility (Fig. 6) or morphology (Fig. 7).

In the patients undergoing cooling treatment, there was no significant difference in the duration of abstinence (median: 5.5 before the study, 4.5 at week 0, 5.0 at week 4, 5.0 at week 8, 5.0 at week 12) and respective ejaculate volume (median: 4.35 before the study, 3.5 at week 0, 4.0 at week 4, 4.0 at week 8 and 3.75 at week 12).

No change in the concentration of FSH and total testosterone was observed before and at the end of scrotal cooling, but a significant increase in LH was observed (P < 0.02; median: 2.35 versus 3.3; and 10–90% percentile: 1.8–4.5 versus 1.7–4.8 miu ml^-1, respectively).

The questionnaire score values of the patients undergoing cooling treatment with regard to genital heat stress at the beginning and end of therapy revealed a significant reduction in factors that influence heat stress. Patients had changed their behaviour, although this had not been requested before the study (P < 0.05; score values for median and 10–90% percentile: 44.5 versus 39; 34–49 versus 28–48). In eight patients, lower scores resulted primarily from fewer rest periods because of increased physical activity during leisure time and in six patients because of less clothing worn at night (no pyjamas or underpants).

**Discussion**

In the present study, patients with oligoasthenoteratozoospermia of idiopathic nature or caused by varicocele showed marked scrotal heat stress compared with normozoospermic
temperatures > 35.5°C. Scrotal temperature profiles showed significantly more genital heat stress. In addition, long-term monitoring of evaluation of score values in questionnaires focusing on men (control group 1). This finding is supported by the evaluation of score values in questionnaires focusing on genital heat stress. In addition, long-term monitoring of patient behaviour towards genital heat stress, indicating that genital heat exposure should be considered as a causal factor of impaired fertility. Scrotal cooling by means of a continuous air stream represents a simple method for reduction of the relatively high scrotal temperatures observed at night (Jockenhövel et al., 1990; Lerchl et al., 1993). Long-term monitoring of scrotal temperatures in patients before and during use of the cooling device revealed a cooling effect of approximately 1°C. Scrotal cooling by applying ice bags in the genital region was suggested as a method for improving semen parameters by Robinson et al. (1968), but a study was not performed. The first such study was performed by Mulcahy (1984) who used a similar method to investigate the effect of nocturnal scrotal cooling on spermatogenesis. The patients had ice packs applied to the scrotum and held in place with shorts, but scrotal temperatures were not monitored and statistical analysis was limited. Repeated cold washings of the genitals has been recommended as another means of scrotal cooling (Davidson, 1954), but pertinent studies are not available. To date, only an evaporative cooling device for reduction of scrotal temperature has been developed for use in practice (Zorgniotti et al., 1980, 1982, 1986). The cooling effect is achieved by evaporation of water from a body-worn reservoir, which is continuously emitted into a scrotal covering. This cooling device offers the advantage that it can be used during the day in the work environment; however, because of the resultant humid environment the duration of use must be limited to allow regeneration of the scrotal skin. Furthermore, dermatological diseases such as tinea inguinalis or erythrasma are considered contraindications. Among 64 patients (infertile for at least 2 years and partner with normal gynaecological findings) who had worn the cooling device for a minimum of 16 weeks, spermiograms showed improvement in 65.6% of patients and pregnancy occurred in 26.6% of cases (Zorgniotti et al., 1986). Overall, patient compliance was only 46%. The study included only patients who had scrotal temperatures above 34.1°C. This inclusion criterion was established in
increased heat stress was demonstrated in patients in the heat exposure in mammals (Setchell, 1998) and presumably especially of spermatocytes and spermatids to testicular interval is in agreement with the high susceptibility support the theory of a placebo effect, whereas the time and 12 weeks, but not after 4 weeks. This finding does not against this explanation is that the effect is observed after 8 weeks, and 12 weeks, but not after 4 weeks. This finding does not also be explained by a marked placebo effect. An argument andrological therapy, improved semen parameters could be assessed more accurately by long-term monitoring and 12 weeks, but not after 4 weeks. This finding does not within the framework of intensified andrological therapy, improved semen parameters could be assessed more accurately by long-term monitoring conditions, are not considered. These environmental factors could be assessed more accurately by long-term monitoring of scrotal temperature under everyday physiological conditions. For example, the temperature-reducing effect of frequent physical activity as compared with physical rest has been demonstrated in the present study by evaluating long-term temperature profiles and the patient’s history. A limitation of the present study is that it cannot be performed in a double-blind manner, because the airstream is perceived subjectively. It is not completely satisfactory to evaluate patients with oligoasthenoteratozoospermia of idiopathic nature or caused by varicocele without therapy (control group 3), who do not show a significant change in sperm parameters. Within the framework of intensified andrological therapy, improved semen parameters could also be explained by a marked placebo effect. An argument against this explanation is that the effect is observed after 8 and 12 weeks, but not after 4 weeks. This finding does not support the theory of a placebo effect, whereas the time interval is in agreement with the high susceptibility especially of spermatocytes and spermatids to testicular heat exposure in mammals (Setchell, 1998) and presumably in humans. A placebo effect is also unlikely because increased heat stress was demonstrated in patients in the present study by means of both the questionnaire on genital heat stress and long-term measurement of scrotal temperature. Apart from nocturnal scrotal cooling during the study, patients showed moderate behavioural changes that reduced scrotal heat factors; therefore, the improvement in the spermiograms cannot be attributed solely to scrotal cooling. Another limitation of the study design was that semen parameters were considered, but pregnancy rates were not. However, the study was not designed for this purpose, because a maximum of two ovulations could be expected during the treatment period with improved spermiogram parameters and an additional gynaecological infertility factor was not an exclusion criterion. It would be unethical to perform a study focusing directly on pregnancy rates without having determined a possible effect on spermiogram parameters. Improvement in the spermiogram alone enables many infertile couples to apply simple methods of assisted reproduction, such as intrauterine insemination, and to avoid more invasive and costly reproductive techniques, for example microinjection.

Serum concentrations of FSH, LH and total testosterone were recorded to determine whether an optimal effect of scrotal cooling resulting in improved spermatogenesis was associated with a slight reduction in FSH concentrations. Similarly, improved testosterone synthesis in the Leydig cells may have led to decreased LH concentrations; therefore, the increased LH concentrations observed in the present study should not be interpreted as resulting from a significant influence of scrotal cooling.

For further investigation of the influence of scrotal cooling on spermatogenesis, a cooling device that can be worn for 24 h would be desirable, coupled with a thermosensor to avoid temperature increases beyond a threshold value, for example 35.5°C. Prospective double-blind studies could then be performed by setting different threshold values.

Warming of the testis as a method of contraception has been investigated in several studies. It was found that scrotal temperatures increased by 1°C as a result of wearing polyester-lined athletic supports, but did not cause suppression of spermatogenesis over several cycles (Wang et al., 1997). However, other studies demonstrated that long-term increases in scrotal temperature as a result of wearing insulating underwear (Rock and Robinson, 1965; Robinson and Rock, 1967) or polyester sling scrotal covers (Moelock, 1995) led to impaired semen quality and azoosperma. Increased scrotal temperatures were also observed in patients wearing a special support that presses the testes close to the inguinal canal (Mieusset and Bujan, 1994) and after surgical fixation of the testes in the inguinal canal (Shafik, 1991). These findings support the results of the present study.

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