Lymphatic preservation using methylene blue dye during laparoscopic varicocelectomy: early results

Danny M. Rabah, MD, Ayman A. Adwan, MD, Mohamed A. Seida, MD King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia

RABAH DM, ADWAN AA, SEIDA MA. Lymphatic preservation using methylene blue dye during laparoscopic varicocelectomy: early results. The Canadian Journal of Urology. 2009;16(5):4826-4830.

Background and objectives: Hydrocele caused by the division of lymphatic vessels during varicocelectomy is a common complication. Preservation of these lymphatics is the aim of many studies. We evaluated patient outcomes after laparoscopic varicocelectomy that involved intratunical methylene blue dye injection just prior to the procedure.

Materials and methods: This prospective study included all adult patients (over age 14 years) with clinically palpable varicocele who presented to our clinic between December 2005 and July 2007. Prior to laparoscopic surgery, methylene blue dye was injected in the intratunical space between the tunica albuginea and the tunica vaginalis. Laparoscopic intraperitoneal varicocele ligation was performed. Patients were assessed for early postoperative complications and consumption of analgesia. They were reassessed at 1 and 6 months

Introduction

Varicocele is the dilatation of the testicular veins and pampiniform plexus of the testis within the scrotum. It is a relatively uncommon condition in

Accepted for publication April 2009

Address correspondence to Dr. Danny M Rabah, Chief of Urology, King Khalid University, Hospital, King Saud University, PO Box 55068 Riyadh 11534, Saudi Arabia postoperatively by clinical and radiological evaluations to detect hydrocele formation, recurrent varicocele, and testicular pain or atrophy.

Results: Twenty-three consecutive patients with 40 clinically palpable varicoceles were evaluated. The patients had a mean age of 28.4 years. The mean operating time was 37 minutes, (range, 25 to 50 minutes). The patients did not have any intraoperative or early postoperative complications, including any complications related to methylene blue dye injection. Follow up examinations at 6 months revealed hydrocele formation in 2 of the 40 patients (2.5%).

Conclusion: This preliminary study suggests that intratunical injection of methylene blue dye just prior to laparoscopic ligation of varicocele can aid in the identification and sparing of lymphatic vessels, although it did not preserve lymphatic vessels in all patients in this study. It appears to be a safe technique that does not prolong operating time.

Key Words: adult laparoscopic varicocelectomy, lymph sparing, hydrocele

young pediatric patients, but prevalence increases to 13.7% to 16.2% by age 10 to 15 years.¹ Varicocele is the main cause of correctable male infertility. Varicocelectomy is indicated in cases of infertility, as well as when testicular volume is decreased--such as in adolescence --and when varicocele is associated with pain.² The ideal method to treat varicocele remains controversial. Several methods have been used, including open surgery (using the Palomo technique or the Ivanissevich technique),³ laparoscopy, and percutaneous transvenous procedures. The Palomo technique, first described in 1949, involves en masse transection of the testicular vessels in the retroperitoneum above the internal inguinal ring.⁴ The varicocele recurrence rate for the Palomo procedure has been reported to range from 0% to 16% with postoperative hydrocele rates ranging from 7% to 24% in the adolescent population.⁵ In comparison, using microscopic assistance with an inguinal approach, varicocele recurrence rates and hydrocele rates reported in the existing literature range from 0% to 2%, and 1% to 4%, respectively.^{6.7} However, in a study of adult patients, laparoscopic varicocele ligation has been reported to result in a 5% to 8% risk of hydrocele formation compared to 0% in adult patients who underwent the subinguinal microsurgical varicocelectomy.3

Donovan and Winfield first described a minimally invasive surgical technique using laparoscopy for the treatment of varicoceles in an adolescent in 1992.8 The site of varix ligation in this technique is similar to that of the open Palomo approach. Postoperative hydrocele using a laparoscopic approach have been observed in up to 28% of cases.9,10 Analysis of the protein concentration of hydrocele fluid has indicated that postvaricocelectomy hydrocele is mainly attributable to lymphatic obstruction.¹¹ At least half of postvaricocelectomy hydrocele grow to a size large enough to warrant surgical excision secondary to the associated discomfort and size of the hydrocele. The development of a large hydrocele that surrounds the testis with an abnormal insulating layer can impair the efficiency of the counter-current heat exchange mechanism, thereby counteracting some of the benefits of varicocelectomy.¹² Many previous studies have looked at ways to preserve the lymphatics during varicocelectomy with the goal of decreasing the incidence of postvaricocelectomy hydrocele. The current study aimed to evaluate the efficacy of lymph sparing laparoscopic varicocelectomy using methylene blue dye to identify the lymphatic channels, and to evaluate the effect of this procedure on the rate of postoperative hydrocele formation.

Materials and methods

This prospective study included all consecutive adult patients (older than 14 years) who had newly diagnosed unilateral or bilateral grade II to grade III varicocele with an indication for surgical repair, who were seen in our center during December 2005 to July 2007. All varicoceles were graded based on findings from preoperative physical examinations--performed with and without Valsalva maneuver in patients standing in a warm room--and scrotal ultrasound. The 23 study patients presented with scrotal pain (20 patients) or primary infertility (3 patients).

After providing informed consent, all patients underwent laparoscopic varicocelectomy with intratunical injection of methylene blue. All procedures were performed by the same surgeon, and the surgery was performed under general anesthesia. Prior to surgery, each patient underwent sterilization of the abdomen and external genitalia from a supine position and a Foley's catheter was inserted. All patients had an intratunical injection of 0.25 mg (5 ml) of methylene blue dye, given in one injection between the tunica albuginea and the tunica vaginalis. The needle was passed into the substance of the testis without injection and then gently removed until it was felt to be just out of the tunica albuginea but still within the intratunical space. The methylene blue dye was then injected. The testicles were not violated by injecting methylene blue dye into them.

Three laparoscopic ports (10 mm, 5 mm, and 5 mm) were used. Adequate pneumoperitoneum was established followed by insertion of the laparoscopic camera at the umbilicus and the other two ports at the midaxillary line at a point half way between the umbilicus and the anterior superior iliac spine. The internal spermatic vessels were identified, and then the peritoneum overlying the vessels was opened 1 cm proximal to the internal ring, and the gonadal veins were then carefully separated from easily visible blue lymphatic trunks. The separation was easily accomplished with blunt dissection. The vein was then clipped and divided, sparing the lymphatics. The surgery is shown in Figures 1 and 2.

All patients remained in the hospital for 1 day after surgery to observe any immediate postoperative complications and to receive analgesia. Follow up at 1 month and 6 months after surgery included clinical and radiological evaluations. The primary study endpoint was hydrocele formation, and the secondary study endpoint was recurrent varicocele.

Results

The study included 23 consecutive patients with 40 clinically palpable varicoceles. Demographic and surgical data are shown in Table 1. The patients had a mean age of 28.4 years (range, 14 to 56 years). Of the 40 varicoceles, 27 were grade II and 13 were grade III. All patients underwent laparoscopic varicocele ligation with intratunical methylene blue injection. The mean operating time (including methylene blue dye injection) was 37 minutes (range, 25 to 50 minutes). The mean



Figure 1 and 2. Laparoscopic varicocelectomy with intratunical injection of methylene blue.

laparoscopic surgery time was 22 minutes (range, 15 to 30 minutes). There were no intraoperative or early postoperative complications. Methylene blue dye injection did not result in any local or systemic reactions. All patients received nonsteroidal anti-inflammatory drugs for postoperative pain control, and two patients who needed further analgesia received morphine. At the first follow up visit 1 month after surgery, two patients had hydrocele and one patient had persistent varicocele. At the second follow up visit at 6 months after surgery, the same complications, with no new ones, were documented. These complications were confirmed by clinical and ultrasound examinations.

Discussion

There is currently no gold standard treatment for varicocele. Different techniques for varicocelectomy have been evaluated for the two most common late complications: hydrocele formation and varicocele recurrence. The reported incidence of postvaricocelectomy hydrocele varies widely. Some studies have reported a range of 3.1% to 13%, with higher ligation tending to cause more hydrocele.¹³ The pathogenesis of postoperative hydrocele after Palomo varicocelectomy results from lymphatic obstruction, as documented by Szabo and Kessler.¹¹ Another recent study demonstrated a decrease

TABLE 1. Demographic and surgical data in patients who underwent varicocelectomy

| No of patients No of varioceles | 23 patients 40 varicoceles |
|---|--|
| Age, mean (range), years | 28.4 (14-56) |
| Indications for varicocelectomy | pain (20 patients), infertility (3 patients) |
| Grade of varicocele (No. of varioceles) | grade II (27), grade III (13) |
| Operating time, mean (range), minutes | 37 (25 -50) |
| Laparoscopic time, mean (range), minutes | 22 (15-30) |
| Intraoperative complications | none |
| Conversion to open surgery | none |
| Systemic and local reaction | none |
| Hospital stay, days | 1 |
| Findings at 1 month follow up, No. of patients (%) | hydrocele, 2 patients (5%); persistent varicocele, 1 patient (2.5%) |
| Findings at 6 month follow up, No. of patients (%) | hydrocele, 2 patients (5%); persistent varicocele, 1 patient (2.5%) |

in testicular function in patients with postvaricocelectomy testicular edema. This study documented the importance of lymphatic drainage preservation to ensure a better andrological outcome.¹⁴

Certain procedures have been performed to decrease the incidence of post varicocelectomy lymphatic obstruction. Microsurgical varicocele ligation is a procedure in which the arterial and lymphatic supplies to the testis are meticulously dissected, to eliminate the risk of lymphatic obstruction and varicocele recurrence or persistence.¹⁵ Hydrodissection of the spermatic cord is a new method to delineate the lymphatics.¹⁶ This method involves injection of a few milliliters of saline into the spermatic cord to separate the vascular components of the cord from the lymphatic part. In one study, none of the patients had developed postvaricocelectomy hydrocele at a 1 year follow up.¹⁶

Sentinel node mapping for breast cancer, melanoma, and other malignancies is widespread and well established.^{17,18} It uses the property of methylene blue lymphography. The same idea was used to preserve lymphatics during varicocelectomy, to achieve better results. Depending on its magnification power, laparoscopy can be used to visualize lymphatic trunks, but this is not sufficient to ensure total lymphatic preservation. Mapping with methylene blue dye is a good option for all surgical varicocelectomy approaches. To achieve good mapping, the vital dye should be injected into a space that is easily available to the surgeon, with minimal error, and that can give a rapid onset, so that the injection could be performed when the patient is already under general anesthesia.¹⁹

There are three different modes of injection: subdartos, intravaginal and intraparenchymal. Subdartos injection is performed in the space between the dartos and the parietal tunica vaginalis. This is an easy, safe, and rapid method, but the lymphatic pathway preferred is the scrotal one that drains to inguinal nodes and partially to the testicular system. Intravaginal injection is performed in the narrow space between the two layers of the tunica vaginalis. This is probably the most difficult mode of injection. It was first described in the pediatric varicocele population by Tan et al in 2004.²⁰ Intraparenchymal injection is achieved using a fine needle just within the body of the testis. This is the fastest and most specific approach, because it is related to regional lymphatic drainage. It gives the highest rate of successful lymphatic mapping. However, some concerns have been raised regarding testicular tissue inflammation and resultant fibrosis. Makari et al demonstrated this in a recent animal study. Histological examination of the testicles at 3 months after intraparenchymal injection revealed areas with necrosis of seminiferous tubules, thickened tubular basement membranes, interstitial fibrosis and hyalinization, and striking intratubular dystrophic calcification.²¹

Our study showed a low rate of postvaricocelectomy hydrocele. Only two patients (5%) developed hydrocele, and one of these cases involved difficult lymphatic mapping. Methylene blue lymphography was a quick and easy adjunct to the surgical procedure; however, it has yet to be evaluated in comparison with other state-of-theart techniques such as microscopic varicocelectomy.

Conclusion

This preliminary study suggests that intratunical injection of methylene blue dye just prior to laparoscopic ligation of varicocele can aid in the identification and sparing of lymphatic vessels, although it did not preserve lymphatic vessels in all patients in this study. It appears to be a safe technique that does not prolong operating time.

The suggested value of this technique is in potentially decreasing the rate of postoperative hydrocele formation in adult patients undergoing laparoscopic varicocelectomy. This remains to be confirmed in a prospective, randomized trial.

References

- 1. Niedzielshi J, Paduch D, Racynski P. Assessment of adolescent varicocele. *Pediatr Surg Int* 1997;12(5-6):410-413.
- 2. Schwentner C, Oswald J, Lunacek A, Deibl M, Bartsch G, Radmayr C. Optimizing the outcome of microsurgical subinguinal varicocelectomy using isosulfan blue: a prospective randomized trial. *J Urol* 2006;75(3 Pt 1):1049-1052.
- Lipshultz M, Thomas JR A, Khera M. In: Walsh P, Retik A, Vaughan E.D, Wein A, editors. Campbell's Urology. 9th ed. Philadelphia: Saunders;2007:665.
- 4. Palomo A. Radical cure of varicocele by a new technique: preliminary report. *J Urol* 1949;61(3):604-607.
- 5. Misseri R, Gershbein AB, Horowitz M, Glassberg KI. The adolescent varicocele: the incidence of hydrocele and delayed recurrent varicocele after varicocelectomy in long-term followup. *BJU Int* 2001;87(6):494-498.
- 6. Minevich E, Wacksman J, Lewis AG, Sheldon CA. Inguinal microsurgical varicocelectomy in the adolescent: technique and preliminary results. *J Urol* 1998;158(3):1022-1024.
- 7. Schiff J, Kelly C, Goldstien M, Schlegel P, Poppas D. Managing varicocele in children: results of microsurgical varicocelectomy. *BJU Int* 2005;95(3):399-402.
- Donovan JF, Winfield HN. Laparoscopic varix ligation. J Urol 1992;147(1):77-81.
- 9. Koyle MA, Oottamasathien S, Barqawi A, Rajimwale A, Furness PD 3rd. Laparoscopic Palomo varicocele ligation in children and adolescents: results of 103 cases. *J Urol* 2004;172(4 Pt 2): 1749-1752.

- 10. Hassan JM, Adams MC, Pope JC 4th, Demarco RT, Brock JW 3rd. Hydrocele formation following laparoscopic varicocelectomy. *J Urol* 2006;175(3 Pt 1):1076-1079.
- 11. Szabo R, Kessler R. Hydrocele following internal spermatic vein ligation: A retrospective study and review of literature. *J Urol* 1984;132(5):924-925.
- 12. Goldstien M, Eid JF. Elevation of intratesticular and scrotal skin surface temperature in men with varicocele. *J Urol* 1989;142(3):743-745.
- 13. Paduch DA, Niedzielski J. Repair versus observation in adolescent varicocele: a prospective study. J Urol 1997;158(3):1128-1132.
- 14. Kocvara R, Dolezal J, Hampl R, Povysil C, Dvoracek J, Hill M, Dite Z, Stanek Z, Novak K. Division of lymphatic vessels at varicocelectomy leads to testicular oedema and decline in testicular function according to the LH-RH analogue stimulation test. *Eur Urol* 2003;43(4):430-435.
- 15. Lemack GE, Uzzo RG, Schlegel PN, Goldstein M. Microsurgical repair of the adolescent varicocele. J Urol 1998;160(1):179-181.
- Atteya A, Amer M, Abdelhady A, Al-Azzizi H, Ismael E, Abdel-Gabbar M, Shamloul R. Lymphatic vessel hydrodissection during varicocelectomy *Urology* 2007;70(1):165-167.
- Borgstein PJ, Meijer S, Piipers R. Intradermal blue dye to identify sentinel lymph node in breast cancer. *Lancet* 1997;349(9006):1668-1669.
- 18. Ramirez PT, Levenback C. Sentinel nodes in gynecologic malignancies. *Curr Opin Oncol* 2001;13(5):403-407.
- 19. D'Alessio A, Piro E, Beretta F, Brugnoni M, Marinoni F, Abati L. Lymphatic preservation using methylene blue dye during varicocele surgery: a single-center retrospective study. *J Ped Urol* 2008;4(2):138-140.
- Tan HL, Tecson B, Ee MZ, Tantoco J. Lymphatic sparing, laparoscopic varicocelectomy: a new surgical technique. *Pediatr Surg Int* 2004;20(10):797-798.
- 21. Makari JH, Atalla MA, Belman AB, Rushton HG, Kumar S, Pohl HG. Safety and efficacy of intratesticular injection of vital dyes for lymphatic preservation during varicocelectomy. *Urol* 2007;178(3 Pt 1):1026-1030.