Intravenous methylene blue venography during laparoscopic paediatric varicocelectomy

David J.B. Keene *, Raimondo M. Cervellione

Department of Paediatric Urology, Royal Manchester Children's Hospital, Manchester, United Kingdom

ARTICLE INFO

Received 6 November 2013
Accepted 10 November 2013

Key words:
Varicocele
Adolescence
Methylene blue
Lymphography

ABSTRACT

Introduction: One of the challenges of varicocele surgery is to prevent hydrocele formation while still ensuring success. Methylene blue has been used to identify and preserve lymphatic vessels, and venography has been a standard component of sclerotherapy and percutaneous retrograde techniques. The authors have combined both approaches during laparoscopic varicocelectomy and report their experience.

Methods: A prospective study was performed of adolescents with idiopathic varicocele and spontaneous venous reflux on Doppler ultrasound. A pampiniform plexus vein was cannulated via scrotal incision before creating the pneumoperitoneum. A mixture of methylene blue and Omnipaque™ was injected into the pampiniform plexus with fluoroscopic screening. Laparoscopic selective vein ligation was then performed using 5 mm endoscopic clips or a bipolar vessel sealing device such as Plasmakinetic™ or Ligasure™. Venography was repeated to confirm complete ligation of the internal testicular veins. Patients were followed-up at 3, 6, and 9 months post-surgery with clinical examination and Doppler ultrasound. Data are presented as median (interquartile range).

Results: Twenty-four patients underwent laparoscopic selective vein ligation with venography and methylene blue injection. The median age was 14.7 (14.6–15.7) years. The recurrence rate was 12%. No patients developed a hydrocele. The length of surgery was 120 (100–126) minutes.

Conclusion: Intra-operative intra-venous methylene blue injection and venography helps to identify venous duplications of the internal testicular veins and enhances the success rate of laparoscopic selective vein ligation. This approach prevents hydrocele formation but has a 12% recurrence rate, which appears to be higher than some techniques described in the literature.

© 2014 Elsevier Inc. All rights reserved.

Scrotal varicoceles are relatively common in adolescent boys and there have been many techniques described in the literature to treat them [1]. The aim of such surgery is to achieve complete ligation of incompetent veins, preservation of fertility, resolution of pain, restoration of symmetrical testicular volumes while limiting damage to surrounding lymphatic and arterial structures. The anatomy of testicular venous drainage is complicated [2] and recurrence caused by a persistence of collateral veins can be problematic [3]. There is an on-going debate about the merits of lymphatic and artery sparing surgery in reducing hydrocele formation or recurrence [4].

Venography is a standard component of sclerotherapy [5] and percutaneous retrograde techniques [6]. In the majority of recurrences a residual incompetent internal testicular vein is demonstrated by venography [8]. In our practice antegrade venography of the pampiniform plexus identifies a higher incidence (>80%) of anatomical variations compared to 26–65% using retrograde techniques [7,9]. Pre-operative venography has been described to identify the optimum level for varicocelectomy [10]. Intra-operative venography can identify collateral veins [3] however its reliability has been questioned [11].

Methylene blue can identify and preserve lymphatic vessels which may reduce the incidence of hydrocele formation [12–14]. However intra-parenchymal injection can result in testicular loss [13] and injection around the tunica vaginalis may not reliably stain the lymphatic vessels. Methylene blue is only licenced for use intravenously and is excreted in the urine. It has been used intra-operatively during varicocelectomy to identify the veins during an open inguinal approach [15]. To date it has not been described in combination with laparoscopic selective vein ligation. Our aim was to investigate whether combining intravenous contrast with methylene blue could enhance the ability to detect the small residual collateral veins and therefore reduce recurrence and limit complications.

1. Methods

A prospective study was performed of adolescent patients with an idiopathic varicocele and spontaneous venous reflux on Doppler ultrasound. All patients included had a palpable (grade II) or visible (grade III) varicocele on clinical examination using the Dubin and Amelar clinical classification [16]. Doppler ultrasound was performed...
with 5–10 MHz probes with the patient stood upright and spontaneous breathing. The Hirsh classification was used to classify Doppler grade [17]. Puberty was classified as pre-pubertal (absent pubic hair with infantile genitalia) and pubertal (complete development of pubic hair and genitalia).

Indications for surgery included pain [18], testicular volume asymmetry [19,20] and randomisation to early surgery as part of a clinical trial of asymptomatic patients currently running in our hospital REC09/H1013/15 [21]. All asymptomatic patients were part of this trial. The ethical approval obtained for the study was based on using the surgical technique described in this paper. Testicular asymmetry was defined as a difference in testicular volume >20% as measured by testicular ultrasound [20].

**Procedure**

A pampiniform plexus vein was cannulated via a scrotal incision using the method described by Tauber [22]. A mixture of 4 ml 1% methylene blue and 40 ml 300 mg/ml Omnipaque™ (iohexol) was injected into the pampiniform plexus vein and position confirmed with fluoroscopic screening (Fig. 1). Pneumoperitoneum was created and laparoscopic selective vein ligation was then performed (Fig. 2A, B, C). The veins were ligated with 5 mm endoscopic clips or using a bipolar vessel sealing device such as Plasmakinetic™ or Ligasure™. Blue venography was repeated to confirm complete ligation of the internal testicular veins (Fig. 3) with careful inspection both radiological screening and direct laparoscopic visualisation to identify any residual veins.

Patients were seen in clinic at 3, 6 and 12 months post-surgery with clinical examination and Doppler ultrasound. Data are presented as median (interquartile range).

---

**Fig. 1.** Antegrade venography to confirm parallel duplication of the internal testicular vein.

**Fig. 2.** A. Internal testicular vein stained with methylene blue. B. Selective dissection of internal testicular vein. C. Ablation and division of internal testicular vein with bipolar vessel sealing device.

**Fig. 3.** Venogram post-ligation of internal testicular vein.
2. Results

Twenty-four patients were included in the study. The median age for varicocelectomy was 14.7 (14.6–15.7) years. On clinical examination 20 patients had a visible varicocele and 4 patients had a palpable varicocele [16]. On Doppler examination, 21 patients had continuous venous reflux (Hirsh grade 3) and 3 patients had venous reflux which varied with respiration (Hirsh grade 2) [17].

The indications for surgery were pain (n = 7) and testicular asymmetry (n = 11) in the symptomatic group; the other 6 being part of the study of asymptomatic patients randomised to early surgery. Median duration of surgery was 120 (100–126) minutes.

Median follow-up was 18.4 (12–21) months. Three patients had varicocele recurrence diagnosed within 6 months of surgery (defined as persistent spontaneous venous reflux on Doppler ultrasound). There were no postoperative hydroceles, no testicular atrophy or testicular congestion.

Nine of the 11 patients treated for testicular asymmetry demonstrated catch-up growth with symmetrical testicular volumes at follow-up. The median difference in testicular volumes for these 11 patients was 34% pre-surgery and 15% post-surgery. All 7 patients treated for pain reported resolution of their symptoms following surgery.

3. Discussion

Selection of surgical technique for an adolescent varicocele repair remains a hotly debated topic and remains a fine balance between success and complications.

Testicular volume asymmetry has been demonstrated to show a correlation with impaired semen characteristics at 18 years of age and also in early adolescence [19,20]. Varicocele repair can lead to the resolution of testicular asymmetry or “catch-up growth” in 66–93% of adolescent patients [23]. In this study, > 80% of our patients showed “catch-up growth”. It is important that the complication testicular congestion is distinguished from such “catch-up growth”. The key features of testicular congestion are rapid change in testicular volume with an associated hydrocele. No patient in our study developed a hydrocele or testicular congestion.

Adolescent data on the high retroperitoneal ligation (Palomo procedure) show a low recurrence rate of 0–1.9%; however, the incidence of hydrocele may be as high as 23% [12,25,26] as they may improve semen parameters [27].

An inguinal approach to surgery encounters many more dilated veins [1,28] and puts the testis at higher risk of atrophy secondary to inadvertent ligation of the testicular artery. Combining microscopic optical magnification and intra-operative Doppler ultrasound to try and preserve the artery with intra-operative sclerotherapy has reduced recurrence rates to 2.7% and the hydrocele rate to 2.7% in one study [29].

Retrograde embolization has reported recurrence rates between 7% and 40% [6,30]. Recurrent varicoceles are a consequence of unidentified collateral veins [9,29]. Post-mortem studies show that at the lumbar level there are 1–5 left testicular veins and all can have incompetent valves [28]. The commonest type of vascular malformation is a type 3 (Bahren classification) or parallel duplication (Murray classification); however, renal and lumbar malformations also exist [34].

Hydrocele formation is a frequent problem following mass ligation techniques (open or laparoscopic Palomo) with rates varying between 3% and 23% [31]. Dye-assisted lymphatic sparing surgery has reduced the hydrocele rate to 0–5% [12–14,32,33]. These techniques however fail to stain the lymphatic vessels in about 10% of patients [33].

We used a Doppler ultrasound definition of persistent spontaneous venous reflux to identify varicocele recurrence which is more sensitive than relying on clinical examination alone. The 3 recurrences occurred within 6 months of surgery and all were successfully treated by antegrade sclerotherapy of the residual internal testicular vein(s). Antegrade sclerotherapy appears to be the procedure of choice for a recurrent varicocele with a high success rate 97% and minimal complications [8]. Primary antegrade sclerotherapy in high grade varicoceles has a somewhat lower success rate of 80–90% [22,25,35] which may be the result of the higher venous flow diluting the effect of the sclerosant.

The recurrence rate for the technique described in this study (12%) is higher than we might expect considering the significant efforts used to detect collateral veins. We are now using a 3 mm Plasmakinetic™ device to seal the vessels which allows injection of the contrast mixture with more sustained pressure. The recurrent varicoceles encountered early in this study may have been prevented with more sustained pressure antegrade contrast injection. With more experience we anticipate that the recurrence rates described in this study will decrease further. It may be however that the only way of achieving a low recurrence rate and hydrocele incidence is to combine laparoscopic selective ligation of the main internal testicular vein with sclerotherapy of the smaller Collins. This combination approach has been described in open inguinal surgery with good results [29].

Methylene blue has a wide variety of medical applications and the therapeutic dose is < 2 mg/kg [36]. This led the authors to use 4 ml of 1% methylene blue mixed with Omnipaque™ in our adolescent population. Omnipaque™ 300 mg/ml was chosen because the higher concentration allows better visualisation of small collaterals. The recommended dose of 300 mg/ml as a single injection in children is up to 1.75 ml/kg [37]. Hence no patient required more than the 40 ml per procedure.

The authors describe a safe, new technique of laparoscopic selective vein ligation with blue venography. However it has several technical challenges including cannulation of a pampiniform plexus vein, preparation of the solution for injection, radiographic screening, and laparoscopic dissection. This has led to a slow learning curve with most procedures lasting 2 hours. However, we believe that zero rate of hydrocele or testicular atrophy and the excellent demonstration of venographic anatomy justifies our continued use of this surgical technique. Further efforts are needed to improve the relatively high recurrence rate associated with this technique.

References

Discussion

Unknown discussant: Two hours for a varicocele procedure?

Response: Mr Keene: There are several components of the technique which are challenging. From the very beginning, we went to Germany to bring the scrotal component from Germany, and to use that for both antegrade sclerotherapy and for this laparoscopic technique which we present. We have been training surgeons in it as well, so it is not just one surgeon doing it but different trainees doing different components. I am sure that other centres will attest that there can be problems with the laparoscopic equipment, and if you have worked in Manchester there have been quite a few problems with that! The actual technique is logically targeting the veins, and this makes more sense than trying to preserve the lymphatics, preserve the artery, if we stain the veins and go straight for them. That is what we are trying to achieve.

Question: Have you had any complications with methylene blue, such as anaphylaxis? Or are there any cardio-vascular concerns following methylene blue injection?

Response: Mr. Keene: We titrate the dose so obviously the weight of the patient is important, so we have chosen 4 ml per patient. The dose of methylene blue is 1.75 ml per kilo and the dose of Omnipaque is 2 ml per kilo. We haven’t needed more than 40 ml which is the little bottles of Omnipaque. We haven’t had reactions to either of the solutions. Obviously part of the length of the procedure is having 4 solutions: local anaesthetic, saline, methylene blue and Omnipaque, and making sure that you are injecting the correct solution. We have not had any serious complications at all. In fact it is the recurrences that I have focussed on.

Question: Wouldn’t you suggest that this technique only be used in recurrence?

Response: Mr Keene: We are using this technique on the very big varicocele, the ones with the highest flow, on the ones where you would be worried about sclerotherapy where it won’t cause the concentration effect on these huge veins. I think this is a perfect technique for that. For recurrence, our experience with antegrade sclerotherapy shows that it is a very good technique for the recurrent varicocele and we would advocate that as the best method of treating recurrent varicocele.

Question: Have you had problems taking referrals from other centres with funding in England?

Response: Mr Keene: We are starting to get referrals where patients are looking at our website and are coming straight to us. We do want to get GPs to refer, particularly with recurrent varicoceles. We would like centres to think about referrals to us for the antegrade sclerotherapy – primary surgery can be performed by radiologists or by whatever centre it is you are involved in. We are trying to reduce the hydrocele formation which is associated with the standard technique which is mass ligation obviously. We have had some patients who have had to go privately to have the techniques as described on our web site. We have had funding issues, but these are usually solved by writing to GPs or other funding bodies and they are happy to refer to either ourselves or the local urology services.