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Retroperitoneal Varix ligation with sclerotherapy: a prospective randomized comparative study

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Introduction The aim of this article is to compare the results of high varix ligation with and without sclerotherapy.

Material and methods Between November 2014 and December 2015, sixty patients with varicocele were included in this study. Patients were divided into two equal groups; group I (underwent high varix ligation), and group II (underwent high varix ligation with a retrograde injection of 2 mL of 5% ethanolamine oleate in the lower end of the bisected gonadal vein). The operative time, intra- and postoperative complications, postoperative pain, improvement of semen parameters, incidence of recurrence and achieving of unassisted pregnancy were recorded for both groups.

Results The age range was 19–34 years in group I and 21–37 years in group II. The operative time was shorter in group I (34.6 ±7.81 min) than group II (43.3 ±8.5 min) (P <0.001), which was statistically significant. Improvement of semen parameters and the occurrence of spontaneous pregnancy were insignificant between both groups. No intraoperative complications occurred. The postoperative complications were statistically insignificant in both groups.

Conclusions Combined varix ligation with retrograde sclerotherapy does not offer significant advantages over high varix ligation alone with a longer operative time and prolonged post-operative pain.

Key Words: ligation ‹› retroperitoneal ‹› sclerotherapy ‹› semen ‹› Varix

INTRODUCTION

Varicocele is the most common surgically correctable cause of male subfertility. Significant improvement in sperm concentration, motility, normal morphology and pregnancy rate are associated with its treatment [1]. Indications for varicocelectomy include male subfertility with poor semen parameters, testicular pain, androgen deficiency, progressive testicular atrophy and non-obstructive azoospermia even in men who have undergone micro-dissection testicular sperm extraction [2].

Multiple techniques of treatment are available including open surgery, microsurgery, laparoscopic surgery, interventional radiology and sclerotherapy [3, 4, 5]. Herein, we will compare the results of retroperitoneal varix ligation with and without retrograde sclerotherapy regarding the intraoperative and postoperative outcome in two randomized groups of patients with varicocele.

MATERIAL AND METHODS

Sixty patients with different degrees of varicocele were included in this prospective randomized study, which took place between November 2014 and December 2015. Written informed consent was obtained from all patients after the study was approved by the local ethical committee. Patients with primary or secondary infertility with isolated left-sided varicocele associated with seminal changes were included in this study. Exclusion criteria were; recurrent varicocele, testicular atrophy, normal spermiograms, azoosperma, and abnormal hormonal profile.

Patients were divided into two equal groups; group I underwent high varix ligation, and group II underwent high varix ligation plus retrograde injection of 2 mL of 5% ethanolamine oleate in the lower end of the bisected gonadal vein. The choice of either technique was made using the 'closed envelope' method. Each procedure was performed under spinal anesthesia.

Preoperative preparation

A thorough history was taken and physical examination was performed for all patients. Varicocele was graded as follows: grade I: palpable with Valsalva maneuver, grade II; palpable without Valsalva maneuver and grade III: visible without palpation [6]. Scrotal duplex ultrasound and hormonal assay including LH, FSH and testosterone levels were performed for all patients. Semen samples were collected after 3–4 days of abstinence. A second sample was obtained 15 days after the first. The mean value of both results was calculated preoperatively. A further two samples were collected 4 months postoperatively to evaluate the result of surgery. Basic parameters of semen analysis were standardized according to the WHO 2010 guidelines [7].

Surgical procedure

1. Retroperitoneal approach

A 3–4 cm transverse incision was made 3 finger breadths medial and 2 finger breadths cranial to the anterior superior iliac spine as described by Palomo in 1969 [8]. After exposure of the testicular vein (s), it was ligated and the wound was closed in layers.

2. Sclerotherapy

The operative procedure was the same as group I. In addition, the upper end of the transected testicular veins was ligated and the lower end was cannulated using a 24-gauge cannula. Then, 2 ml of ethanolamine oleate was injected slowly in a retrograde manner. The spermatic vein at the site of injection was ligated by 3/0 Vicryl. If multiple veins were present, the largest one was chosen for injection of the sclerosing material after ligation of smaller ones.

Both techniques were compared regarding the operative time (calculated in minutes), intra-and postoperative complications (according to the modified clavien system), postoperative pain, improvement of semen parameters, incidence of recurrence and achieving of unassisted pregnancy. The pain score was subjectively recorded on a scale from 0–10 as described by Aubrun et al., in the first, second and fourth week postoperatively as follows [9]: none (0): no pain, mild (1–3): pain reported in response to questioning only without any behavioral signs, moderate (4–6): pain reported spontaneously without questioning and severe (7–10): strong verbal response accompanied by facial grimacing or tears. Follow up included clinical examination, duplex ultrasound and semen analysis for one year postoperatively.

RESULTS

The mean age of the patients was 24.76 ±3.51 (range 19-34) years in group I and 25.10 ±3.66 (range 21–37) years in group II, with no statistically significant difference (P 0.77). Eleven patients presented with testicular pain in group I and 23 in group II. Grades of varicocele in group I were as follows; grade I in 6 patients, grade II in 7 and grade III in 17. The corresponding grades in group II were present in 1, 5 and 24 patients respectively with no significant difference. The operative time was statistically significant less in group I (34.6 ±7.81 min) than group II (43.3 ±8.5 min) (P <0.001).

No intraoperative complications occurred in either group. According to the modified clavien system, grade I occured in 4 (13.3%) patients, 2 in each group, in the form of fever and simple wound infection, which was treated with antipyretics and local

Table 1. *Pre- and post-operative semen parameters in each group*

Semen Parameter	Group I Mean± SD		Group II Mean± SD		P. Value	Improvement %		P. Value
	Preoperative	Postoperative	Preoperative	Postoperative		GI	GII	
Sperm concentration (10^6/ml)	10.24 ±8.73	16.37 ±12.81	13.14 ±19.15	18.63 ±23.15	<0.001	6.1 (0.62%)	5.49 (41.7%)	0.62
†Sperm progressive motility (%)	11.53 ±9.38	21.83 ±16.37	14.17 ±10.09	24.33 ±17.45	<0.001	10.3 (0.59%)	10.16 (71.7%)	0.59
Sperm abnormal forms (%)	36.5 ±9.5	30.5 ±7.69	36.83 ±11.60	31.66 ±8.34	<0.001	6 (0.91%)	5.17 (14.3%)	0.91

†Sperm progressive motility (A+B): A – rapid forward progressive motility; B – slow or sluggish progressive motility.

antibiotic spray. Delayed postoperative complications in the form of secondary hydrocele and varicocele recurrence occurred in 1 (3.33%), 2 (6.66%) patients and 6 (20%), 2 (6.66%) patients in both groups respectively with no significant statistical difference (P 0.950 and 0.254 respectively). Postoperative testicular atrophy did not occur in either group.

The pre- and postoperative semen parameters in both groups are shown in Table 1. A statistically significant difference was present between the preoperative and postoperative results in each technique. However, the difference between both groups regarding improvement of semen parameters postoperatively was statistically insignificant.

Concerning postoperative pain, the difference between both groups was statistically insignificant in the first week post-operatively (3.63 ±1.85 in group I, 3.96 ±2.29 in group II) (P 0.69). It became significant during the second week (0.80 ±1.12 and 1.80 ±1.63 respectively) (P 0.02) and at one month post-operatively (0.17 ±0.64 and 0.60 ±0.72 respectively) (P 0.01), although the pain was mild. Spontaneous unassisted pregnancy in the first year postoperatively occurred in 4 (13.3%) patients in group I and in 6 (20.0%) patients in group II, which was statistically insignificant (P 0.128).

DISCUSSION

Surgical correction of clinical varicocele has a positive impact on the postoperative semen parameters and pregnancy rates [10]. Many surgical procedures for the treatment of this condition are available but the ideal one is still controversial. However, the treatment should be safe, effective and minimally invasive [3, 4, 5].

Sclerotherapy was first attempted in the treatment of varicose veins of the lower limbs in order to shrink and obstruct the diseased veins [11]. In varicocele, sclerotherapy may be an antegrade scrotal sclerotherapy, foam sclerotherapy or a retrograde approach. Advantages of the antegrade approach are its short operative time and smaller recurrence rates. Its disadvantages are scrotal hematoma, epididymo-orchitis and thrombophlebitis of the pampiniform plexus [12]. Foam sclerotherapy has the advantages of reducing the diameter of testicular veins and number of recurrences. However, venous thromboembolism, thrombophlebitis and allergic reaction are among its drawbacks [13]. Retrograde sclerotherapy during high retroperitoneal varix ligation has the same advantages of the previous techniques and less systemic complications, as the sclerosing agent is injected toward the testis after ligation of the upper end of the cut vein. This procedure does not require fluoroscopy, as do the other sclerotherapy techniques [14].

In our study, the mean operative time for group I was significantly less frequent (34.6 ±7.81 min) than in group II (43.3 ±8.5 minutes) (P value <0.001). This may be due to the amount of time required in the second group to carefully cannulate the lower end of the testicular vein, followed by the slow injection of sclerosing agents. The operative time in group I was consistent with that for high varix ligation as reported by Koji Shiraishi, where it was 29.1 ±4.4 minutes [15]. However, it was somewhat longer than that reported by Gauda El. Labbon,where the average time was 25.3 minutes for th same procedure [16]. The mean operative time for group II was 43.3 minutes which is markedly longer than that for antegrade scrotal sclerotherapy reported in other studies where the mean operative time was 25 minutes [17].

In our study, after varix ligation, a major improvement in the sperm motility parameter was observed [13] (89.3% in group I and 71.7% in group II). Also, semen parameter improvement in the present study, although statistically insignificant between the two studied groups as shown in Table 1, was consistent with others. A study by Agarwal demonstrated that sperm concentration increased by 9.71 x 106/mL, motility by 9.92% and sperm morphology by 3.16% after treatment [18].

Other approaches of sclerotherapy are also associated with improvement in spermiograms. Long Li et al. used trans-catheter foam sclerotherapy and found that the mean values of sperm concentration and motility increased from 14.73 x 106/mL and 44% pre-operatively to 50.56 x 106/mL and 70% postoperatively after treatment as also shown in group II of our study [14].

Spontaneous pregnancy rate after varicocele treatment ranged between 30–60% [19]. In a controlled trial comparing the pregnancy rate at one year after surgery versus no surgery in infertile men, the rate was 44% compared to 10% respectively [20]. In the current study, spontaneous pregnancy at one year occurred in 4 cases (13.3%) in group I, and 6 cases (20%) in group II, with no statistically significant difference. The pregnancy rate in group I was less than that reported by Evers, who reported 21% pregnancy rate at one year after high varix ligation alone [21]. Our pregnancy rate, of the two techniques, was less than that reported by others of 33.3% [22].

The microsurgical repair plus sclerotherapy may be more effective than the inguinal or supra-inguinal approaches in terms of varicocele recurrence and persistence. The retroperitoneal approach is asso-

ciated with 15% recurrence rate, which is considered a major disadvantage of this approach. This may be due to the presence of parallel inguinal or retroperitoneal collaterals [23]. However, surgeon's preference is an important determinant of the surgical technique [24]. We chose the retroperitoneal approach as it is easily applicable; no microsurgical instruments were needed- which necessitate a sufficient learning curve and higher costs. In our study, the recurrence rate was 6 (20%) patients in group I and only 2 (6.66%) in group II. This might be due to the obliteration of the pampiniform plexus by the sclerosing effect of ethanolamine. Koji Shiraishi, reported 4 recurrences (9.3%) after retroperitoneal varix ligation which was less than our results in group I [15]. In our study, the recurrence rate in group II was 6.6% which was less frequent than that encountered by Zaupa et al. (21.9%) using antegrade sclerotherapy. This might be due to retrograde rather than antegrade injection [25].

Hydrocele formation is a common complication after conventional non-microscopic varicocelectomy. Its incidence varies between 3–33% (average 7%). This is due to failure to preserve the lymphatics with subsequent obstruction. Use of magnification to identify and preserve these lymphatics can decrease the risk of postoperative hydrocele to less than 3% [26]. The effect of hydrocele formation on sperm function and fertility is uncertain. However, large hydrocele creates an abnormal insulating layer that surrounds the testis. This will impair the efficiency of the counter current heat exchange mechanism and therefore reduce some of the benefits of varicocelectomy [27]. In the current study, postoperative hydrocele occurred in one (3.33%) patient in group I and in 2 patients (6.66%) in group II with no statistically significant difference. Arain et al. reported no postoperative hydrocele after high varix ligation, which is better than our results [28]. In group II, hydrocele formation was 6.7% which is less than similar studies which reported a hydrocele formation of 13.4% [29].

Testicular atrophy after varix ligation, which occurs in 1% of patients, is caused by spermatic artery ligation, which represents 2/3 of the testicular blood supply. Vasal and cremasteric arteries supply the remaining 1/3 [30, 31]. The incidence of testicular atrophy is less frequent in high varix ligation due to the collateral circulation below the level of ligation. In children, the potential for neovascularization and compensatory hypertrophy of the vasal and cremasteric vessels is probably greater than in adults, making atrophy after testicular artery ligation less likely [20]. In our study, testicular atrophy did not occur in either technique. This was consistent with other studies [17, 28].

Postoperative pain after sclerotherapy might be due to the inflammatory reaction that may persist for 45–90 days after injection of the sclerosing agent [32]. In our study, the postoperative pain during the first week was statistically insignificant between both techniques. However, it was statistically significantly higher during the 2nd and 4th week in group II. Arain et al. reported the occurrence of persistent pain in 2 patients (7.7%) [26].

In conclusion, retrograde sclerotherapy during retroperitoneal varix ligation does not seem to offer a significant benefit over retroperitoneal varix ligation alone in treatment of primary varicocele with a longer operative time and prolonged postoperative pain.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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