



Antegrade sclerotherapy in adolescent varicocele patients



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Summary

Introduction

In the 1970s, Tauber described the antegrade sclerotherapy technique to treat varicoceles, and reported a 10% recurrence rate. The present study aimed to evaluate paediatric success rates and the effect of modifications to the surgical technique.

Methods

A prospective study was performed of all adolescent patients undergoing antegrade sclerotherapy surgery. Each patient had an idiopathic varicocele with spontaneous venous reflux on Doppler examination, and underwent cannulation of a pampiniform plexus vein via a scrotal incision under general anaesthetic. Aethoxysklerol® 3% (2 ml/kg) maximum 3 ml was injected into the pampiniform plexus vein under fluoroscopic monitoring. Success was assessed by clinical examination and Doppler ultrasound 3, 6 and 9 months after surgery. Data were presented as median (interquartile range). Patients were split into three groups: Group A – liquid sclerotherapy with Y connector; Group B – liquid sclerotherapy

direct to cannula; and Group C – foam sclerotherapy direct to cannula. Fisher's exact test was used to compare the success rates in each group.

Results

A total of 91 patients underwent antegrade sclerotherapy. The median age was 14.8 years (range 13.7–15.5). Eleven persistent varicoceles occurred and were diagnosed by Doppler ultrasound. The success rate of surgery was 58% in Group A, 90% in Group B and 96% in Group C. Success was significantly higher in Group B and Group C compared with Group A. No testicular atrophy occurred; two wound infections, two haematomas and one hydrocele were recorded (Table).

Conclusion

Introduction of antegrade sclerotherapy in the adolescent population resulted in a safe and cost-effective method for the management of adolescent varicocele. Several modifications to the technique have been introduced to achieve a high success rate (96%) with minimal complications.

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Table Group-wise comparison of success rates using Fisher's exact test.

Group	A	B	C
Modifications to technique	Liquid sclerotherapy + intravenous connector	Liquid sclerotherapy direct to cannula	Foam sclerotherapy direct to cannula
Number of patients	14	50	27
Age of patients (yrs)	14.6 (13.5 – 15.0)	14.7 (13.6 – 15.4)	15.2 (14.1 – 16.6)
Success (%)	58%	90%	96%

*P = 0.03 (Gp A vs B), **P = 0.01 (Gp A vs C).

Introduction

Varicocele is a common urological condition and presents in 8–16% of adolescent males [1]. The majority of adolescent patients with a varicocele remain asymptomatic. Varicoceles are associated with an increased risk of subfertility in adult males [2]. The challenge for managing children and adolescents with varicoceles is to avoid under or over treatment [1].

Testicular asymmetry (>20%) is seen in approximately 10% of teenagers with a varicocele [2]. Patients with larger volume differentials have more impaired semen parameters [3]. “Catch-up growth” following varicocele surgery is seen in this group [4,5]. Other indications for varicocele surgery include symptoms of pain or heaviness, which is usually described as a dull ache around the scrotum that is worsened after long periods of standing [6,7]. Routine sperm analysis is being increasingly offered to physically mature adolescents and young adults [3,8], with varicocele surgery being offered when subfertility is detected [1].

Many techniques have been described for the management of varicocele, including: open inguinal [9], high retroperitoneal [10], laparoscopic (with or without artery and lymphatic sparing) [11] and sclerotherapy [12]. There is great variability in practice regarding choice of surgical technique, and with each technique comes differing complication rates [13,14]. Tauber described the antegrade sclerotherapy (AS) technique in the 1970s to treat varicoceles, and reported a 10% recurrence rate [12]. Within the paediatric population, a 10% recurrence rate and 14% risk of hydrocele was reported [15].

The present study aimed to: further evaluate paediatric outcomes following AS in the management of varicocele; assess complications; and demonstrate the effect of modifying the surgical technique on success.

Methods

A prospective study was performed of all adolescent patients presenting to the Varicocele Clinic with idiopathic left sided varicocele. All varicoceles that were included were clinically evident: Grade II or Grade III according to the Dubin and Amelar clinical classification [16]. Every patient underwent testicular venous Doppler and only those with spontaneous venous reflux on Doppler ultrasound were included [17]. Paediatric testicular volume was predicted using the formula: volume in ml = $0.52 \times L \times W \times H$, with the definition of asymmetry being a difference in volume of >20% [18,19]. Patients included underwent surgery between 2012 and 2016. The indications for surgery included: pain; testicular asymmetry >20%; subfertility on sperm analysis at 17 years of age (sperm concentration <15 millions/ml and/or forward motility <32%); and randomisation to early surgery as part of a randomised controlled study of early surgery versus conservative management [20].

The procedure was performed as follows: an upper scrotal incision was made over the spermatic cord. The internal and external spermatic fasciae were opened. The fat was identified within the cord, which accurately located the pampiniform plexus veins. One vein was mobilised and isolated proximally and distally with ties. A yellow 24

French cannula with wings was inserted. The ties on the vein were then tied and the cannula was secured. The cannula was seen to bleed back and then flushed with normal saline. An X-ray screening arm was brought into position. The patients were positioned on a spinal extension to the operating table so the kidney could be imaged easily. Omnipaque 300 mg/ml was injected to confirm the venous anatomy. Group A patients had a Y-shaped intravenous connector attached to the cannula and liquid Aethoxysklerol® 3% (2 ml/kg) with a 1 ml air block was injected, as described by Tauber [12]. Group B patients had a syringe with the liquid Aethoxysklerol® 3% (2 ml/kg) and 1 ml air block directly connected to the cannula for injection. Group C had foam sclerotherapy with the syringe directly connected to the cannula for injection. All patients were positioned 30° head up with a short Valsalva manoeuvre at the time of sclerosant injection. The foam was prepared immediately before injection. A microfoam was prepared from Aethoxysklerol® 3% (2 ml/kg), maximum 3 ml was mixed with 7 ml of air, using a three-way connector, 20 times before injection. The foam was injected and seen to displace the omipaque on the fluoroscopic images, with the injection being stopped before the foam reached the renal vein. As the cannula was carefully removed the vein was re-tied to prevent any leak of sclerosant. The spermatic fascia was closed, local anaesthetic injected and the wound closed with vicryl and dermabond.

Success was defined as absence of varicocele and resolution of venous reflux, as assessed by clinical examination and Doppler ultrasound 3, 6 and 9 months after surgery. Postoperative complications were also recorded. Data were presented as median (interquartile range). Fisher’s exact test was used to compare the success rates in each group.

Results

A total of 213 adolescent patients with varicoceles were seen during the study period. Of these, 100 were managed conservatively (those without spontaneous venous reflux on Doppler examination or those who did not meet the criteria for surgery), 22 underwent laparoscopic selective vein ligations, and 91 underwent antegrade sclerotherapy (AS).

The median age at the time of AS was 14.8 years (range 13.7–15.5). Thirteen patients had palpable varicoceles (Grade 2), 78 had visible varicoceles (Grade 3) [16]. A total of 18 patients were pre-pubertal, 33 were peri-pubertal, and 40 were post-pubertal. The indications for surgery included: testicular asymmetry (28 patients); pain (38 patients); subfertility on sperm analysis (three patients); and enrolment into a randomised controlled study of early surgery versus conservative management (22 patients).

The median postoperative follow-up was 1.8 years (range 1–3.5). Eleven persistent varicoceles occurred and all underwent successful repeat sclerotherapy. The success rate of surgery was 58% in Group A, 90% in Group B and 96% in Group C. Success was significantly higher in Group B and Group C compared with Group A. One postoperative hydrocele occurred in a patient who required redo-sclerotherapy and this needed surgical treatment with a Jaboulay procedure. No postoperative testicular atrophy

occurred during the study. Two wound infections and two haematomas were recorded. Testicular asymmetry improved in all 28 patients who had an initial median volume difference of 33.9% (range 26–40.8) and a final volume difference of 10% (range 0–17).

All 38 patients treated for pain had resolution of pain symptoms following surgery. One of the three patients treated for sub-fertility had, to date, performed a repeat sperm test postoperatively. His sperm parameters were all improved: sperm concentration from <2 million/ml to 4 million/ml, forward motility from 16% to 32%, morphology from too low to count to 4%. The mean dose of radiation used during the venography and sclerotherapy procedures was 0.67 (± 0.55) mGy.

Discussion

Varicocele remains a leading reversible cause of infertility in men [21]. The mechanisms explaining how a varicocele interferes with sperm production are not clearly understood, and theories include: venous hyperaemia, increased testicular temperature and testicular hypoxia [15]. Pathological changes occur in Leydig and Sertoli cells, many of which improve following varicocele repair [22]. The effect of varicocele surgery in a sub-fertile adult population is weakly positive, with the number needed to treat being 17 to achieve one additional pregnancy [23].

In this series of adolescent patients, 26 of the 28 patients who underwent AS for testicular asymmetry had full resolution of the asymmetry to <20% (catch-up growth) after surgery, although there was improvement in all 28 patients. The median testicular volume differential improved from 33.9% to 10%. This supports the findings of a meta-analysis reporting that catch-up growth occurred in 76% of patients following varicocele surgery [24]. All 38 patients in the present study had resolution of pain symptoms. Three patients elected to undergo surgery, after lengthy discussion, because of subfertility, all were Tanner stage V of pubertal development. Two of these patients had sperm concentrations <2 million/ml, the third had a sperm concentration of 7 million/ml and forward motility of 19%. One patient has subsequently undergone repeat sperm analysis post sclerotherapy, which showed improvement in all parameters. The other two patients are still waiting to repeat their sperm analyses.

To understanding the pros and cons of the different approaches to varicocele surgery, an appreciation of the complexity of the venous anatomy in varicoceles is essential. The present study reported that the incidence of parallel duplications is 74%, which is higher than previously reported in the literature. Lumbar and renal collaterals (Fig. 1a) comprise 3% and 5% of patients, respectively, and trans-scrotal collateral veins are rarely described [25]. Tauber described the complex anatomy around the spermatic cord with pampiniform plexus veins surrounding the testicular artery, cremasteric veins and vassal vessels. When selecting an approach for varicocele surgery, the surgeon needs to appreciate the limitations and risks of each technique. The advantages of mass ligation of internal testicular artery, lymphatic and venous vessels in terms of success may be outweighed by the chances of producing

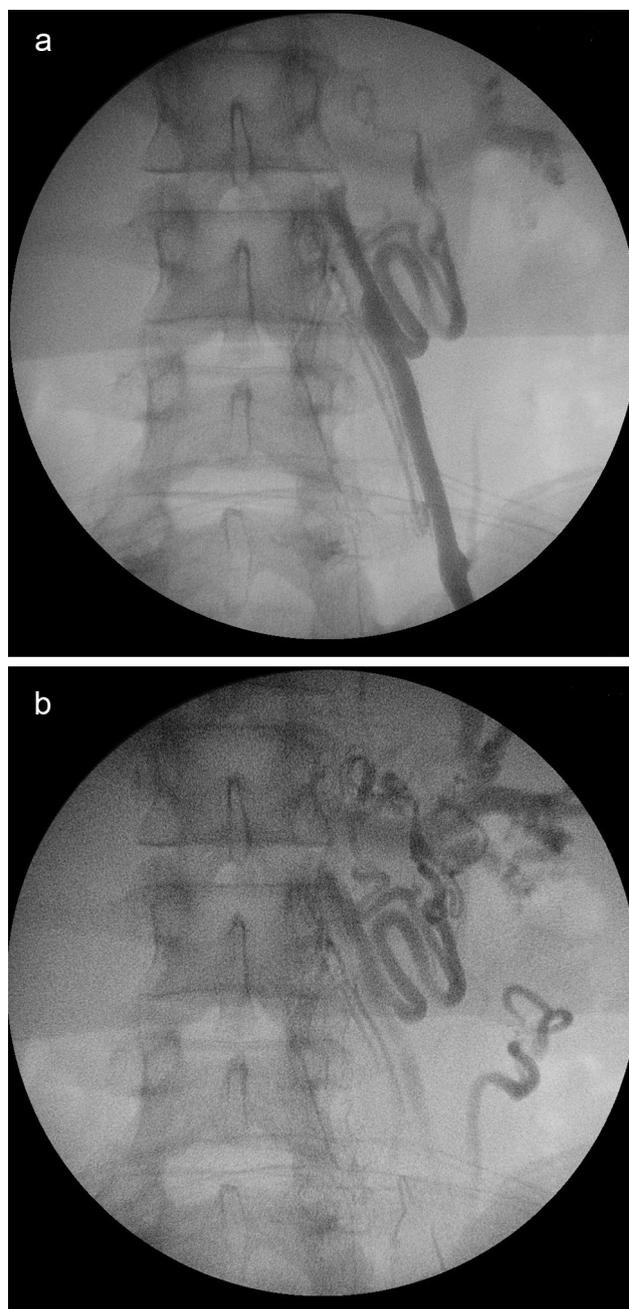


Figure 1 a. Antegrade venography demonstrates parallel duplications and renal collaterals of the internal testicular vein. b. Foam sclerotherapy is seen to displace the contrast within the main veins and collaterals.

lymphatic congestion around the testis (hydrocele) and the unforeseen risks of testicular loss if the men subsequently undergo a vasectomy. Peri-operative antegrade venography enabled the present study to appreciate the diversity of venous anatomy, aid treatment by either laparoscopic selective vein ligation [22] or by varying the amount of sclerosant required to fill the veins in antegrade foam sclerotherapy (Fig. 1b and Fig. 2b). The mean dosage of radiation used for antegrade venography was 0.67 mGy (± 0.55), which was much lower than that used in another commonly performed paediatric urological examination: video-urodynamics, 2.18 mGy (± 2.0) [26]. Fig. 2a.

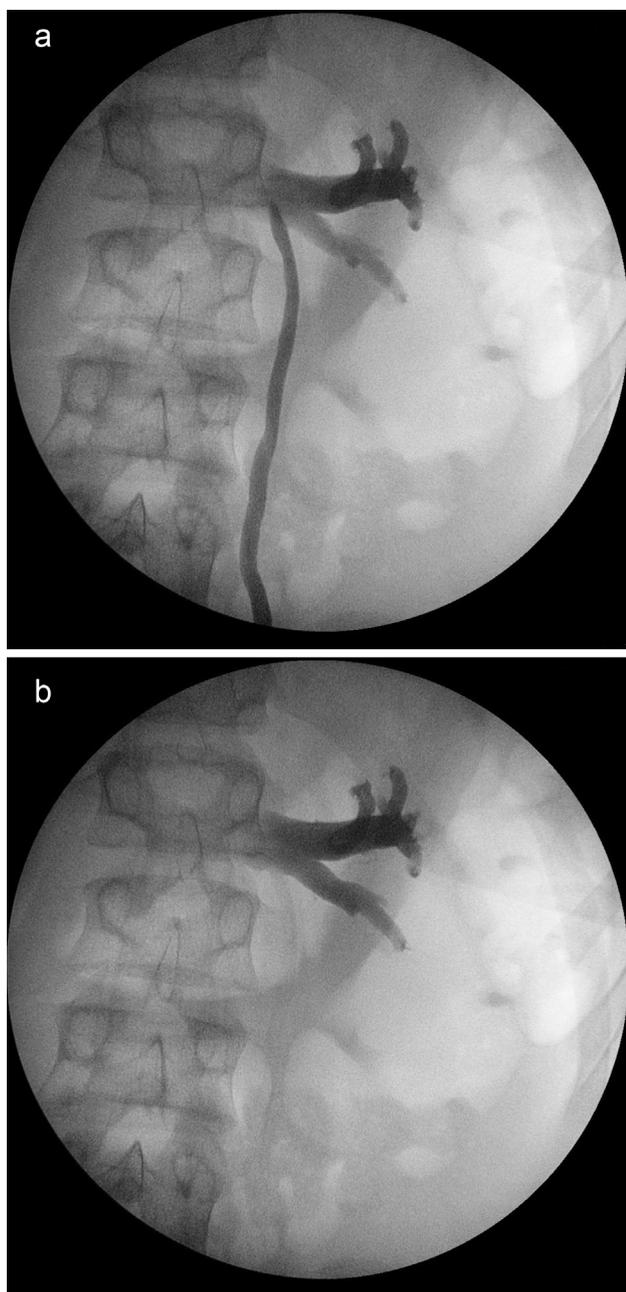


Figure 2 a. Antegrade venography demonstrates a single internal testicular vein. b. Foam sclerotherapy is seen to fill the internal testicular vein and displace the contrast up to the renal vein.

Antegrade sclerotherapy was initially described in the 1970s. It has shown to have the highest economic effectiveness of all forms of surgical management for varicocele, costing £36.64 per case when performed under local anaesthetic [27], and has a low complication rate in adults [13,23]. Paediatric studies have reported persistent varicocele rates of 2% [28], 4.5% [29], 7% [30] and 10% [15]. The variations in recurrence rates may be due to the differences in the clinical grades of varicoceles treated in each study. Those studies using screening to identify patients have a higher proportion of small varicoceles (Grades 1 and 2), which may be less prone to persistence [12]. Zaupa

reported that less than half of their patients had Grade-3 varicoceles [30] compared to 86% in the present series.

Adult studies have reported complications of AS, including: scrotal haematoma in 2.2% of patients, testicular atrophy at a rate of 0.6%, haematoma and wound infections in 3% [30]. In the present series, two patients (2.2%) experienced a scrotal haematoma and there were no cases of testicular atrophy.

Postoperative hydrocele formation has its highest complication rate following mass ligation procedures (open or laparoscopic Palomo) with rates quoted between 3 and 23% [31]. Laparoscopic surgery remains the most widely used surgical method for the management of adolescent varicocele [32]. Techniques utilising methylene blue either to stain the lymphatic channels or to inject into the veins effectively reduce the rate of hydrocele formation by 0–5% [33]. These techniques are more time consuming and costly compared with AS. Antegrade sclerotherapy is naturally lymphatic sparing, and so results in low rates of post-operative hydroceles, which was confirmed in the present study that reported a 1% hydrocele rate.

The present study reported 11 recurrences following antegrade sclerotherapy, which were confirmed by Doppler ultrasound. All recurrences were treated successfully with repeat AS. Group A had the highest recurrence rate (58%); this was thought to be due to the use of a Y-shaped intra-venous connector between the cannula and syringe. When injecting such a small volume of sclerosant (maximum 3 ml) a significant portion remained within the connector, thus reducing its efficacy. After the first 14 procedures (Group A), the syringe was connected directly to the cannula (Groups B and C). This ensured that all the sclerosant was delivered into the vein, ensuring maximum efficacy. The combined success rate after this adjustment to the technique was 93% in Groups B and C, which was similar to the 90% success rate reported by Tauber [12].

A second modification was introduced (Group C) with the Aethoxysklerol[®] being prepared as a microfoam instead of a liquid. The preparation technique described by the manufacturer involves mixing the Aethoxysklerol[®] with 7 ml of air and making it into a foam using a micro-foam adaptor to produce 10 ml of a stable, homogenous and viscous microfoam with fine bubbles [34]. The micro-foam fills the internal testicular vein(s), displaces the omnipaque, and allows precise radiological control over the foam volume required (Figs. 1b and 2b). The viscosity of the microfoam reduces fast “run-off” into the renal vein and systemic circulation; the white foam can be seen remaining in the pampiniform plexus veins during wound closure. The microfoam increases the surface area and contact time between the sclerosant and vessel wall. This technique has been described for varicose vein treatment, with improved efficacy and no safety concerns [35]. The median volume of the microfoam injected in the present study was 6 ml (range 5.5–8). Group C had a higher success rate (96%) than Group B (90%); however, with the smaller numbers in Group C, to date, this did not achieve significance. The authors suggest that a relative contraindication to the microfoam preparation of Aethoxysklerol[®] may be pre-pubertal patients with very small pampiniform plexus veins. The high viscosity of the microfoam can occlude very small pampiniform plexus veins before sufficient sclerosant has flowed

into the main internal testicular veins. In these patients, the sclerosant may be better injected "neat" with the 1 ml air-block technique, as described by Tauber [12] and as per Group B patients.

Overall, the complication rates for this procedure compared favourably to those reported in the literature. This experience of AS in the adolescent population has demonstrated an initial steep learning curve to optimise the technique by direct injection of the sclerosant into the cannula without the need for an intravenous connector. Preparation of the sclerosant as a micro-foam has made the technique much more controlled, with reductions in the amount of sclerosant injected and potential gains in success rates.

Conclusion

Introduction of antegrade sclerotherapy in the adolescent population has resulted in a safe and cost-effective method for the management of adolescent varicocele. Several modifications to the technique have been introduced to achieve a high success rate (96%) with minimal complications.

Conflict of interest statement

None.

Funding source

No external funding was received. The authors are both National Health Service Employees.

Ethical approval

NHS trust audit approval was obtained. Ethical approval was not required, except for the 21 patients co-enrolled in the randomised controlled study of early varicocele surgery versus conservative management [20] REC 09/H1013/15.

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