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Varicocele: An overview

Bharat Goel[1]*, Kanhaiya Pathak[1], N. A. Khan[2] and Mohammad Abid[2]
1, Department of Pharmaceutics,
Indian Institute of Technology (Banaras Hindu University), Varanasi, (U.P.) - India
2, Department of Pharmacology and Clinical Research,
IFTM University, Moradabad, (U.P.) - India

Abstract

Varicocele is defined as an abnormal dilatation of the veins of the pampiniform plexus in the spermatic cord. It is estimated to affect 10–15% of men and adolescent boys. The management of varicocele is likely to prove an increasingly important and challenging aspect of medical practice for urologists and general physicians. Over the last decade, research into pathophysiology of varicoceles has focused on three main areas. These are oxidative stress-related damage, tissue hypoxia- and hormonal imbalances. Oxidative stress in turn may result in damage to sperm membrane and DNA. Patients with varicoceles are typically asymptomatic. If symptomatic, most patients present with changes such as atrophy of the testes, histological changes within the testes, changes in Leydig and Sertoli cell function and their seminal parameters, and endocrine abnormalities. The symptoms are Enlarged, twisted veins in the scrotum, Infertility, Painless testicle lump, scrotal swelling, or bulge within the scrotum. Diagnosis of varicocele is mainly done by sonographic quantitative evaluation of scrotal vein diameters. Varicocele treatment has traditionally involved open surgery, usually performed by a urologic surgeon, or urologist. In recent years, however, a safe and effective nonsurgical alternative called varicocele embolization is becoming the treatment of choice for many patients and their physicians. Our present study is to evaluate the current literature on the varicocele and their possible method of treatment.

Key-Words: Male infertility, Percutaneous embolization, Varicocele, Varicocelectomy

Introduction

Varicoceles (L. *varix*, twisted vein, + Gr. *Kele*, tumor, swelling) [1] are a relatively common condition (affecting approximately 10 percent of men) that tends to occur in young men, usually during the second or third decade of life [2]. A testicular varicocele represents an abnormal degree of venous dilatation of the pampiniform plexus [3]. Varicocele is caused by dysfunction of the valves in the spermatic vein [4]. Anatomically, varicoceles present as dilatation of the internal spermatic vein and pampiniform plexus of the testis, which may lead to testicular injury via several mechanisms [5]. The presence of varicocele has been linked to decreased testicular volume [6]. The growing awareness of the potential damage associated with long-standing varicoceles has stimulated urologists to become more diligent in their pursuit of the adolescent varicocele [7]. Varicocele is potentially a progressive condition that may affect fertility [8].

*** Corresponding Author**
E.mail: bharat.goel.phe11@iitbhu.ac.in,
fromabid@yahoo.com

Incidence

A number of groups have studied the incidence of varicoceles. Oster examined a group of 837 males in the age in the age group of 10-19 years and found that 16.2 % of boys had detectable varicoceles [9]. Yerokhin found a similar incidence in about 10,000 males between the age group 10-17 years of whom 12.4 % had detectable varicoceles [10]. Horner found an incidence of 15.1% in the group aged 17-31 years which corresponds with that in adolescent boys (16.2%) [11].

In an analysis of WHO data on 904 men 25.4% of those with abnormal semen analysis and 11.7% with normal semen analysis had varicoceles [12]. In the elderly population, the prevalence of varicoceles was found to be 42% which was greater than that for historic control younger populations, suggesting either an increase with age or examiner sensitivity bias [13].

Pathogenesis

Research in the pathogenesis of varicoceles has focused on three main areas: oxidative stress related damage, tissue hypoxia and hormonal imbalances.

Oxidative stress in turn may result in damage to sperm membrane and DNA. In order to accept these hypotheses, it will be first important to first document elevated levels of reactive oxygen species (ROS), in infertile men with varicoceles, show an association between raised ROS levels and sperm membrane and DNA damage [14].

Reactive Oxygen Species (ROS)

Varicoceles may be associated with an increase in the ROS generation and oxidative stress. In an experimental study evaluating the association of varicoceles with oxidative stress, Weese et al [15] found that the ROS amount to be higher in the semen samples of men with varicoceles, irrespective of their fertility status. Further, Mostafa et al demonstrated improved ROS parameters after surgical treatment of varicoceles [16].

Tissue Hypoxia

Lee et al found significantly higher level of HIF-1 (Hypoxia Inducible Factor – one of the principal regulators of response to hypoxia) in the patients with varicoceles [17].

Hormonal Imbalances

Varicoceles may exert their damaging effects on spermatogenesis through changes in hormonal milieu. A number of studies have shown a decline in the level of testosterone in men with varicoceles, when compared with those without varicoceles [18]. Other mechanisms responsible for a decline in testosterone levels may be a decreased responsiveness to hCG, decreased binding of hCG to Leydig cells, abnormality of peak secretions, or abnormalities of sex hormone binding globulin (SHBG) [18].

Diagnosis

Clinical

Varicoceles may be symptomatic with pain and swelling. Physical examination is still the standard diagnostic method for varicocele but it is usually difficult to estimate the existence of varicocele using physical examination since most of the varicoceles are impalpable, asymptomatic and diagnosed only with ultrasound evaluation [19]. The clinical view of a varicocele depends on the experience of the evaluating physician. Varicoceles greater than 3–4 mm in diameter are usually clinically apparent [20]. Dubin and Amelar [21] devised a useful clinical grading system for palpable varicoceles. Grade 1 varicoceles are considered to be those palpable only during a Valsalva manoeuvre. Grade 2 varicoceles are palpable without the Valsalva manoeuvre. Grade 3 varicoceles are visible on examination before palpation. In a World Health Organisation multicentre study on 141 men with sub-fertility, the sensitivity of clinical examination was approximately 50% for the detection of a varicocele when compared with venography [22]. This false rate for clinical examination makes it essential that a practising radiologist be familiar with the radiological features and variations of testicular varicoceles.

Imaging

Imaging techniques used in the diagnosis of the testicular varicocele are discussed in the table 1 [3].

Clinical Features

Male sub-fertility [23]

The relationship between varicocele and sub-fertility was first reported in 1952 by Tulloc, who found that spermatogenesis returned to normal in an azoospermic patient after surgical treatment of a bilateral varicocele.

Testicular hypertrophy [24]

Varicocele is associated with testicular atrophy and the rate of testicular atrophy increased depending on varicocele grade.

Palpability of spermatic veins [24]

The palpability of the spermatic vein can be assessed by imaging modalities.

Dysmenorrhea in females [25]

Varicocele occurs in both sexes. Although no association with infertility in the female has been reported, a dilation of veins of pampiniform plexus within the broad ligament does occurs and may cause dysmenorrhea.

Treatment

The varicocele can be repaired surgically or by interventional radiology. The former may be performed at different levels, including retroperitoneal, inguinal and subinguinal, and by open surgery, with or without the aid of optical magnification, or by laparoscopy. Radiological treatment, instead, is accomplished by percutaneous embolization of the internal spermatic vein in either a retrograde or antegrade fashion.

Surgical treatment

Surgical treatment is the most popular form of treatment for varicocele and can be achieved by open varicocelectomy, laproscopic varicocelectomy and microsurgical varicocelectomy.

Open varicocelectomy [26]

Conventional open varicocelectomy can be performed using different incisions to expose the spermatic vessels at various levels. High retroperitoneal ligation of varicocele, also known as the paloma technique, is performed through a horizontal incision medial and inferior to the ipsilateral anterior superior iliac spine and extending medially. The external oblique fascia is incised in the direction of the fibers and the internal oblique muscles retracted cranially to expose the internal spermatic veins proximal to the internal inguinal ring. In the inguinal approach, an incision is

made in the groin above and lateral to the ipsilateral pubic tubercle and extending laterally along the skin lines of the inferior abdominal wall. Incision of the open sublingual varicocelectomy is made at the level of the external inguinal ring to allow delivery of the spermatic cord without dividing any muscle or fascia of the abdominal wall. Complications include hydroceles, inadvertent arterial ligation, testicular atrophy, injury to vas deferens, epididimitis, hematoma and wound infection [27].

Laproscopic varicocelectomy

Laproscopic varicocelectomy has the advantage of isolating the internal spermatic veins proximally, near the point of drainage into the left renal vein. Only few veins are to be ligated. Laproscopic varicocelectomy result in higher recurrence rates (3.5-20%). Failure of laproscopic varicocelectomy is due to presence of parallel inguinal or retroperitoneal collaterals, which may exit the testis and bypass the ligated retroperitoneal veins rejoining the internal spermatic vein proximal to the site of ligation [28]. Complications of laproscopic varicocelectomy include air embolism, inadvertent arterial division, genitofermoral nerve injury, hydrocele, intestinal injury and peritonitis [26].

Microsurgical varicocelectomy [29]

Microsurgical approach has been shown to result in a fewer recurrences and complications than conventional open varicocelectomy. The procedure is safe to perform and can be performed under local/general anesthesia. Operating time is very less. Testicular arteries are clearly identified under 10-25x magnification and preserved.

Percutaneous embolization [30]

In case of varicocelectomy, hydrocele formation remains one of the most frequent complications, occurring in 3-40% of patients after treatment. Recent laparoscopic and microsurgical techniques have been developed in an attempt to prevent the hydrocele formation. Although, these methods have decreased the formation of postoperative hydroceles, but have not totally eliminated this complication. The technique of percutaneous embolization has been extensively reported for treatment of the adult varicocele. In this technique, after obtaining informed consent, the patient is sedated using midazolam and fetanyl. Lidocaine is infiltrated above the right femoral vein to achieve a local anesthetic. A vascular sheath is then inserted into the right femoral vein and a 6-Fr curved guiding catheter is advanced into the left renal vein where a venogram is performed while the patient performs a valsalva maneuver. If reflux of contrast through the spermatic vein is seen to the level of the scrotum, a 4-Fr catheter is then advanced into the inferior spermatic vein and fibered coils are placed to occlude the spermatic vein at the level of the internal inguinal ring. In order to demonstrate collateral and parallel veins, a venogram is then performed through the 4-Fr catheter. If collaterals are visualized, additional coils are placed within these veins at their branch points. 3% sodium tetradecyl sulphate foam is then injected while the catheter is pulled back to the more superior portion of the gonadal vein, where additional coils are placed to obliterate the vein. A repeat venogram is performed to confirm occlusion of the spermatic vein and patency of the renal vein. The catheters are then removed and a pressure dressing is applied to the right femoral vein. The patient is awakened and transferred to an observation unit. After 6 h, the pressure dressing is removed, and the patient is allowed to ambulate and is discharged home.

Sclerotherapy [31]

The sclerotherapy is done with Ethoxysklerol (KreusslerPharma, active substance: Polidocanol). It is available in concentrations of 0.25–4%. An ampoule contains 2ml solution. Ethoxysklerol leads to a local thrombophlebitis that induces a thrombosis. We apply the 4% solution in cases of large varicoceles, 3% for medium-sized and 2% for small ones. A very high concentration causes an increased inflammatory reaction in the perivenous area. The patient is ordered to stay in bed for two hours and to avoid sports and heavy lifting for 3 days. After approximately 3 months, the clinical and Doppler sonographic re-examination takes place. Any existing pathological spermiogram is also controlled.

Conclusion

Varicocele is an important disorder leading to significant symptoms like testicular atrophy, Palpability of the spermatic vein, sub-fertility in males while dysmenorrhea in females. Literature survey showed that it occurs in 12-16 % of males out of which 90% of cases on left side and 10% are bilateral. Accurate diagnosis is important as correct treatment may lead to resolution of symptoms and improvement in sperm count in sub-fertile patients. Since, most of the patients are asymptomatic; it is usually difficult to estimate the existence of varicocele using physical examination. Hence, imaging techniques are most reliable for the assessment of varicoceles. The technique of percutaneous embolization has been extensively reported for treatment of the adult varicocele. However, surgical methods are also widely used for the repairing of varicoceles.

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References

1. Thomas C.L. (1997). Taber's Cyclopedia Medical Dictionary. 18th ed. Philadelphia: F. A. Devis Company;39-43
2. Varicoceles.com. Varicocele embolization, a non-surgical treatment of varicocele. Website. http://www.varicoceles.com/what-is-a-varicocele.htm. Published 2001. Accessed August 14, 2012.
3. Beddy P., Geoghegan T., Browne R.F. and Torreggiani WC. (2005). Testicular varicoceles. *Clin Radiol*. 60:1248-55.
4. Biyani C.S., Cartledge J. and Janetschek G. (2009). Varicocele. *Clin Evid*, 01:1806.
5. Johnson C.W., Fisch H., and Hensle T.W. (2004). American Urological series, vol. 23. Linthicum: Education and Research Inc; p. 266-271.
6. Kolon T.F., Clement M.R., Cartwright L., Bellah R., Carr M.C. and Canning DA. (2008). Transient Asynchronous Testicular Growth in Adolescent Males With a Varicocele. *J Urol*. 180;1111-4.
7. Kubal A., Nagler H.M., Zahalsky M. and Budak M. (2004). The adolescent varicocele: diagnostic and treatment patterns of pediatricians. A public health concern. *J Urol*. 171;411-3.
8. Keene DJ, Sajad Y, Rakoczy G, Cervellione RM. Testicular volume and semen parameters in patients aged 12 to 17 years with idiopathic varicocele. J Pediatr Surg. 2012; 47:383-5.
9. Oster J. (1971). Varicocele in children and adolescents. An investigation of the incidence among Danish school children. *Scand J Urol Nephrol*. 5:27-32.
10. Yerokhin AP. Classification and frequency of varicocele in children. Klin Khir. 1979; 6:45-6.
11. Horner JS. The varicocele: A survey among secondary school boys. Med Officer. 1960; 104:377-81.
12. World health organization: The influence of varicoceles on parameters of fertility in a large group of men presenting to infertility clinics. Fertil steril. 1992; 57:1289.
13. Canales B.K,, Zapzalka D.M., Ercole C.J., Carey P., Haus E. and Aeppli D. (2005). Prevalence and effect of varicoceles in an elderly population. *Urology*, 66:627-31.
14. Kumar R., and Gupta N.P. (2006). Varicocele and the urologist. *Indian J Urol*, 22: 98-104.
15. Weese D.L., Peaster M.L., Himsl K.K., Leach G.E., Lad P.M. and Zimmen P.E. (1993). Stimulated reactive oxygen species generation in the spermatozoa of infertile men. *J Urol*, 3: 149:64-7.
16. Mostafa T., Anis T.H., El-Nashar A., Imam H. and Othman I.A. (2001). Varicocelectomy reduces reactive oxygen species levels and increases antioxidant activity of seminal plasma from infertile men with varicocele. *Int J Androl*, 24: 261-5.
17. Lee J.D., Jeng S.Y. and Lee T.H. (2006). Increased expression of hypoxia inducible factor-1α in the internal spermatic vein of patients with varicocele. *J Urol*, 175: 1045-8.
18. Naughton C.K. and Nangia A.K. (2001). Agarwal A. Pathophysiology of varicoceles in male infertility. *Hum Reprod Update*, 7: 473-81.
19. Kocakoc E., Serhatlioglu S., Kiris A., Bozgeyik Z., Ozdemir H. and Bodakci MN. (2003). Color doppler sonographic evaluation of inter relations between diameter, reflux and flow volume of testicular veins in varicocele. Eur J Radiol.; 47:251-6.
20. Demas BE, Hricak H, McClure RD. Varicoceles. Radiologic diagnosis and treatment. Radiol Clin North Am. 1991; 29:619-27.
21. Dubin L. and Amelar R.D. (1970). Varicocele size and results of varicocelectomy in selected subfertile men with varicocele. *Fertil Steril*, 21:606-9.
22. World Health Organization. (1985). Comparison among different methods for the diagnosis of varicocele. *Fertil Steril*. 43: 575-82.
23. Turek P.J. and Lipshultz L.I. (1995). The varicocele controversies I. Etiology and pathophysiology. AUA Update Series XIV, 13: 105-11.
24. Cornud F, Belin X, Amar E, Delafontaine D, Hélénon O, Moreau JF. Varicocele: strategies in diagnosis and treatment. Eur Radiol. 1999, 9: 536-45.
25. Saypol DC. (1981). Varicocele. J Androl, 2: 61-71.
26. Chan P. (2011). Management options of varicoceles. *Indian J Urol*, 27: 65-73.
27. Szabo R. and Kessler R. (1984). Hydrocele following internal spermatic vein ligation: A

retrospective study and review of the literature. *J Urol*.; 132:924-5.

28. Murray R.R., Jr, Mitchell S.E., Kadir S., Kaufman S.L., Chang R. and Kinnison M.L. (1986). Comparison of recurrent varicocele anatomy following surgery and percutaneous balloon occlusion. *J Urol*, 135:286-9.
29. Lemack G.E., Uzzo R.G. and Schlegel P.N. (1998). Goldstein M. Microsurgical repair of the adolescent varicocele. J Urol, 160: 179-81.
30. Storm D.W., Hogan M.J. and Jayanthi V.R. (2010). Initial experience with percutaneous selective embolization: A truly minimally invasive treatment of the adolescent varicocele with no risk of hydrocele development. *J Pediatr Urol*, 6: 567-71.
31. Wunsch R. and Efinger K. (2005). The interventional therapy of varicoceles amongst children, adolescents and young men. *Eur J Radiol*.; 53: 46-56.