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Platelet Changes Following Partial Splenic Artery Embolization in Cirrhotic Patients with Hypersplenism

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Abstract

Background: Hypersplenism is a common complication of cirrhosis, leading to thrombocytopenia and leukopenia. Partial splenic artery embolization (PSE) has been introduced as an effective alternative to surgical splenectomy, effectively increasing hematologic indices particularly the platelets and lowering risk of bleeding.

Aim of Study: To investigate the effect of partial splenic Artery embolization (PSE) on platelet Count in cirrhotic patients with Hypersplenism.

Patients and Methods: Fifteen patients with chronic liver disease were included. All patients had Cirrhosis with hypersplenism and all patients underwent PSE in one session with follow-up after one month.

Results: The mean age of the selected patients was about 49 years old.

All patients showed significant increase in the platelet count after one session and remained at appropriate levels during the follow-up period.

Postembolization syndrome was the most common complication and noted in in 14 patients (93.3%). Ascites reported in 3 patients (20%). Portal vein thrombosis reported in 2 patient (13.3%) left sided pleural effusion developed in 1 patient (6.6%). No pancreatitis or splenic abscess reported. None of the patients developed septic shock. No post procedure mortality occurred.

Conclusion: Partial splenic artery embolization is not without risks, but proven to be effective treatment for thrombocytopenia in cirrhotic patients with hypersplenism. It is performed under local anesthesia, thus is suitable in surgically unfit patients. It achieves improvement of hematological status with less complications as well as preservation splenic role in immunity.

Key Words: *Partial splenic artery embolization (PSE) – Hypersplenism – Liver cirrhosis – Thrombocytopenia – Platelets.*

Introduction

IT is well known that Egypt is one of the world's highest of hepatitis C virus (HCV) infection. "Just about every family in Egypt is touched by hepatitis C", says Dr. Henk Bekedam, WHO representative in the country. The bloodborne virus, kills an estimated 40,000 Egyptians a year and at least 1 in 10 of the population aged 15 to 59 is infected. Estimates of HCV prevalence in Egypt range from 11% to 14% with 8 to 10 million having HCV antibodies and 5 to 7 million having active infections [1].

According to the WHO data, liver disease deaths in Egypt reached 41,400 or 7.9% of total deaths. This ranks liver cirrhosis as the third cause of death in Egypt [2].

Along with HCV infection, clinical studies showed 70% to 90% of patients with chronic hepatitis, cirrhosis, or hepatocellular carcinoma had HCV infections. Co-infections with schistosomiasis caused more severe liver disease than infection with HCV alone [3].

Portal hypertension in the setting of cirrhosis commonly leads to splenomegaly [3].

Hypersplenism refers to a clinical syndrome characterized by splenomegaly, a variable combination of anemia, leucopenia and/or thrombocytopenia. Thrombocytopenia in portal hypertension is due to the dual mechanism of splenic sequestration of platelets and reduced hepatocellular function. TIPS treats portal hypertension but does not improve liver synthetic function and has not been found effective in Hypersplenism [4].

Cirrhosis is frequently associated with decreased hematologic indices, including thrombocytopenia and anemia. The prevalence of leukopenia amongst cirrhotic patients is more common than in the general population, and varies from 5% to 61% [5].

The pathogenesis of each hematologic deficiency in cirrhotic patients is multi-factorial in nature [3].

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Decreased hematologic indices can have significant clinical Results. Thrombocytopenia increases a patient's risk of spontaneous bleeding, and may prevent surgical or endovascular interventions. Leukopenia decreases the patient's ability to overcome infection, and may serve as a contraindication to the use of chemotherapy in hepatocellular carcinoma. Anemia places a patient at increased risk should bleeding occur, may prevent surgical or endovascular interventions and can leave a patient dependent on transfusions [5].

Operative splenectomy can be used to treat splenomegaly in cirrhotic patients. While splenectomy is an effective treatment of splenomegaly in the setting of cirrhosis, it is not without risk. Major complications include portal vein thrombosis and sepsis. Additionally, some cirrhotic patients may be poor surgical candidates, thus necessitating alternative approaches to splenomegaly in some cirrhotic patients [3].

In 1973, Maddison performed the first splenic artery embolization. An intra-arterial embolization of the splenic artery utilizing autologous clot as the embolic agent. The patient responded well and no complications were reported at 5-months follow-up [6].

Despite Maddison's early success, numerous complications of total splenic artery embolization were soon discovered. Complications included splenic abscess, splenic rupture, pneumonia, septicemia, and death. In response to these complications, Spigos et al., transitioned to partial splenic embolization (PSE) paired with antibiotic prophylaxis and demonstrated significantly better outcomes [7].

Now partial splenic embolization gained popularity and served as a therapeutic option for cirrhotic patients with Hypersplenism who were poor surgical candidates [3].

PSE has a direct effect on the spleen and may cause improved hepatic function. The improvement may be due to an immunologic mechanism, or because of decreased splenic venous flow, leading to compensatory increase in flow in the hepatic artery and superior mesenteric and vein, which may result in more nutritious flow of blood to the liver [8].

Patients and Methods

Study place: Interventional Radiology Unit, Ain Shams University Hospitals, Cairo, Egypt.

Sample size: 15 consecutive patients from July 2017 to December 2018.

The patients were referred form Gastroenterology department for correction of thrombocytopenia in cirrhotic patients with splenomegaly not suitable for surgical splenectomy.

The study included 14 male patients and 1 female patient ranging from 35-56 years old with average 49 years.

Written consent was obtained form all patients after full explanation of the procedure and its outcomes as well as complications.

Inclusion criteria: Cirrhotic patients with hypersplenism and Bleeding tendency.

Exclusion criteria: Elevated liver functions total bilirubin more than 2.5mg/dl, hepatocellular carcinoma, patients with a history of alcohol consumption, smoking, or the administration of drugs that could affect platelet function, such as aspirin and anticancer drugs, 4. Pyemia or other severe infections, Renal disease and high Serum creatinine.

Equipment: Monoplane angiographic machine (Toshiba Infinix Cath lab)-5 French cobra catheter-hydrophilic guide wire 150cm-Iodinated contrast (Scanlux® 370mg/ml) - Embolizing material (Emboshere particles or Gelfom).

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

Paired sample *t*-test of significance was used when comparing between related sample.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *p*-value was considered significant as the following:

- Probability (*p*-value).
- *p*-value <0.05 was considered significant.
- *p*-value <0.001 was considered as highly significant.
- *p*-value >0.05 was considered insignificant.

The study was approved by the Ethics Board of Ain Shams University.

Indications of partial splenic artery embolization in liver cirrhosis.

Cirrhotic patients with Hypersplenism and symptoms of thrombocytopenia.

Technique and methods:

Two techniques can be used to perform Partial splenic artery embolization.

1- *Low pressure flow control protocol (Non-selective):* The tip of the catheter placed at the main splenic artery distal to last pancreatic branch **[9]**.

2- *Embolization of the lower or upper polar splenic artery (Selective):* The catheter tip is positioned in the main branch of the lower polar splenic artery **[10]**.

In this study, nonselective method is used:

Under strict aseptic conditions, PSE performed in the following processes:

- A 5.0 French catheter inserted into the femoral artery using Seldinger maneuver.
- Angiography of the Celiac trunk and selective angiography of the splenic artery is performed to investigate the splenic arteries distribution and collateral circulation.
- The tip of the catheter then placed as proximal as possible to the hilum of the spleen, insuring it is distal to last pancreatic branch to avoid non desirable embolization of the spleen that may cause the pancreatic complication.
- Then gelfoam particles or Emboshere particles, suspended in contrast medium are used to achieve proper Embolization.
- The target of embolization is 40-60% of splenic parenchyma. To achieve this, embolization is performed by repeated injections of gelfoam particles or Emboshere particles under angiography control.
- Immediate angiography is performed after each injection with assessment of the extent of embolization, roughly, by comparing the percentage of the ablated splenic parenchyma seen at post-embolization angiography with the total splenic parenchyma area in pre-embolization angiography.
- After reaching the targets of 40-60% ablation of the splenic parenchyma, the embolization session ended.
- The catheter and vascular access device then removed followed by manual compression for hemostasis.

Post embolization care:

Analgesics and antibiotic for 5-10 days is given to the patients. follow-up after one month of the procedure by clinical examination, Platelet count, creatinine level and abdominal ultrasound and/or CT abdomen.

The study was approved by the Ethics Board of Ain Shams University.

Results

The aim of this work was to evaluate the effect of partial splenic artery embolization on platelet count and improving the thrombocytopenia in cirrhotic patient with hypersplenism. Fifteen patients with chronic liver disease and hypersplenism were included.

HCV infection and bilharzial disease are the causes of cirrhosis in our study group. HCV infection only founded in 8 patients (53%), bilharzial disease only in 1 patient (6.7%) and mixed HCV and bilharzial infection in 6 patients (40%) (Table 2).

All of the 15 patients (100%) showed Bleeding tendency, while 10 patients (66.6%) showed anemic manifestations, history of hematemesis or melena was found in 12 patients (80%), left upper quadrant paint was found in 7 patients (46.6%) and abdominal enlargement was found in 6 patients (40%) (Table 3).

Significant increase in the platelet count were noticed and the results were all statistically highly significant (p-value <0.001). Mean platelet count was 36.313± 12.198/uL before the maneuver and changed to 109.625±36.683/uL after one month follow-up (Table 4).

As regarding complications, Postembolization syndrome was the most common complication which was reported in 14 patients (93.3%) (Fig. 1). Ascites developed in 3 patients (20%). Portal vein thrombosis was developed in 2 patients (13.3%) which was most likely as result to rapid increase of the platelets with decrease of the blood flow in the portal vein resulting in hypercoagulable state of the portal vein flow (Fig. 3), the patient was admitted to the hospital, treated with liver support medications, anticoagulant, antibiotic as well as diuretics for the ascites. Left sided effusion was reported in 1 patient (6.7%) (Fig. 2) which is related mainly to the restriction of breathing caused by the left upper quadrant pain after PSE, pleural reaction, and inadequate lymph drainage of inflammatory effusions. No other complications have been reported (Table 5).

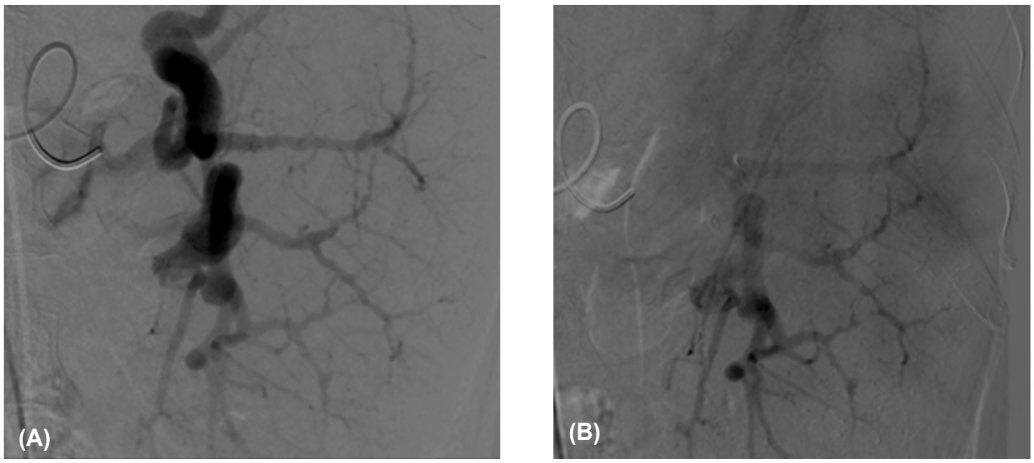

Fig. (1): 53 years old male patient with HCV infection, splenomegaly, liver cirrhosis and thrombocytopenia (platelets 19,000 /1 L) presented with repeated bleeding varices underwent PSE (A): Pre-embolization angiogram reveals normal splenic plush. Non-selective PSE was done with the catheter tip positioned in the main splenic artery with injection of the embolizing material (Gelfoam). (B): Post embolization angiogram showing occlusion of multiple small branches. Following the procedure, the platelet count reached 88,000/1 L Patient showed symptoms of Post-embolization syndrome which was managed conservatively by administration of antibiotic and analgesics with patient reassurance and follow up with recovery in 2 days and hospital discharge.

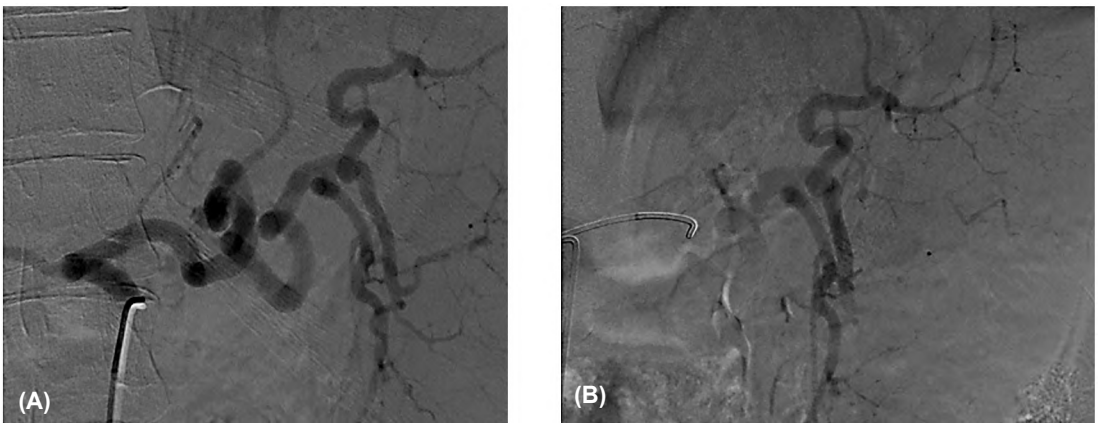

Fig. (2): A 48 years-old male patient with HCV and bilharzial infection, periportal fibrosis, splenomegaly, and Thrombocytopenia (platelets 52,000/1 L) presented with hematemesis and melena. Partial splenic artery emolization was done (A): Pre-embolization angiogram reveals normal splenic plush. Non-selective PSE was done with the catheter tip positioned in the main splenic artery with injection of the embolizing material (Embosphere). (B): Post embolization angiogram reveals occlusion of multiple small branches. Following the procedure, the platelet count reached 122,000 / 1 L. One week after embolization the patient showed cough and fever, CT scan was done diagnosing pleural effusion which managed with antibiotic and analgesics. No thoracentesis was needed

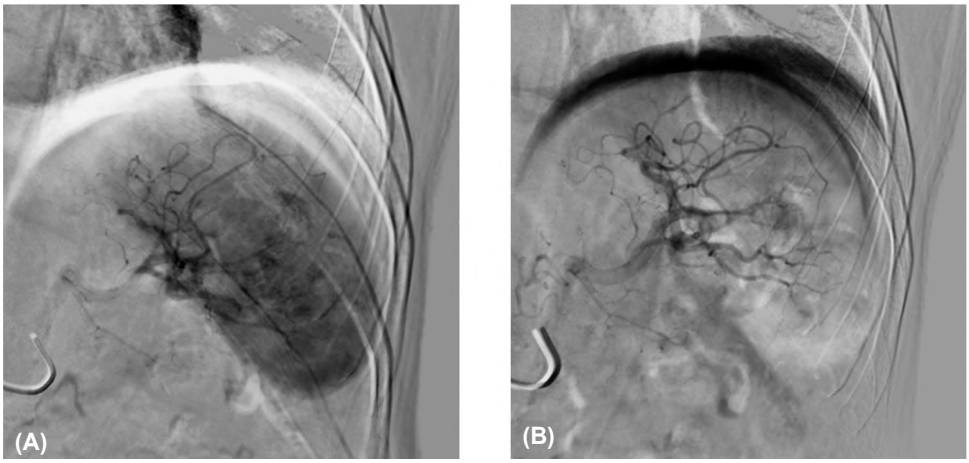

Fig. (3): A 52 years-old female patient with HCV and bilharzial infection, periportal fibrosis, splenomegaly, and Thrombocytopenia (platelets 37,000/1 L) presented repeated melena. Partial splenic artery emolization was done (A) Pre-embolization angiogram reveals normal splenic plush. Non- selective PSE was done with the catheter tip positioned in the main splenic artery with injection of the embolizing material (embosphere). (B) post embolization angiogram reveals decrease in splenic plush. Following the procedure, the platelet count reached 221,000/ 1 L. One week after the procedure the patient presented to the ER with abdominal pain more on the right hypochondrium and abdominal distension, CT scan was done revealed thrombosis of the right branch of the portal vein, the patient was admitted to the hospital, treated with liver support medications, anticoagulant antibiotic as well as diuretics for the ascites.

Table (1): Causes of chronic liver disease and hypersplenism.

Causes of chronic liver disease and hypersplenism	Number	Percentage
HCV infection	8	53
Mixed HCV and Bilharzial infection	6	40
Bilharzial infection	1	6.6

Table (2): Signs and symptoms of Cirrhosis in the studied group.

Symptoms	Number	Percentage
Bleeding tendency	15	100
Anemic manifestation	15	60
Hematemesis and/or melena	12	80
Left upper quadrant pain	7	46.6
Abdominal enlargement	6	24

Table (3): Value of the platelets before and after the Embolization.

	Platelets /μL				Paired *t*-test	
	Mean	SD	Min.	Max.	*t*	*p*-value
Before embolization	36,313	12.198	19,000	61,000	8.544	<0.001**
After embolization	109.625	36.683	67.000	221,000		

Table (4): Complications reported after the Embolization.

Complications	Number	Percentage
Postembolization syndrome	14	93.3
Ascites	3	20
Portal vein thrombosis	2	13.3
Left side pleural effusion	1	6.7
Pancreatitis	–	–
Splenic abscess	–	–

Discussion

Hypersplenism is a well-known complication of portal hypertension in cirrhosis, which can result in thrombocytopenia and/or leukocytopenia. In some patients, severe peripheral cytopenia may prevent treatments, such as interferon therapy, antineoplastic chemotherapy and major surgery, Spontaneous bleeding events may also occur [11]. Surgical splenectomy can eliminate hypersplenism induced blood cell destruction, but the morbidity of severe complications after splenectomy still ranges from 9.6% to 26.6%, including laparoscopic and open splenectomy. In addition, splenectomy is often associated with an increased long-term risk of septic events. PSE has been proposed as an effective alternative to splenectomy [12].

Since Maddison first described splenic artery embolization in 1973 [6] and Spigos developing PSE technique in 1979 to overcome the complications reported by Maddison in total artery embolization the procedure has developed greatly in materials and techniques, many studies were conducted with variable results and different success rates [7]. Many complications were noted over time. Despite those complications PSE is still very appreciable option in the treatment of thrombocytopenia in cirrhotic patients with hypersplenism as it avoids the complications arise form surgical splenectomy as well as patient with bleeding tendency not suitable for surgical intervention [10].

Our study was conducted to assess the efficacy of the partial splenic artery embolization on the platelet count in cirrhotic patient with hypersplenism in a country that is considered among highest incidence of chronic liver disease with death rate of 67.54per 100.000 of population ranks Liver Cirrhosis as the third cause of death in Egypt according to WHO [2]. This high rate of liver cirrhosis and its complications is considered major cause of disability in the country, limiting treatment options and increasing the risk of complications. One of these major complications is thrombocytopenia resulting from hypersplenism, increasing bleeding tendency, specially from esophageal varices.

Partial splenic artery embolization (PSE) is a simple, rapid procedure that is easily performed under local anesthesia. It has been demonstrated to effectively increase hematologic indices in cirrhotic patients with splenomegaly. This is particularly valuable amongst those cirrhotic patients who are not viable candidates for splenectomy [3].

Comparison between the current study results with other nearly similar studies:

Regarding platelet count:

Mean platelet count was 36.313 ± 12.198/uL before the PSE and changed to 109.625 ±36.683/uL at one month follow-up. Appreciable increase in the platelet count was noted and the results were all statistically highly significant (p-value <0.001).

This agrees with other studies investigating PSE in cirrhotic patients with hypersplenism.

Including Elmonem et al., (2011) [13], Hayashi et al., (2007) [14], Zhu et al., (2009) [12], N'Kontchou et al., (2005) [15] and Zhu et al., (2008) [16] who performed PSE in cirrhotic patients with thrombocytopenia using gelfoam, PVA and emnosphere.

Zhu et al., (2008) [16] reported that mean platelet count was 47.060± 14.850/ μL before the maneuver

and changed to 113.200 ± 17.600/ [illegible] after one month follow-up. Elmonem et al., (2011) **[13]** reported that mean platelet count was 41.300 ± 13.000/ [illegible] before the maneuver and changed to 115.8 ± 18.4/ [illegible] after one month follow-up. Hayashi et al., (2007) **[14]** reported that mean platelet count was 45,000 ± 11.700/ [illegible] before the maneuver and changed to 116.000 ± 51.000/ [illegible] after one month follow-up. Zhu et al., (2009) **[12]** reported that mean platelet count was 37.400 ± 12.300/ [illegible] before the maneuver and changed to about 110.000 / [illegible] after one month follow-up. N'Kontchou et al., (2005) **[15]** reported that mean platelet count was 48.000 ± 14.000/ [illegible] before the maneuver and changed to 137.500 ± 77.400/ [illegible] after one month follow-up.

So, this study confirmed the previous results showing that PSE is highly effective in improving thrombocytopenia in patients with chronic liver disease.

Regarding the Complications following the procedure:

Postembolization syndrome was the most frequent complication and occurred in 14 out of 15 patients (93.3%). These results agree with:

Zhu et al., (2008) **[16]** found that the post-embolization syndrome was the most common complication and occurred in more than 90.6% of cases with gelfoamas embolization material and 100% in patients with PVA as embolization materials. Zhu et al., (2009) **[12]** found that the post-embolization syndrome was the most common complication and occurred in more than 91.2% of cases. Elmonem et al., (2011) **[13]** found that the post-embolization syndrome was the most common complication and occurred in more than 91.3 % of cases.

Also, Kim et al., (2007) **[17]**, Hayashi et al., (2007) **[1]** and Lee et al., (2007) **[18]** who reported Postembolization syndrome as the most common complication and occurred in 100% of cases.

This complication was managed conservatively by antipyretics and antibiotics, and the patients was discharged from the hospital as soon as symptoms withdrawal.

In this study, three patients (20%) developed transient ascites. Similar results were seen in the study of:

- Lee et al., (2007) **[18]** who reported ascites in 10%.
- Zhu et al., (2009) **[12]** who reported ascites in 116.6%.
- Zhu et al., (2008) **[16]** who reported ascites in 9.4 with gelfoam and 10.7% with PVA.
- Amin et al., (2009) **[19]** who reported ascites in 10%.

It was managed by diuretics and liver supportive treatment, the ascites resolved within a month. In this study, one patient (6.6%) developed mild left sided pleural effusion which confirmed by ultrasound and CT scan. This goes with Elmonem et al., (2011) **[13]** and who reported the complication in 8.7% of the patients. Zhu et al., (2008) **[16]** who reported the complication in 10.7% of the patients.

The condition resolved within 2 weeks with conservative treatment only, no intervention or aspiration needed.

In this study, two patients (13.3%) developed Portal vein thrombosis. While; Zhu et al., (2008) **[16]** reported Portal vein thrombosis in 7.1% of cases. N'Kontchou et al., (2005) **[15]** who reported Portal vein thrombosis in 6.3% of cases.

Other possible complications of partial splenic artery embolization as pancreatitis, peritonitis and Splenic abscess were not reported in our patients.

These results confirm the Findings of previous studies showing that partial splenic artery embolization is not without risks, but with good preparations, proper technique and good selection of the patients; complications can be minimized with better outcome and prognosis.

Conclusion:

Partial splenic artery embolization is not without risks, but proven to be effective treatment for thrombocytopenia in cirrhotic patients with hypersplenism. It is performed under local anesthesia, thus is suitable in surgically unfit patients. It achieves improvement of hematological status with less complications as well as preservation of splenic role in immunity.

There is statistically significant improvement in platelet count before and after partial splenic artery embolization.

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التغير فى الصفائح الدموية كنتيجة للحقن الجرئى لشرايين الطحال فى حالات تضخم الطحال المصاحب للتليف الكبدى

تضخم الطحال المصاحب للتليف الكبدى هو أحد المضاعفات المعروفة لإرتفاع ضغط الوريد البابىالكبدى، ومما قد يؤدى إلى الإصابة بنقص الصفائح الدموية بل ونقص عام فى الدم قد يحد من قدرتنا على إعضاء العلاج المناسب بل ويمنع إجراء الجراحات الضرورية وقد يؤدى بالمريض إلى النزيف.

الإستئصال الجراحى للطحال قد يكون حلاً فى علاج نقص مكونات الدم، ولكن قد يتعرض المريض للعديد من المضاعفات الجراحية بنسبة ٢٧٪، كما أن إستئصال الطحال يرفع من نسب إصابة المريض بالعدوى، ولذا فإن الحقن الجرئى لشرايين الطحال قد يكون بديلاً فعالاً فى العلاج.

منذ الظهور الأول لحقن شرايين الطحال على يد ماديسون عام ١٩٧٣ والتعديلات التى أدخلها سبيجون للتغلب على المشكلات التى واجهها ماديسون ، تطورت المعدات والوسائل المستخدمة كثيراً، كما تم إجراء العديد والعديد من الدراسات، وخلال تلك الفترة ظهر العديد من المضاعفات للعملية و لكن على الرغم من ذلك مازال الحقن الجزئى لشرايين الطحال علاج مناسب لنقص الصفائح الدموية فى مرضى تضخم الطحال المصاحب للتليف الكبدى وذلك للتغلب على مضاعفات الإستئصال الجراحى وكذلك بعض الحالات التى من الغير المناسب إجراء التدخل الجراحى كحالات النزف الشديدة.

ولهذا تم إجراء هذه الدراسة لتقييم كفاءة الحقن الجرئى لشرايين الطحال فى زيادة عدد الصفائحالدموية فى مرضى التليف الكبدى فى دولة تعتبر من أعلى الدول فى معدل الإصابة بالتليف الكبدى المزمن ومعدل وفاة يجعله ثالث أكبر مسبب للوفاة بالبلاد طبقاً لمنظمة الصحة العالمية. وهذا المعدل المرتفع يجعل مضاعفات المرض من أكبر مسببات الإعاقة فى البلاد ويحد من القدرة على إستخدام العلاجات المناسبة وخصوصاً فى حالات نقص الصفائح الدموية والتى ترفع من إحتمالات النزيف باستمرار كما فى دوالى المرئ.

لقد تم إجراء هذه الدراسة على خمسة عشر مريضاً بنقص الصفائح الدموية الناتج عن تضخم الطحال فى حالات للتليف الكبدى فى الفترة من ٢٠١٧ وحتى ديسمبر ٢٠١٨ جميع المرضى تم العديد من الفحوصات للتأكد من جاهزيتهم لإجراء العملية وشملت صورة دم كاملة ووظائف كبد وكلى وكذلك فحوصات الموجات الصوتية على البطن قد كان أشهر سبب لتضخم الصحال الإلتهاب المزمن بفيروس الكبد الوبائى ج (٥٣٪) يليه الأصابة بمرض البلهارسيا (٧٪) وباقى المرضى مصابون بالمرضين معاً (٤٠٪).

تم شرح الفوائد والمخاطر المحتملة لكل مريض والحصول على الموافقة المسبقة. يتم إدخال قسطرة عبر شريان الفخذ صعوداً عبر الشريان الأورطى مروراً بالجذع البطنى ثم الوصول إلى شريان الصحال وفى البداية يتم تصوير شريان الطحال لتحديد حجم الطحال. وبعد ذلك يتم حقن المغلقة المتناهية الصغر عبر القسطرة وتتوقف العملية عندما يتم إنسداد حوالى٤٠ إلى ٦٠ بالمائة من الشرايين المغذية للطحال.

وبعد إجراء العملية يتم وصف المضادات الحيوية اللازمة للمرضى لمدة عشرة أيام وتتم متابعة المريض لمدة شهر بعد العملية بالتحاليل والفحوصات الازمة ويمكن عمل أشعة مقطعية عند الأشتباه فى تكوين خراج بالطحال أو وجود علامات تسمم بالدم.

ومن دراسة دالصفائح الدموية فى عينات الدم المسحوبة من المرضى بعد إجراء العملية والتى أرتفع فيها متوسط الصفائح الدموية من ٣٦.٣١٣ إلى ١٠٩.٦٢٥/ميكرو لتر مما يؤكد أم الحقن الجرئى لشرايين الطحال هو وسيلة علاجية فعالة لعلاج نقص الصفائح الدموية فى حالات فرط نشاط الطحال الثانوى لمرض الكبد المزمن. وهو إجراء بسيط وسريع يتم تنفيذه بسهولة تحت التخدير الموضعى. ويسمح بالحفاظ على أنسجة الطحال حتى تكون كافية لحماية الجسم ضد العدوى.