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Percutaneous Sclerotherapy for Management of Large Hepatic Haemangioma: First Series from Bangladesh

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ABSTRACT

Introduction: Hepatic haemangiomas are non-malignant hepatic vascular malformations, which are usually asymptomatic, but may be a potential cause of life-threatening complications requiring urgent surgical intervention. Methods: Of the wide range of treatment modalities currently available for hepatic haemangiomas, we opted for percutaneous sclerotherapy with a combination of bleomycin and lipiodol. Results: We included 20 patients with hepatic haemangiomas in this single arm, single centre study, all underwent percutaneous sclerotherapy with combination bleomycin and lipiodol. Patients tolerated the procedure well, with no significant adverse event reported. Reduction of size of hepatic haemangiomas was achieved in 70% of patients at 6-month follow-up. Conclusion: The study shows that percutaneous sclerotherapy with bleomycin and lipiodol is safe and effective for management of hepatic haemangiomas.

INTRODUCTION

The International Society for the Study of Vascular Anomalies classifies vascular anomalies into vasoproliferative or neoplasms and malformations without mitosis. Hepatic haemangiomas are now classified as venous malformations [1,2], glucose transporter 1-negative, low-flow venous malformations composed of clusters of blood-filled cavities lined by endothelial cells and fed by the hepatic artery [3].

Hepatic haemangioma is the most typical benign hepatic space-occupying lesion. It has been estimated that up to 20% of people have this condition in their livers. The prevalence is higher in those between 30 years to 50 years of age and in females [4,5]. Hepatic haemangiomas usually do not increase in size. Large hepatic hemangioma (>5cm) may cause non-specific symptoms like pain in the upper right abdomen, early satiety, nausea and vomiting, and are also a potential cause of heart failure, consumptive thrombocytopenia, spontaneous or traumatic rupture, that may be life-threatening [6,7,8].

Ultrasonography, computed tomography (CT) and magnetic resonance imaging confirm the diagnosis. The characteristic finding of hepatic haemangioma on triphasic abdominal CT scan is centripetal peripheral discontinuous nodular enhancement [5]. Wide range of treatment modalities are available for hepatic haemangiomas, ranging from surgical resection to trans-arterial embolization (TAE), radiofrequency ablation (RFA), microwave ablation and percutaneous sclerotherapy [7]. Despite having access to TAE and RFA, we opted for percutaneous sclerotherapy, as between these three, the later one is easier to perform.

Bangladesh is a middle-income country, where treatment cost is not reimbursed. Cost is therefore an important factor while opting for any treatment in Bangladesh, especially for a benign diagnosis like hepatic haemangioma.

Complications of hepatic haemangiomas are rare and depend on the size and location of the lesion. Common complications include acute and chronic inflammation, rupture, intralesional and intraperitoneal bleeding, thrombosis, and fibrosis, to name a few.

In this present study we share our experience of treating hepatic haemangiomas by percutaneous, transhepatic sclerotherapy for the first time from Bangladesh. Bangladesh.

METHODS

All patients included in this study had hepatic haemangiomas (Table 1). After skin sterilization, 10 ml to 15 ml local anaesthetic agent (2% lidocaine hydrochloride) was injected around the hepatic capsule and in the intercostal space and overlying sub-cutaneous tissue. Prophylactic intravenous antibiotic ceftriaxone (1 gm) was administered in every patient.

Table 1: Patient characteristics and study outcomes

Patient characteristics	
N	20
F:M	12: 8
Age	25 - 55 years
Right lobe hepatic haemangioma	15
Left lobe hepatic haemangioma	5
Size	
At baseline	3.5 - 7.4 cm
At 6-month follow-up	3 - 4.5 cm
Reduction of hepatic haemangioma at 6-months follow up	14
Adverse events	
Mild right hypochondriac pain	10
Pain radiating to the right shoulder	5
Post-procedure nausea	3

Hepatic haemangioma was punctured percutaneously through transhepatic route, under ultrasound guidance with 2-gauge spinal Chiba needle. Needle weas carefully placed at the centre of the haemangioma to avoid peripheral scar formation, as central scars do not seem to have significant connection with the venous channels of hepatic haemangiomas. Combination of approx. 50 IU to 60 IU bleomycin sulfate (Injection Bleonix, 15 unit/vial; Beacon Pharmaceuticals PLC, Bangladesh) diluted with 10 ml distilled water and mixed with 10 ml lipiodol was then slowly injected under ultrasound guidance into the hepatic haemangiomas over approx. 30 sec to 45 sec.

Needle was removed slowly and manual pressure applied to the puncture site for approx. 5 minutes. Next tight, pressure gauge bandage was applied to the puncture site and patient placed in right lateral position for approx. 2 hours.

Procedures were performed under total intravascular anesthesia using injection propofol (1 mg/kg body weight) by a qualified anesthetist. The patient's vital signs and cardiac rhythms were monitored continuously. Patients were monitored for approx. 6 hours post-procedure. International normalized ratio > 1.5 and/or platelet count <100,000/μL were considered as contraindications for the procedure and corrected with fresh frozen plasma and aphaeresis platelet transfusion respectively before the procedure. Patients were monitored for 24 hours post-procedure before being discharged. Injection proton pump inhibitor (40 mg; intravenously), injection timonium methyl sulphate (5 mg; intravenously) and acetaminophen (500 mg; orally) were used to relieve minor symptoms of the patients. At follow-up, liver function tests and abdominal ultrasounds were performed at 6 months.

DISCUSSION

Treatment for hepatic hemangiomas is usually unnecessary as they have no malignant potential and do not cause hormonal or biochemical derangements. Treatment is however recommended for patients with significant (≥5 cm) and/or symptomatic hepatic haemangiomas [1]. In our case, however, the indication was extended. In Bangladesh, the risk of major abdominal trauma is not insignificant. For example, we have a high incidence of road traffic accidents. The country's sudden economic expansion has seen infrastructural development over the last decade. New roads and highways are coming up, clogged with slow to vast moving vehicles, from paddled trishaws to heavy vehicles and expensive sedans and sports utility vehicle. However, in sharp contrast, there is an acute shortage of skilled drivers and general traffic sense. In January 2024 only, there were 989 road traffic accidents on the Padma Expressway, unprecedented anywhere in the world [9]. The country is a riverine one, and riverway accidents are also common here. Our economic boom has seen a boom in our construction sector and construction site accidents are also frequent as protective measures and general awareness are lacking. Natural calamities are part and parcel of Bangladeshi life, for example regular floods and cyclones add to our miseries. On the contrary, Hepatobiliary surgery is still in its infancy in the country, restricted to a handful of centers in major cities. As such, such patients are often left with no other option, but conservative management due to lack of appropriate resources, although emergency surgery is indicated for this life-threatening complication. It is therefore not infrequent to come across patients with traumatic ruptured hepatic haemangiomas with catastrophic outcome in Bangladesh. We opted for percutaneous sclerotherapy for large hepatic haemangiomas (≥5 cm) and symptomatic ones, like any advanced centre worldwide. However, we have also expanded our treatment indication (Table 2). Patients with risk of potential complications were excluded from the study (Table 3).

Table 2: Indications for treating hepatic haemangiomas

Giant hepatic haemangiomas (≥5 cm)
Symptomatic hepatic haemangiomas
Left lobe hepatic haemangiomas close to the heart
Hepatic haemangiomas close to the hepatic surface with little or no intervening hepatic tissue

Table 3: Exclusion criteria

Hepatic impairment
Renal impairment
Pulmonary fibrosis
Allergy to contrast media

Although prolonged retention of sclerosing agents in low-flow vascular malformations is always associated with risk of endothelial damage, thrombus formation, tissue ischaemia and necrosis [10], such an approach is not new. It has been adopted especially for management of non-visceral vascular malformations in the head and neck region. Studies have shown that intra-lesional bleomycin injection is effective in complete or partial resolution in head and neck haemangiomas and vascular or venous malformations and facial malformations [11,12].

Various sclerosing agents have been used for hepatic haemangioma management including bleomycin, pingyangmycin (bleomycin A5 hydrochloride), lipiodol, ethanol and polyvinyl alcohol [13]. The first report of percutaneous sclerotherapy for hepatic haemangioma used ethanol in two patients [4]. Bleomycin is an mTOR inhibitor, which has been explored more in TAE to manage hepatic haemangiomas [14]. Bleomycin destroys vascular endothelial by inhibiting DNA synthesis and causing sclerosis. It is often preferred as it is associated with lower incidence of adverse events compared to other sclerosing agents [15]. Lipiodol, on the other hand, is radio-opaque and can deliver drugs. However, its role in percutaneous sclerotherapy is yet to be clarified [13]. In our center, we use bleomycin in combination with lipiodol for percutaneous sclerotherapy to manage hepatic haemangiomas.

Our results are comparable with that of studies conducted in other centres in different parts of the world. One of the earliest series of sclerotherapy for hepatic haemangioma using bleomycin and lipiodol involving five patients reported 25% to 63.5% reduction of tumor size at 5-months follow up [8]. A much larger study on 28 patients subsequently reported 65.7% tumor size reduction at 6-months [5]. We achieved reduction of size of hepatic haemangiomas in 14 out of 20 patients (70%). Our data is more or less consistent with the findings of a meta-analysis [15] and another review of 18 cohort studies that reported 89.9% volume reduction [16].

Another important aspect of our study is the low incidence of adverse events in our treated patients. Several studies have reported major complications like decrease in haemoglobin level, iscahemic cholecystitis and persistent post-embolization syndrome in 3.8% to 12% cases [17, 18, 19, 20]. Unusual complications like leakage of contrast to sub-segmental portal vein and leakage of sclerosing agent around liver surface leading to severe pain have also been reported in the literature. Minor complications like post-embolization syndrome, elevated liver enzymes and transient abdominal pain have been seen in 68% to 100% cases in different studies [5, 17, 18, 19, 20]. In our series, 50% of patients complained of transient abdominal pain, which resolved with conservative treatment. None of our patients experienced any serious complications.

Our study, however, has some limitations. It was a single centre, single arm study without any control arm. We used fixed dose bleomycin and lipiodol, without dose adjustment for body weight or size of hepatic haemangioma. Having said so, this may be noted that this same fixed dose approach has been adopted by other studies and in fact, the optimal dose of bleomycin for this indication is yet to be determined. The dose of bleomycin and lipiodol, that we used is consistent with other studies.

This study demonstrates the safety and efficacy of percutaneous sclerotherapy with bleomycin and lipiodol combination for treatment of hepatic haemangiomas. Our technique was flawless

and patient benefit was significant. We propose larger, prospective, multi-centre, randomized clinical trial to determine the best possible treatment option for hepatic haemangiomas.

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