Physical activity as a possible aggravating factor for athletes with varicocele: impact on the semen profile

Luigi Di Luigi¹, ⁶, Vincenzo Gentile², Fabio Pigozzi³, Attilio Parisi⁴, David Giannetti¹ and Francesco Romanelli⁵

¹Unit of Endocrinology, Laboratory of Endocrine Research, University Institute of Motor Sciences (IUSM), ²Division of Urology, University ‘La Sapienza’, ³Sport Medicine Unit, University Institute of Motor Sciences (IUSM), ⁴Sports Medicine Institute, FMSI, CONI and ⁵Division of Andrology, University ‘La Sapienza’, Rome, Italy

The aim of the present study was to evaluate the influence of physical exercise on seminal parameters of male athletes with varicocele. Sixty healthy male volunteers (athletes and non-athletes, n = 30 + 30) and 60 volunteers affected by varicocele (athletes and non-athletes, n = 30 + 30) were randomly selected for a clinical study. All subjects provided at least two semen samples for routine microscopic analysis. Determinations for basal luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin, oestradiol, total and free testosterone under resting conditions were also performed. In both groups with varicocele the percentage of total and progressive forward sperm motility and the percentage of normal spermatozoa were significantly reduced. The percentage of both progressive forward motility and normal spermatozoa were significantly lower in athletes with varicocele compared with non-athletes with varicocele (P < 0.05). Only athletes with varicocele had mean left testis volume significantly lower than the contralateral testis (P < 0.05). No modifications of hormonal parameters at rest were observed in any groups. Physical activity might represent an aggravating factor for spermatogenesis in athletes with varicocele. In countries where sport eligibility is granted by an authoritative body, these results suggest the need to establish general medical criteria to guarantee the continuation of an athlete’s training whilst at the same time taking care of his reproductive health.

Key words: exercise/FSH/LH/semen/testosterone

Introduction

Physical exercise is a potent modulator of the release of a large number of hormones and has been widely studied as a stimulus for hormonal secretion (Howlett, 1987; Cumming, 1995). In particular, physical stress has a range of effects on the hypothalamus–pituitary–gonadal (HPG) axis, depending both on the type, intensity and duration of the activity and on the fitness and the characteristics of the individual (Ayers et al., 1985; Hackney et al., 1988; Cumming et al., 1989a,b; Bagatell and Bremmer, 1990; Arce et al., 1993; Roberts et al., 1993; De Souza et al., 1994; De Souza and Miller, 1997).

In women, exercise-induced alterations of the HPG axis are expressed clinically by delayed menarche, oligo- or amenorrhoea, inadequate luteal phase and anovulatory cycles. In male athletes, such evident clinical alterations are lacking and a number of areas still remain unexplored, such as: (i) the relationships between physical stress and correlated factors (i.e. doping, ergogenics, supplementations, etc.) and male fertility; (ii) the clinical consequences of the observed exercise-dependent serum testosterone reduction (Hackney et al., 1988; Cumming et al., 1995; De Souza and Miller, 1997) in male athletes (on bone tissue, muscles, central nervous system, immune system, etc.) and (iii) the impact of physical activity on body physiology in hypoandrogenic subjects (prepubertal age, ageing, male hypogonadism, etc.).

Regarding the effects of physical activity on an athlete’s seminal fluid, some authors (Ayers et al., 1985; Bagatell and Bremmer, 1990; De Souza and Miller, 1997) have found no significant modifications of semen parameters, whereas others have found reduced total sperm count, reduced normal sperm motility and morphology (Arce et al., 1993; Roberts et al., 1993; De Souza et al., 1994). To date, the evaluations concerning the seminal fluid of athletes have been carried out on healthy athletes, while nobody has ever considered evaluating the impact of physical activity on the spermatogenesis of male athletes with andrological diseases. Perhaps this is also due to the fact that in-depth andrological evaluations are not common during the athlete’s pre-participation physical examinations. Varicocele, which may result from venous incompetence of the spermatic veins, has a high incidence in the general population (Hargreave, 1993) and, in particular, in athletes...
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(Di Luigi et al., 1994; Scaramuzza et al., 1996). Varicocele represents the most frequent cause of sub-fertility or infertility in men because it is frequently associated with morphological and functional alterations of the seminal parameters (Pryor and Howards, 1987; WHO, 1992a). The aim of the present cross-sectional study was to determine whether sport activity influences the seminal parameters of male athletes suffering from varicocele.

Materials and methods

Sixty trained male competitive athletes, training (football, volleyball, basketball and handball) 4–5 days a week (2–4 h per day) for a minimum of 4 years and 60 age-matched non-obese male subjects who participated at maximum in educational or recreational physical activities (2–3 h per week) (non-athletes), were selected for the study. The athletic group was divided into two subgroups: athletes with varicocele (group A: n = 30; age 22.2 ± 2.6 years; height 179.1 ± 6.3 cm; weight 70.2 ± 5.9 kg) and healthy athletes without varicocele (group B: n = 30; age 22.6 ± 4.1 years; height 183.4 ± 7.5 cm; weight 75.2 ± 7.8 kg). The non-athletic group was also divided into two subgroups: non-athletes with varicocele (group C: n = 30; age 23.5 ± 4.3 years; height 171.2 ± 8.3 cm; weight 69.2 ± 7.9 kg) and healthy non-athletes without varicocele (group D: n = 30; age 21.9 ± 2.3 years; height 173.1 ± 5.9 cm; weight 68.9 ± 4.9 kg). The subjects of each group were randomly extracted from four larger groups of subjects selected during the pre-participation physical examinations carried out in order to grant sport eligibility (athletes), and during andrological examinations performed in order to assess male fertility status (non-athletes). The nature of the study was explained to each subject in detail and informed consent was obtained.

All the subjects underwent a complete clinical and andrological examination. All the volunteers were in good health (in terms of non-andrological diseases), their weight was stable (no weight variation of more than 2–4 kg within the past year) and they all had normal physical and sexual development. Except for the varicocele in groups A and C, none of the subjects had a history of diseases influencing their andrological status or showed andrological and/or physical alterations (cryptorchidism, inflammatory processes, etc.) influencing the reproductive tract. None of the subjects had taken medication or nutritional supplements that could affect the HPG axis (Conte et al., 1999; Di Luigi et al., 1999) in the preceding 6 months and none had ever taken anabolic steroids. None worked in professions where the activity might influence reproductive capacity. In each group there were 4 to 6 habitual smokers (not more than 20 cigarettes a day). Only a few subjects were married (five non-athletes and three athletes) and only three (one in group B, C and D respectively) had one child with their habitual partner (wife). Routine biochemical and haematological analyses were in the normal range in all the subjects.

In all the subjects with clinical varicocele, the diagnosis was confirmed by an ultrasound-Doppler examination of the testicular vessels and only subjects with a left second degree varicocele (reflux throughout the Valsalva’s manoeuvre in Dubin classification) were selected for the study. Ultrasound examination was performed on all the subjects by the same operator to evaluate testicular volume (0.525×a×b×c; a, b, c are testis diameters). A testicular vascular Doppler examination was also performed on all the control subjects (healthy athletes and healthy non-athletes) in order to exclude the presence of ‘sub-clinical’ varicocele.

All the subjects maintained their usual dietary habits and, in athletes, the training was stopped 2 days prior to each semen sample and 3 days prior to blood samples.

Semen analyses

In an effort to account for the inherent variability observed in semen analyses, all the subjects collected at minimum two samples of seminal fluid, after 2–5 days of sexual abstinence (intercourse or masturbation) and with a minimum interval of 3 weeks between the semen collections. More than two samples (up to 4–5 samples in some subjects) were collected from a given individual when total normal motile count varied by more than 20% from the previous sample (five). Semen was generally collected by manual masturbation into a sterile container on site and examined within 60 min of ejaculation. In some cases (group A: three subjects; group B: five; group C: four; group D: four) the semen samples were delivered to the laboratory within 30 min of home collection.

Semen analysis including pH, viscosity, semen volume, sperm concentration, motility and morphology was performed by the same technicians according to the general World Health Organization guidelines (WHO, 1992b).

Endocrine evaluation

The blood collection sessions for hormone analysis began for all subjects between 0800 h and 0900 h and the environmental conditions were always identical (temperature 20–22°C; humidity 52–62%). The subjects were requested to have a similar breakfast (without chocolate or caffeine) 1 h before blood collections. All the subjects were settled and made comfortable for about 30 min, then an i.v. catheter was inserted into an ante-cubital vein and maintained in situ for 30 min. Blood collections were performed immediately after catheter insertion (0) and then again after 15 (+15) and 30 min (+30).

After the first two blood samples were taken the catheter was flushed with a 0.9% isotonic saline to avoid blood clotting. Following blood sample collections the serum was separated, frozen and stored at –40°C until assayed for luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin, total testosterone, free testosterone and oestradiol.

Hormone determinations of all the volunteers were performed in duplicate in the same assay. LH, FSH and prolactin were assayed in all samples (0, +15, +30) whereas testosterone, free testosterone and oestradiol were assayed only in the last sample (+30). LH and FSH were measured in unextracted serum by immunoradiometric assay kits (Sorin Biomedica Diagnostics, Vercelli, Italy). Prolactin and testosterone were measured in unextracted serum by radioimmunometric assay kits (Ares Serono Diagnostici, Milano, Italy). Free testosterone and oestradiol were measured in unextracted serum by radioimmunometric assay (DSL, Webster, Texas and CIS Bio International, Gif-Sur-Yvette Cedex, France respectively). The intra- and inter-assay coefficients of variation (%CV) were 4.7 and 5.9% for LH, 3.3 and 5.8% for FSH, 4.0 and 4.6% for prolactin, 3.5 and 3.2% for testosterone, 5.2 and 7.3% for free testosterone, 6.5 and 10.5% for oestradiol respectively. The sensitivity for LH was 0.2 mIU/ml, for FSH 0.2 mIU/ml, for prolactin 1.0 ng/ml, for testosterone 0.064 ng/ml, for free testosterone 0.18 pg/ml and for oestradiol 1.35 pg/ml. The reference ranges reported for men (20–30 years) are as follows: LH: 1.5–10 mIU/ml; FSH: 1.0–12 mIU/ml; prolactin: <20 ng/ml; testosterone: 2.8–9.8 ng/ml; free testosterone: 15–40 pg/ml; oestradiol: 15–50 pg/ml.

Statistical analyses

All data are expressed as means ± standard deviation. The mean hormonal data ± standard deviations were calculated both from the single absolute hormone plasma concentrations (testosterone, free testosterone, oestradiol), and from the means of the three hormone assays performed for each subject (LH, FSH, prolactin).

After testing the normal distribution of data, the analysis between
were in the normal ranges in all groups and no significant differences were observed between groups (Figure 1).

In both athletes and non-athletes the percentage of total sperm motility and the percentage of progressive forward motility (moderate and very active forward progression) were significantly lower in subjects with varicocele compared with their healthy controls ($P < 0.01$ for both parameters) (Figure 2). Interestingly, the percentage of progressive forward motility was significantly lower in the athletes with varicocele compared with the non-athletes with varicocele ($34.3 \pm 11.3\%$ versus $41.6 \pm 9.8\%$ respectively; $P < 0.05$). However, no difference in the percentage of total sperm motility between the same groups was observed.

As with forward motility, regarding sperm morphology the percentage of normal spermatozoa was significantly reduced in both groups of subjects with varicocele, compared with their healthy controls ($P < 0.01$). Furthermore, this reduction in normal morphology was significantly lower in athletes with varicocele compared with non-athletes with varicocele ($34.1 \pm 10.1\%$ versus $42.4 \pm 11.3\%$ respectively; $P < 0.05$) (Figure 2).

No significant differences were observed between healthy non-athletes and healthy athletes without varicocele for sperm motility and morphology.

**Hormone evaluations**

All evaluated hormonal parameters are reported in Table I. All plasma hormone concentrations were in the normal range and no significant differences between all the evaluated groups were observed.

**Testis volume**

No differences between the mean left and right testis volumes were found in healthy athletes and non-athletes, both intra- and inter-groups (Figure 3).

A reduction of mean left testicular volume (compared with the mean right testis volume of the same group) was observed in both groups of subjects with varicocele. Only athletes with varicocele had mean left testis volume significantly lower than the contralateral testis ($16.9 \pm 2.2 \text{ml}$ versus $18.4 \pm 1.7 \text{ml}$ respectively; $P < 0.05$). No differences in testis volumes compared with healthy subjects within non-athletes or athletes between the two varicocele groups were observed.

**Discussion**

Varicocele is the andrological pathology of greatest incidence (from 4–23% of the general population) and represents the most frequent disease found in sub-fertile men. Epidemiological studies correlating exercise and andrological diseases are rare. Furthermore, in a recent clinical trial, evaluating the role of sport medicine in the diagnosis and prevention of andrological diseases, a high incidence of varicocele in athletes was observed (about 29%) (Di Luigi et al., 1994).

As demonstrated by many studies, varicocele can influence the quantitative and qualitative characteristics of seminal fluid, yet its relevance to fertility is still unclear. In the general population, the most common semen alterations observed in untreated subjects affected by varicocele are: decreased motility
(qualitatively and quantitatively), increased atypical spermatozoa, presence of immature cells and reduced number of spermatozoa (Cheval and Purcell, 1992).

In the present cross-sectional clinical study we wanted to evaluate whether competitive sport activity has an exacerbating affect on seminal parameters and testis size of men with varicocele. Our goal was not to evaluate how physical activity influences varicocele formation and/or aggravates the degree of varicocele. In this sense, as for fertility, longitudinal studies would be more appropriate. We selected only subjects with a second degree varicocele in order to standardize the study. Furthermore, in our country it is very difficult to find competitive athletes (with at least 4–5 years of sport activity) affected by a higher degree of varicocele, because they usually cannot obtain sport eligibility.

To our knowledge, this is the first study evaluating the semen profile and the testis volume of athletes with varicocele in comparison with both healthy athletes and non-athletes (with and without varicocele). Our results show that in the athletic group with varicocele the percentage of spermatozoa with forward progression and normal morphology was significantly lower than in the non-athletes group with the same degree of varicocele, whereas no such effects were observed in the seminal fluid of healthy athletes. Interestingly, whereas a reduction of mean left testicular volume was observed in both groups of subjects with varicocele (athletes and non-athletes), mean left testis volume was significantly lower than the contralateral testis only in athletes with varicocele.

In healthy athletes, seminal characteristics have mainly been evaluated in endurance-trained subjects (Ayers et al., 1985; Bagatell and Bremmer, 1990; Arce et al., 1993; Roberts et al., 1993; Jensen et al., 1995; De Souza and Miller, 1997). Only athletes with a high-volume of training (runners >108 km/week) had reduced total sperm count, reduced sperm motility and reduced normal sperm morphology, compared with sedentary controls. In highly trained runners, a greater percentage of immature cells and reduced sperm penetration in bovine cervical mucus have also been found and the observed seminal characteristics have been significantly correlated with the number of kilometres run per week (De Souza et al., 1994).

On the basis of the present preliminary investigation, it is postulated that the athletic condition might be an aggravating factor in the pathogenesis of the varicocele-linked sperm alterations observed in athletes. Furthermore, while the literature indicates that physical activity seems to influence negatively seminal fluid only in healthy athletes with a high level of training (De Souza and Miller, 1997), in athletes with varicocele a lower level of training might favour testicular and/or sperm alterations.

In the general population, the alterations associated with male varicocele are probably linked to factors acting locally on testicular tissues (high local temperature, low oxygen exchange, adrenal toxic factor, prostaglandin production, etc.) (Isidori et al., 1980; Conte et al., 1985). Furthermore, the spermatogenesis alterations in varicocele are also dependent on individual endogenous (genetic, biochemical, hormonal, etc.) and/or exogenous factors (physical activity, ‘anti-spermatogenesis’ toxic substances, daily living habits, type of work activity, etc.) that may directly or indirectly influence spermatogenesis via metabolic and endocrine control (Takahara et al., 1991). In athletes with varicocele exercise-linked deleterious testicular and seminal alterations might be a result of both local (increased temperature, increased spermatic blood reflux, increased action of exercise-related adrenal ‘spermio-toxic’ factors, etc.) and general [altered gonadotrophin secretion, increased antigenic stress-dependent hormones, i.e. corticotrophic hormone (CRH), cortisol, opioids, etc.] causes.

Concerning the endocrine control of spermatogenesis, none of the groups showed any modification in the serum quantitative reproductive hormone concentrations in resting conditions. From the literature, the experiments evaluating the quantitative gonadotrophin responses to acute exercise or training in healthy
athletes have shown conflicting results (Hackney et al., 1988; De Souza et al., 1994), and the variability between different studies is probably due to all the factors influencing hormonal response to exercise and/or training (Cumming et al., 1989a, 1989b; Williams et al., 1995). Several authors have indicated the importance of the qualitative evaluation of gonadotropin secretion in male athletes (Bagatell and Bremmer, 1990; Hackney, 1996). In this sense, despite conflicting results, in healthy male athletes physical stress has been shown to disturb the quality of LH secretion (Rogol et al., 1984; MacConnie et al., 1986; McColl et al., 1989; Wheeler et al., 1991).

In order to define the exact role of physical activity on sperm functional capacity, further semen evaluations (sperm electron microscopy, penetration tests, semen biochemical evaluations, lipid peroxidation analysis, etc.) and a follow-up for a longitudinal evaluation of fertility in athletes with varicocele is necessary.

This preliminary clinical study lacks proof of both the direct influence and the pathways involved in the sport-linked deterioration of semen characteristics and testis volume reduction observed in athletes with varicocele. However, from a clinical standpoint our study may stimulate both further studies in athletes with varicocele and an in-depth pre-participation andrological evaluation in all men practising both competitive and non-competitive physical activity. Furthermore, the reported need for early treatment of varicocele in the general population (Di Silverio et al., 1991; Lenzi et al., 1998; Ismail et al., 1999) together with the possibility that physical activity may represent an aggravating factor for spermatogenesis, lends support to the need for an in-depth follow-up of athletes with varicocele and/or for preventive treatment, when indicated, particularly in younger athletes.

In countries where sport eligibility is granted by an authoritative body, the lack of a systematic approach to varicocele remains a problem. In fact, it is necessary to develop a standard procedure to be used by sport physicians in granting sport eligibility (Di Luigi et al., 1995). In our opinion, the general guidelines should guarantee the continuation of an athlete’s training while at the same time providing care for his reproductive health. This would avoid ethical problems and facilitate relationships among sport physicians and andrologists, endocrinologists and urologists.

References


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