Effect of Varicocele Catheter Guided Glue Embolization on Male Fertility

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ABSTRACT

Background: Varicoceles; dilation of veins within the pampiniform plexus, are present in 15% of the general male population. It is also one of the most frequent causes of male-factor infertility, with a prevalence of 30%–40% among men presenting for primary infertility evaluation and up to 85% in secondary infertility.

Aim of work: The purpose of this study is to measure the success rate of the embolization technique in patients with clinical and radiological varicocele by U/S complaining of infertility.

Patients and Methods: A prospective interventional study including 21patients suspecting varicoccele presented by testicular pain or infertility, the patients underwent Varicoccele embolization under local anesthesia with digital subtraction, then follow up was done after 2 weeks, 3 months and 6 months. The study was conducted in the Radiology Department at Ain-Shams University Hospitals, the period was between January 2018 till the end of September 2019.

Results: The procedure done for the different categories of the patients in our study, 15 patient underwent left ISV embolization, 4 cases underwent bilateral ISV, in one patient we embolized right ISV, and failed at one case to cathetrize ISV.

The study showed that there was statistically significant increase in number and motility of the studied cases with p-value = 0.030 and 0.002 respectively on follow up. 47.6 % of our patients underwent minor complications with 23.8 % of them underwent post procedural pain, 9.5 % ISV peroferation, 4.7 % underwent extravasation and we failed to catherterize the ISV in 4.7 % of the cases.

Conclusion: Gonadal Vein Embolization is an effective way in treating varicocele, with our study showing significant improve as regard sperm count /ml, with significant decrease in the patient in comparison to pre and post procedural data, with highly significant improve of sperm motility in 3 months follow up.

INTRODUCTION

A varicocele consists of abnormally dilated and tortuous veins within the pampiniform plexus of the spermatic cord [1].

Varicocele is prevalent, occurring in approximately 15% of all men, 35% of men with primary infertility, and up to 80% of men with secondary infertility. While the majority of men with varicocele are asymptomatic, there is clear evidence that varicocele is associated with a progressive decline in testicular function resulting in impaired semen parameters and possibly decreased serum testosterone ^[2]. It is likely to be multifactorial. Recent studies showed that it resulted mainly in higher levels of reactive oxygen species (ROS) ^[3].

This excessive ROS is associated with sperm DNA fragmentation, which may mediate the clinical manifestation of poor sperm function and fertilization outcome related to varicocele ^[4].

Accordingly, treatment of varicocele has been shown to arrest continued decline in testicular function, improve semen parameters and, in some reports, serum testosterone ^[5].

Thus, in some men with primary or secondary infertility, treatment of varicocele may obviate the need for assisted

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reproduction, thereby sparing additional interventions, cost, and psychological stress.

Varicocele can also lead to scrotal pain, and correction of varicocele can benefit men with scrotal pain who have failed conservative measures. ^[6]

Both surgical and nonsurgical approaches to the treatment of varicocele have been described. The conventional inguinal or subinguinal operative approach involves an inguinal incision with surgical ligation of all visibly dilated spermatic veins and careful avoidance of the testicular artery. Laparoscopic varicocelectomy utilizes a minimally invasive operative technique to ligate the internal spermatic veins proximally ^[2]

Radiographic approaches involve venography to identify the internal spermatic and collateral veins with subsequent venous occlusion via a variety of occlusion and embolization techniques. Efficacy of varicocelectomy for the treatment of infertility is determined based upon improvement in serum testosterone levels, semen parameters, and, ultimately, pregnancy rates following treatment. In patients with scrotal pain, the primary objective is alleviation of pain ^[2].

Percutaneous embolization is the least invasive of all treatment approaches. In contrast to traditional surgical therapies, percutaneous interventional approaches do not require surgical incisions and thus, can be performed under local anaesthesia, whereas surgical approaches require more extensive anaesthetic preparations. Surgical failure may be the result of pre-existing collateral gonadal veins, Varicocele embolization is therefore better suited to identify and eliminate these collaterals ^[7]

The use of venography enables the precise identification of the internal spermatic veins, in addition to any collateral venous vascular supply that may contribute to the clinical pathology ^[8].

In addition, the transvenous method virtually eliminates the potential for damage to the testicular artery, which results in theoretically reduced complications related to testicular pain and atrophy ^[2]

AIM OF WORK

The purpose of this study is to measure the success rate of the embolization technique in patients with clinical and radiological varicocele by U/S complaining mainly of infertility.

PATIENTS AND METHODS

Patients

During a period of 20 months duration from August 2017, thirteen patients were enrolled in the study. All patients with varicocele, diagnosed by ultrasound and scrotal Doppler, 6 patients presented with infertility (46.2 %), 6 patients presented with pain (46.2 %), and one patient presented with recurrence after surgery (7.7%).

Inclusion criteria

- Patients complaining from symptomatic varicocele (infertility).
- No age predilection.
- Patient complaining of infertility.

Exclusion criteria

- Bleeding tendency.
- Any contraindication to the injection of contrast: high serum creatinine or allergy.

Ethical consideration

An informed consent is obtained from the patient concerning the complication of the procedure, the complication of the glue and the acceptance to be enrolled in the study.

Ultrasound imaging

 U/S examination revealed 10 patients to have unilateral left varicocele and 3 patients to have bilateral varicocele.

Semen analysis

6 patients had infertility, 3 patients with low number only, 3 patients with low motility and 1 patient with both.

Statistical analysis

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 23. Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using Chi² and paired t test.

Chi-square test P-value > 0.05 Nonsignificant

P-value < 0.05 Significant

P-value < 0.01 Highly significant

RESULTS

The 13 patients enrolled in this study were ranging from 16 to 42 years with mean age of 28.6 years.

Table 1:	Representing the statistical data analysis fo	r
	lifferent ages enrolled at our study.	

Age(years)	No.= 13
Mean ± SD	28.60 ± 7.61
Range	16 - 42
Age< 30	7 (53.8%)
Age> 30	6 (46.2%)



Diagram 1: Showing that in our study 7 patients were less than 30 years (53.8%), and 6 patients were older than 30 years (46.2%).

Presenting complain

6 patients presented with infertility (46.2 %), 6 patients presented with pain (46.2 %) and 1 patient presented with recurrence after surgery (7.7%).

Table 2. Demonstrating statistical analysis as regard the clinical indication for varicocele embolization.

Clinical indication	No.	%	
Dain	No	7	53.8%
Palli	Yes	6	46.2%
Infortility	No	7	53.8%
intertity	Yes	6	46.2%
Pogurronco	No	12	92.3%
Recuitence	Yes	1	7.7%

By imaging assessment

All patients were examined by U/S, the examination revealed, 3 of them had bilateral varicocele, 10 cases had unilateral varicocele.



Diagram 2: Representing the percentage of patient with unilateral varicocele (76.9 %), and bilateral varicocele (23.1%).

Table 3: Demonstrating the percentage of patients with right and left side varicocele according to the grade.

			No.	%
	Side	Ι	1	7.7%
Right Grade		II	2	15.4%
		III	0	0.0%
	Side	Ι	2	15.4%
Left Grade		II	6	46.2%
		III	2	15.4%

Semen analysis

3 patients had low number only, 2 patients had low motility and 1 patient had low number and decreased motility.

Table 4: Demonstrating the statistical data for patientspresented with infertility, abnormal number range from
(3-11 million/ml), and abnormality in motility range
from 5-15 %.

		No.= 13
	Low	3 (23.1%)
Semen analysis	Decrease	
abnormality	motility	2 (15.4%)
	Both	1 (7.7%)
Number (million /ml)	Mean ± SD	7.00 ± 2.65
Number (minion/mi)	Range	3 – 11
Motility 04	Mean ± SD	11.80 ± 4.15
Mounity %	Range	5 – 15

The procedure done for 10 patients was left ISV embolization, 3 cases underwent bilateral ISV.

Table 5: Demonstrating the data for the procedure eitherembolization of left or bilateral ISV. All patients weredone via right jugular approach.

		No.	%
Drogoduro	Left		100.0%
Procedure	Right	3	23.1%
Approach	Jugular	13	100.0%

Table 6: Concerning the complications occurred.

		No.	%
Complications	No	8	61.5%
complications	Yes	5	38.5%
Pain		5	38.5%

It occurred in 5 case (38.5%) in the form of self-limited hypochondrial pain after the procedure for one week that resolved over analgesics.



Diagram 3: Representing the percentage of patients with and without complications.

Table 7: Comparison between pre-procedure and post	t
procedure regarding pain.	

		Pre		Post		Test	P-	Sig
		No.	%	No.	%	e*	ue	•
Pai n	No	7	53. 8%	11	10 0%	2 000	0.0	c
	Ye s	6	46. 2%	0	0%	2.089	31	3

*: Chi-square test:

P- value > 0.05 Nonsignificant

P-value < 0.05 Significant

P-value < 0.01 Highly significant

The previous table shows that there was statistically significant decrease in percentage of pain from 53.8% preprocedure to 0% post procedure with p-value= 0.031.

		Pre	Post	Test value*	P-value	Sig.
Number (million (ml)	Mean ± SD	7.00 ± 2.65	28.00 ± 10.89	2 000	0.030	S
Number (million/ml)	Range	3 - 11	15 - 37	-3.909		
Motility %	Mean ± SD	11.80 ± 4.15	45.80 ± 6.94	7 (11	0.002	110
	Range	5 - 15	34 - 50	-7.041	0.002	н2

Table 1: Comparison between pre-procedure and post procedure regarding number and motility.

*: Paired t-test:

HS: Highly significant; S: Significant; NS: Nonsignificant

The previous table shows that there was statistically significant increase in number and motility of the studied cases with p-value= 0.030 and 0.002 respectively.

Concerning three months follow up, one patient had improvement of the motility, but the number is not improved, all patient with pain are improved.

DISCUSSION

The methods of varicocele repair continue to evolve. Many favours the percutaneous trans-catheter technique as a first-line treatment because it is a minimally invasive outpatient procedure and has minimal complication rates [9].

Trombetta et al., 2013 mentioned that the targeted overall reported technical success rate, as cited by the Journal of Vascular and Interventional Radiology quality improvements guidelines, is 83 to 96% ^[10]. *In our study*, we included 13 patients, we failed to catheterize the right internal spermatic vein in one case with technical success rate of 93.75%.

Gat et al., 2005 concluded that clinical outcomes of percutaneous ISV embolization or sclerotherapy are quite similar to surgical procedures. Semen parameters such as sperm concentration and motility improve in 70 to 82% of patients, which is almost the same situation concerning the morphology [11]. *In our study*, we had 6 patients with infertility (46.2 %), 3 patients had low number only, 2 patients had low motility and 1 patients had low number and decreased motility, our results after embolization showed that there was statistically significant increase in number and motility of the studied cases with P-value = 0.030 and 0.002 respectively.

Nabi et al., **2004**, regarding improvement of semen parameters after varicocele embolization recorded improvement in semen motility and morphology in those with retreatment semen density 10-30 million/ml ^[12]. **Gandini et al.**, **2008**, Another study performed on 244 patients also concluded improvement in all semen parameters after treatment ^[13].

Jargiello et al., 2015 answered the question of how we manage recurrent varicocele after surgery as he said: if the varicocele recurs, endovascular treatment is still performed via a retrograde way by accessing the left gonadal vein via the left renal vein, either from a right internal jugular or right femoral vein approach ^[14]. Jargiello et al., 2015 published 100 % technical success in the endovascular treatment of surgically recurrent varicocele. In our study, we have one case of recurrence after surgery that we treated via right jugular approach successfully.

Alqahtani et al., 2002 patients with cardio-pulmonary comorbidities can undergo varicocele embolization using only local anaethesia, whereas general anaesthesia is routinely necessary with surgical repair. Additionally, bilateral varicocele patients can undergo catheter-based embolization with only one single jugular vein access, in contrary to two separate surgical incisions with operative interventions. Without the need to create a surgical incision, catheter-based varicocele embolization is associated with a significant lower risk for wound complications such as infection or dehiscence [15]. In our *study*, we included patients from different age groups without any restrictions, because there is no contraindication to perform our procedure in patients with other comorbidities or systemic diseases. We also did bilateral embolization in 3 cases successfully without any need for hospital stay or complications.

Cassidy et al., 2012 discussed the technical and clinical success based on a larger scale, and his results were quite similar to us as he published a review with the largest recent series of the outcomes currently available in the literature regarding varicocele embolization. The overall technical failure rate 13.9% is consistent with the published meta-analysis rate of 13.05%. However, the high technical failure rate seen in patients with right-sided embolization attempts of 19% in Cassidy's series hadn't been previously addressed. The 3.2% overall failure rate for left-sided embolization attempts is comparable to the 3.25% published failure rate for surgical varicocele repair; for that these two options are equally effective, however embolization offers some advantages in terms of recovery time and safety ¹⁶.

In our study, as regard post procedural complications: 5 of our 13 patients had hypochondrial pain related to the site of gonadal vein embolization that last from 5 days to week that was controlled with analgesics.

Nabi et al., 2004 agreed with our rates of complications as he mentioned that the complications of percutaneous therapy are infrequent and typically mild Complication rates in recent literature have been reported from 0%, to 5% and 11% [¹²].

Reiner et al., 2011 concluded that occurrence of postembolization pain seems to be more frequent when using cyanoacrylate and sclerosing agents rather than coils, and this symptom is related to the secondary phlebitis that they cause [17].

Limitaions of the study

A limitation of this study is that it's small sample size. It would be beneficial to conduct a comparative study with the standard treatment using coil embolization or surgery.

Conclusion

In our study there was significant improvement in patients complaining of scrotal pain, with significant improvement regarding the sperm count /ml in comparison to pre and post procedural data, and highly significantly improve of motility in 3 months follow up.

In conclusion, the use of NBCA as an embolic agent for percutaneous treatment of varicoceles is a therapeutic alternative that is effective, safe, simple. NBCA triggers a local inflammatory reaction that promotes sclerosis and thrombosis. The liquid nature of the embolization product allows diffusion through the gonadal vein and their collaterals, which appears to reduce recurrence and improve results.

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Figure (1): DSA images: (A) catheter tip at the origin of left ISV, with reflux seen along the vein (B) catheter advanced till lower left ISV, with contrast injection showing reflux. (C) Cyanoacrylate cast seen occluding left ISV up to near its origin.

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Figure (2): DSA images (a) left internal spermatic vein embolization. (b) Arrowhead pointing to catheter tip at right ISV, with contrast injection for evaluation of reflux. (c) Venography of right ISV, with cyanoacrylate cast seen occluding left ISV. (d) Bilateral ISV embolization successfully done.