The Paediatric Urology section of the BJU International has always been a particularly strong part of the journal, and it will continue to be so. Papers in this issue come from the North American continent and from Europe and there is an even wider geographical spread in paediatric urology studies reported in subsequent issues. The papers cover a wide range of topics, all of which relate to clinical practice. For example, the effect of reconstructive procedures on the bladder in children when examined in later life, particularly assessing the effect on growth. In addition, the effect on testicular growth of varicocele repair is also commented upon, and an experimental study into a method of urethroplasty is described.

Testicular growth and gonadotrophin response associated with varicocele repair in adolescent males

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OBJECTIVE

To measure testicular volume and the gonadotrophin response to gonadotrophin-releasing hormone (GnRH) stimulation in adolescents undergoing left varicocelectomy.

PATIENTS AND METHODS

Thirteen adolescents undergoing varicocelectomy had their testicular volume and endocrine function evaluated before and after surgery.

RESULTS

The initial left testicular volume was consistently smaller than the right but after surgery both increased. Baseline follicle-stimulating hormone (FSH) levels and the FSH response to GnRH stimulation increased after surgery. There were no differences in luteinizing hormone and testosterone levels, and no changes in Tanner staging.

CONCLUSIONS

Unilateral varicocelectomy with ipsilateral testicular atrophy results in bilateral testicular growth and increased FSH levels. In adolescent development, elevated FSH levels in conjunction with an increased response to the GnRH stimulation test represent a normal physiological response. The GnRH stimulation test cannot be used to determine which adolescent would benefit from surgical repair.

KEYWORDS

varicocele, testicular compensatory growth, GnRH stimulation test

INTRODUCTION

A varicocele is an abnormal dilation of the internal spermatic veins and pampiniform plexus that occurs in 15–20% of adolescent boys and men [1]. Although usually asymptomatic, deleterious effects of varicoceles on testicular size and function have been reported [2–5] and they may be associated with male infertility [6]. After varicocele repair, improvements in sperm density and motility have been well documented in oligospermic men [7,8]. Currently, the most common indications for the operative repair of varicoceles include symptomatic lesions, testicular volume loss ipsilateral to the varicocele, bilateral palpable varicoceles and abnormal semen values. However, obtaining semen samples from adolescent boys can be a sensitive topic; thus adolescent boys with varicoceles continue to present a treatment dilemma to the urologist, as objective outcome measures of varicocelectomy, e.g. semen quality or fertility, are not readily attainable or appropriate.

Testicular volume loss is thought to represent an inhibitory effect of the varicocele on the growing adolescent testis. Early intervention in the treatment of varicoceles has been proposed, with the observation of ipsilateral testicular compensatory growth after varicocelectomy [3–5]. However, there has been no objective assessment of testicular endocrine function in conjunction with measurements of testicular size in the paediatric population. The GnRH stimulation test is effective in documenting gonadal dysfunction in cases of testicular injury [9]. In the present study, we prospectively measured both testicular volume and evaluated the gonadotrophin response to provocative GnRH stimulation testing in adolescents undergoing inguinal varicocelectomy.

TABLE 1 Testicular volume and hormonal levels before and after surgery, and the gonadotrophin response to provocative GnRH stimulation testing

Mean (SD) variable	Before	After	*P*
Testicular volume, mL			
Left	10.0 (2.3)	21.3 (2.0)	< 0.005
Right	15.3 (2.2)	22.7 (2.3)	< 0.005
P	< 0.025	NS	
Hormone levels, mIU/mL			
FSH	2.9 (0.4)	3.9 (0.5)	< 0.005
LH	1.9 (0.5)	2.5 (0.5)	NS
Testosterone	365 (75)	402 (72)	NS
GnRH testing (T30 – T0)			
FSH	1.6 (0.3)	2.5 (0.4)	< 0.005
LH	14.7 (2.2)	13.0 (1.4)	NS

PATIENTS AND METHODS

Over a 1-year period, 17 adolescent males (mean age 15.8 years, SD 0.7, range 12.6–19.7) with a Grade II or III/III left varicocele were evaluated for testicular growth discrepancy and underwent left varicocelectomy by the same surgeon using the modified Ivannisevich technique. These adolescents and their parents were all approached before surgery and asked to participate in the study. Fourteen patients agreed to participate and informed consent was obtained from all. Thirteen patients completed the assessments before and after surgery.

Testicular volume and endocrine function were evaluated just before surgery and the measurements repeated at the 6-month follow-up office visit. Testicular volume was measured using a Prader orchidometer by the same observer before and after surgery. Serum testosterone and gonadotrophin levels, and FSH and LH were measured at baseline (T0) and 30 min (T30) after an intravenous bolus of 100 μg of synthetic GnRH [10]. The response to GnRH was determined as T30 – T0.

The volumes and gonadotrophin levels before and after surgery were compared using a two-tailed Student's *t*-test for paired observations, with $P < 0.05$ taken to indicate significant differences.

RESULTS

All repairs were successful with no recurrences. The growth discrepancy before surgery was confirmed by Prader orchidometry in all patients. The left testicular volume was significantly smaller than the right (Table 1). After surgery, in all subjects both the left and right testicles grew significantly compared with their initial size. After varicocelectomy, there was no significant difference in size between the testicles. There was no change in Tanner stage in all patients.

Baseline FSH levels were higher after surgery than before (Table 1) but there were no significant differences in baseline LH and testosterone levels before and after surgery.

The response of FSH to GnRH stimulation (T30 – T0) was significantly greater after than before surgery but there were no significant differences in LH and testosterone levels after stimulation, either before or after surgery (Table 1).

DISCUSSION

Varicoceles have been described since the time of Celsius and it was recognized that varicoceles have an adverse affect on the ipsilateral testis. Despite the several hundred studies published and the thousands of young men treated for varicoceles, the exact cause or pathophysiology is unknown. Many theories have been proposed to explain the mechanisms by which varicoceles adversely affect the testis but there is no agreement on the cause.

Ponchietti *et al.* [11,12] described many of the ultrastructural changes in the testis of the peri-pubertal adolescent with a varicocele. These changes include a reduced number and atrophy of the Sertoli cells, germ cells and Leydig cells. They also reported fibrotic changes in the testicle, as well as sclerosis of the capillaries within the testis. Hienz *et al.* [13] reported that testicular histological abnormalities are present as early as 12 years old, with changes usually observed bilaterally.

Measuring testicular volume has become extremely important in evaluating the adolescent with a varicocele. A significant size discrepancy between the testicles has become the main indication for surgical treatment. Steeno *et al.* [2] were the first to observe a loss of testicular volume and/or a change in the consistency of the testis ipsilateral to the varicocele, most often the left testis, in about a third of children with Grade II varicoceles and in ≈80% of boys with Grade III varicoceles. Lyon *et al.* [14] reported a volume loss of the left testis in 77% of adolescent boys with a clearly palpable left varicocele. These investigators suggested that a varicocele might have its most damaging effect on the rapidly growing testis in adolescence. The present results agree with the findings of preoperative testicular volumetric asymmetry by these investigators, and support the view that a large adolescent varicocele can be responsible for testicular growth retardation.

Others have also reported that reversal of testicular growth failure [3–5], or compensatory growth of the ipsilateral testis occurs after varicocele ligation. Kass and Belman [3] ligated the varicoceles in 20 adolescent males with Grade II/III left-sided varicocele and loss of testicular volume. After varicocelectomy, with a follow-up of 1–6 years, there was a significant increase in volume of the left testis in 16 of 20 patients ($P < 0.001$). In many of the patients, the volume of both testes became equal. In a more recent study, Lund *et al.* [4] performed 27 laparoscopic varicocelectomies; before surgery the affected side was smaller than the contralateral testicle but afterward all volumes were equal bilaterally. Paduch and Niedzielski [5] described an improvement in left testicular volume in 88 prospectively studied male adolescents who underwent varicocelectomy, with a mean atrophy index of 12.7% at surgery and 3% 12 months later.

The present results show not only compensatory growth but also bilateral testicular growth (Table 1), with a significant increase in both the ipsilateral and contralateral testicular volumes. This occurred within 6 months of varicocele surgery, with no individual showing any change in Tanner stage. The bilateral improvement after unilateral varicocele ligation might support the experimental animal data of Saypol *et al.* [15], in which bilateral testicular temperature elevations were reported in rats and dogs after creating a left varicocele. The correction of scrotal hyperthermia with ligation of a unilateral varicocele would create a scrotal environment in which both testes would show favourable growth.

Although endocrine testing on adolescents with varicoceles has been well established, the GnRH stimulation test is not standardized. Kass *et al.* [16] used GnRH stimulation tests in 104 adolescents with palpable left varicoceles and defined an abnormal value to be 2 SD above the means obtained from matched controls. They noted an abnormal response in 30% of the patients. However, Osuna *et al.* [17] studied the gonadotrophin response in adolescents with unilateral varicoceles and concluded that it was independent of the venous dilatation, but was instead influenced by the patient's age and their pubertal stage of development.

In the present patients the baseline serum FSH levels (Table 1) were significantly higher 6 months after unilateral varicocele ligation. This supports an increase in bilateral testicular endocrine function, a change that is not unexpected when evaluated in the context of the normal physiology of pubertal progression. The bulk of the testis is composed of seminiferous tubules; as such, an increase in testicular volume should be reflected by an increase in seminiferous tubule growth if the varicocele ligation created a favourable scrotal environment for testicular growth. Lee and Migeon [18] characterized the normal changes in baseline plasma levels of FSH, LH and testosterone during puberty in boys. An increase in circulating FSH levels, followed later by an elevation of baseline testosterone levels, is always observed in the process of normal testicular growth during puberty. The rising levels of gonadotrophins that characterize male puberty is a result of increased GnRH stimulation, which continues until the response reaches a normal adult pattern [19].

That baseline FSH levels increased in boys 6 months after varicocele ligation with no changes in their Tanner stage or baseline testosterone levels is evidence for the normalization of endocrine function in growing testes. The present results show an increased FSH response (Table 1) to GnRH stimulation in the adolescent male assessed 6 months after ligation of their unilateral varicocele. This amplification in testicular response to provocative GnRH stimulation again supports the increase in the testicular endocrine function in these adolescents, who have not undergone changes in Tanner staging over the 6-month follow-up. An increased FSH response to provocative GnRH stimulation in adolescents is expected in the setting of both an increased baseline FSH level and bilateral testicular growth, i.e. during adolescent development, the increase in gonadotrophin response to the GnRH stimulation test does not represent testicular dysfunction as the hyper-response to provocative GnRH stimulation is a normal physiological finding [19]. This is in contrast to adults where an increase in baseline FSH levels and an exaggerated gonadotrophin response to GnRH stimulation indicate impaired testicular function.

In summary, the surgical ligation of unilateral Grade II-III/III varicoceles in the adolescent with ipsilateral testicular atrophy results in a reversal of ipsilateral testicular growth arrest, significant bilateral testicular growth and a physiological increase in testicular endocrine function. Whether these enhancements in growth and endocrine function will ultimately result in better fertility potential for these adolescent males requires further investigation. Also, given the observation of testicular compensatory growth associated with an increase in FSH levels, the exaggerated gonadotrophin response to the GnRH stimulation test represents a normal physiological response during adolescent development. Therefore, in adolescents, the GnRH stimulation test cannot be used to determine which adolescent would benefit from surgical repair.

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