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Balloon venoplasty as primary modality of treatment in children with Budd–Chiari syndrome

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ABSTRACT

Introduction: Budd–Chiari syndrome (BCS) is a rare condition affecting children. It is characterized by occlusion of venous outflow from liver at the level of hepatic veins (HV) or inferior vena cava (IVC). The management of BCS in children revolves around forming new collaterals for venous outflow or by elimination of blockage in the venous outflow tracts. These can be achieved by balloon venoplasty (BV), transjugular intrahepatic portosystemic shunting (TIPSS) or open shunt surgeries.
Aim: The aim of this study is to evaluate the management of BCS in children with balloon venoplasty as primary modality of treatment.
Materials and methods: This is a retrospective study which includes children diagnosed with BCS managed by balloon venoplasty by a single surgeon at a single institute. Once confirmed, the child was posted for balloon venoplasty and liver biopsy. When venoplasty was successful, child was subsequently heparinized and dose titrated. Routine follow up was mandated and dose adjustments were continued during follow up. In case of unsuccessful venoplasty, depending on the liver biopsy report, shunt procedure or liver transplantation is offered to patients. An algorithm was then designed for management of BCS in children.
Results: A total of 35 children who underwent evaluation of symptoms associated with Budd–Chiari syndrome were included in the study. Of all the children, 14 are alive and symptom free, 9 are deceased and 12 lost to follow up. Hepatic vein was the most common site of obstruction (85%), followed by both IVC and HV (15%). Overall, in 35 children, 26 had a successful balloon venoplasty, in 3 venoplasty was not done (2 spontaneous resolution and 1 died awaiting), in 6 it was unsuccessful (3 technical failures: 1 underwent TIPSS and 2 lost to follow up, 3 clinical failures: portocaval shunt for failed venoplasty).
Conclusion: Budd–Chiari syndrome is a rare condition affecting children. Balloon venoplasty as a primary modality of treatment for BCS is a promising option for management in children. Early and aggressive use of radiological intervention can help achieve recanalization in children.
Type of study: Clinical research paper.
Level of evidence: Level IV.

Budd–Chiari syndrome (BCS) is a rare condition affecting children. It was first described by George Budd in 1845 and later its pathological features were added by Hans Chiari in 1899. It is characterized by occlusion of venous outflow from liver at the level of hepatic veins (HV) or inferior vena cava (IVC). It can be either primary owing to intrinsic blockage of hepatic veins or secondary owing to external compression from tumors on the hepatic veins. This being a rare condition in children, often it is missed earlier until florid state is reached with massive hepatosplenomegaly, ascites and portal hypertension. It requires a high index of suspicion for diagnosing BCS which usually presents with triad of hepatomegaly, ascites and pain in abdomen. The management of BCS in children revolves around forming new collaterals for venous outflow or by elimination of blockage in the venous outflow tracts. The former can be achieved by transjugular intrahepatic portosystemic shunting (TIPSS) procedures or open shunt procedures with use of vein grafts. The latter can be managed by a relatively newer technique where a balloon is passed over guide wire into the narrowed hepatic vein and dilated to establish venous outflow. If the liver is cirrhotic, a liver transplantation is required. This study is aimed at evaluating the management of BCS in children with balloon venoplasty as primary modality of treatment.

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1. Materials and methods

This was a retrospective study which includes children diagnosed with BCS managed by balloon venoplasty by a single surgeon at a single institute between 2000 and 2018. Children with suspected BCS were evaluated and the diagnosis was confirmed by blocked hepatic venous outflow either at the level of hepatic veins or suprahepatic IVC by M mode ultrasound Doppler and magnetic resonance venogram (MRV). Once confirmed, the child was posted for balloon venoplasty (BV) and liver biopsy. Under fluoroscopic guidance, hepatic venogram was performed by femoral, transjugular or transhepatic routes. Once the femoral or internal jugular vein was cannulated, a 4 or 5 Fr sheath is introduced into the vessel and then a guiding catheter is railroaded to locate the hepatic vein ostium. Once inside the desired vein, a balloon catheter is railroaded over the guide wire and balloon is inflated with contrast. Yukon or Terumo balloon catheter is used, 3 mm or upwards in size depending on the age of the patient. Balloon dilatation of the narrow segment was performed and outflow established. At the same time a liver biopsy was performed. When venoplasty was successful, child was subsequently heparinized, and dose titrated as per Vanderbilt protocol [1]. Subsequently, bolus doses of low molecular weight heparin (LMWH) were introduced. At the time of discharge, LMWH was replaced by warfarin sodium (Coumadin®) to maintain a target international normalized ratio (INR) between 2.0 and 3.0. Routine follow up was mandated and the period ranged between 12 months to 180 months with median of 60 months. The dose adjustments were continued during follow up. In case of an unsuccessful venoplasty, the child was offered portosystemic shunt procedure if liver was noncirrhotic on biopsy or liver transplant if liver was cirrhotic on biopsy.

2. Observations

A total of 35 children who underwent evaluation of symptoms associated with Budd–Chiari syndrome were included in the study. Among them, 15 were females and 20 were males with mean age of 30 months (range between 5 and 144 months). Of all the children, 14 are alive and symptom free, 9 are deceased and 12 lost to follow up.

The average age of children at intervention was 30 months. Abdominal distension was the presenting complaint in 88% of children. Ascites and hepatomegaly were seen in 89% of children. Splenomegaly was found in 62% at presentation. Dilated anterior abdominal veins were seen in the 60% of children. In the work up of these children, we found three of them to have deficiency of protein C and protein S (9%) and in one, anti-phospholipid antibodies (APLA) were detected.

Hepatic vein was the most common site of obstruction (85%), followed by both IVC and HV (15%). Isolated IVC block was not seen in any child. None of them developed hepatic encephalopathy. Hematemesis was seen in 3 children in the follow up period (9%). One child developed subdural hematoma (SDH) while he was on anticoagulation and 1 had repeated episodes of epistaxis and was diagnosed to have hemophilia A.

Among the 14 alive and symptom free, all except one underwent an initial venoplasty. Transjugular route was successful in 10 of them. One had transhepatic dilatation who later underwent liver transplant for a failed balloon venoplasty, while in one case, even the transhepatic dilatation failed who later underwent a TIPSS. Transjugular route was successful in opening at least one blocked hepatic vein in the 13 alive children. One child recovered from symptoms while awaiting venoplasty and is currently symptom free.

Of the nine deceased, one died awaiting venoplasty and venoplasty was done in eight of them. It was successful in opening at least one blocked vein in five of them. In the other three, only a venogram was done and it was unable to cannulate the hepatic veins. Among the five postvenoplasty children, two of them died following portocaval shunt which was done in view of persistent symptoms and noncirrhotic liver biopsy, two had persistent symptoms and died owing to liver failure and one died awaiting shunt surgery. Among the three children in whom only venogram was done, one died after portocaval shunt procedure and two succumbed to liver failure. A portocaval shunt was performed after failed balloon venoplasty (technical failure or failure to relive the symptoms) with congested liver on biopsy and Gortex graft was used in all.

Out of the 12 who are lost to follow up, all except three had undergone balloon venoplasty and it was successful in opening blocked hepatic vein in nine of them. One spontaneously improved, while in two only IVC gram could be performed as hepatic vein could not be cannulated.

Post procedure, all were heparinized by bolus followed by infusion drip. Post removal of vascular sheath, the children were then put on LMWH injection and anticoagulation was monitored to keep a close watch on anti-factor Xa levels. An immediate re-balloon venoplasty was required in none of the patients while two required re-balloon venoplasty beyond two months following primary procedure.

Once discharged, they were shifted to warfarin and LWMH was stopped after three days. The dose of warfarin was titrated to maintain INR between 2 and 3. Propranolol was started in children who presented with features of portal hypertension to reduce the risk of bleeding.

3. Discussion

Budd–Chiari syndrome is characterized by blocked hepatic outflow which can be either primary owing to block in the hepatic vein or secondary owing to extrinsic compression. Owing to the blocked hepatic outflow, there is development of portal hypertension which may manifest as ascites, splenomegaly or variceal bleeding. If not managed appropriately, this condition may be fatal by three years after onset.

There are several etiological factors identified and the most widely accepted ones are hypercoagulable states like protein C and protein S deficiency, Antithrombin III deficiency, antiphospholipid antibody syndrome and hyperhomocystenemia among others. The other etiological factors identified include JAK 2 mutation, factor V Leiden mutation and factor II mutation [2].

The common symptoms associated are ascites, hepatomegaly and pain in abdomen. When the diagnosis is delayed, they may present with features of portal hypertension. Imaging modalities have enhanced the accuracy of diagnosis of this condition and earlier detection of suspected cases [3]. Magnetic resonance venogram provides anatomical details of hepatic veins, its confluence with the intrahepatic IVC and portal vein anatomy among other details to rule out an extrinsic compression causing outflow obstruction [4].

Once diagnosed, the treatment modalities described are to either essentially bypass the obstruction by shunting or to eliminate the obstruction. The operations described are portocaval shunting and TIPSS [5]. Balloon venoplasty is a relatively newer technique with less morbidity compared to the shunt procedures [6]. This was the choice of procedure in all our children and open shunts were performed when this failed to establish blood flow or had repeated episodes of reblockages of the hepatic veins without evidence of cirrhosis. Liver transplantation is another treatment option which has remained the cornerstone in the management of BCS in the Western world [7].

Balloon venoplasty was performed under general anesthesia in the cath lab. Transjugular route was the preferred route and most underwent venoplasty through this route except for two cases. In these two cases, venoplasty was performed by transfemoral route in one and percutaneous transhepatic route in the other.

Once access has been achieved through the routes described above, under fluoroscopic guidance the area of narrowing is identified and dilated with balloon catheter over guide wire. Post procedure the flow across recanalized vein is confirmed and the child is heparinized with a loading dose followed by maintenance dose. The activated partial thromboplastin time (aPTT) is monitored and kept between a tight range of 60 and 85 s and accordingly the dose of heparin is titrated as per Vanderbilt anticoagulation protocol [1].

Subsequently, the child is shifted to low molecular weight heparin (LMWH) injections given at dose of 0.5 mg/kg/day in two divided doses and dose titrated according to the anti-factor Xa levels as per the Vanderbilt protocol [1]. Once the dose of LMWH is established, the child is then discharged and advised follow up for monitoring of the anticoagulation. Post venoplasty, repeat Doppler ultrasonography is performed to check the patency of the occluded veins.

In our setting, oral anticoagulation is preferred over injectable LMWH owing to the difficulty in assessing anti-factor Xa levels in an outpatient setting, so invariably most of our children are shifted to oral warfarin. The INR is maintained between 2.0 and 3.0 and parents are advised to avoid food rich in vitamin K. After a period of one-year post balloon venoplasty, MRV is performed to check the status of the hepatic outflow and anticoagulation is then stopped. Further they are advised for follow up yearly for recurrence of symptoms.

Immediate postprocedure complication reported in other series are hepatic encephalopathy, neck hematoma and hemoperitoneum. We did not have any such immediate postprocedure complications. However, we did have complications associated with anticoagulation like subdural hematoma and prolonged bleeding following trivial injury.

TIPSS has been described in the literature for management of BCS [8]. We have not performed TIPSS for our children and one whose balloon venoplasty was unsuccessful has undergone TIPSS and is currently symptom free. Liver transplant can help ameliorate the signs and symptoms when the liver is cirrhotic [9].

In our hands we have not had much success with open portocaval shunts which were performed with a Gortex graft. Out of four children, three are deceased and one is lost to follow up. The problem we had with the open shunt procedures is the graft suitability. With bigger graft we noted vascular steal phenomenon, and with smaller graft we noted graft occlusion which was evident on Doppler scan.

Overall, in 35 children, 26 had a successful balloon venoplasty, in three venoplasty was not done (2 spontaneous resolution and 1 died awaiting), and in six it was unsuccessful (3 technical failures: 1 underwent TIPSS and 2 lost to follow up, 3 clinical failures: portocaval shunt for failed venoplasty).

A successful venoplasty is when we were able to open at least one blocked hepatic vein which is confirmed on table by performing a venography (Fig. 1). In our study so far, we have been able to recognize any predictors for success vs failure for balloon venoplasty. Technical failures were probably because of variations in the hepatic vein ostia and clinical failure owing to advanced stage of disease (Cirrhosis). Technical failures are identified on table, while clinical failure will have to be identified during the follow up on these patients by restoration of flow across hepatic veins and liver biopsy reports. As outlined in the algorithm mentioned, based on the clinical profile further management of these patients can be taken up.

There are a very few published studies on pediatric BCS and these include studies from Redkar et al., Nagral et al. and Kathuria et al. [10,11]. Our preliminary work was published with 25 cases [12].

The BCS report by Kathuria et al. had 46 children. They reported a mean age of 10.5 years. In their series, radiological intervention was done in 25 of them and the remaining 21 did not undergo any radiological intervention. Angioplasty was performed in three cases, stenting was performed in 19 cases and TIPSS in three cases. Of these children, stent blockage or narrowing of the vein was seen in five of them in whom a repeat intervention was done. They reported a success rate of 96% with only one fatality, a child who underwent TIPSS [11].

The study reported by Nagral et al. had 16 patients. Of these 11 underwent radiological intervention and five did not. Four of the 11 had venoplasty, five underwent TIPSS and two underwent stent placement. Among the five who did not have radiological intervention, four children are asymptomatic while one succumbed to the condition. They reported a success rate of 90 %, with 10 of the 11 doing well after the intervention and only one casualty following venoplasty [10].

Among the 21 without any radiological intervention in Kathuria et al., they reported that 19 of them survived. We had two survivors without any intervention, while Nagral et al. reported four such survivors [10,11].

Among the 9 who are deceased in our series (1 while awaiting venoplasty, 3 following portocaval shunt, 5 following successful venoplasty), all the five children had acute onset of symptoms beginning not more than 30 days. The ages of these children were 10, 6 and 9 years and the rest were less than a year old. Three of them had intractable ascites postprocedure which did not respond to medical line of management. All the children had palpable splenomegaly and dilated abdominal veins at presentation.

As reiterated by Seijo et al. that a stepwise management for BCS will improve long term outcomes [13], we attempt to make an algorithm for patient selection, intervention and postoperative management including follow up as a part of pediatric BCS (Fig. 2).

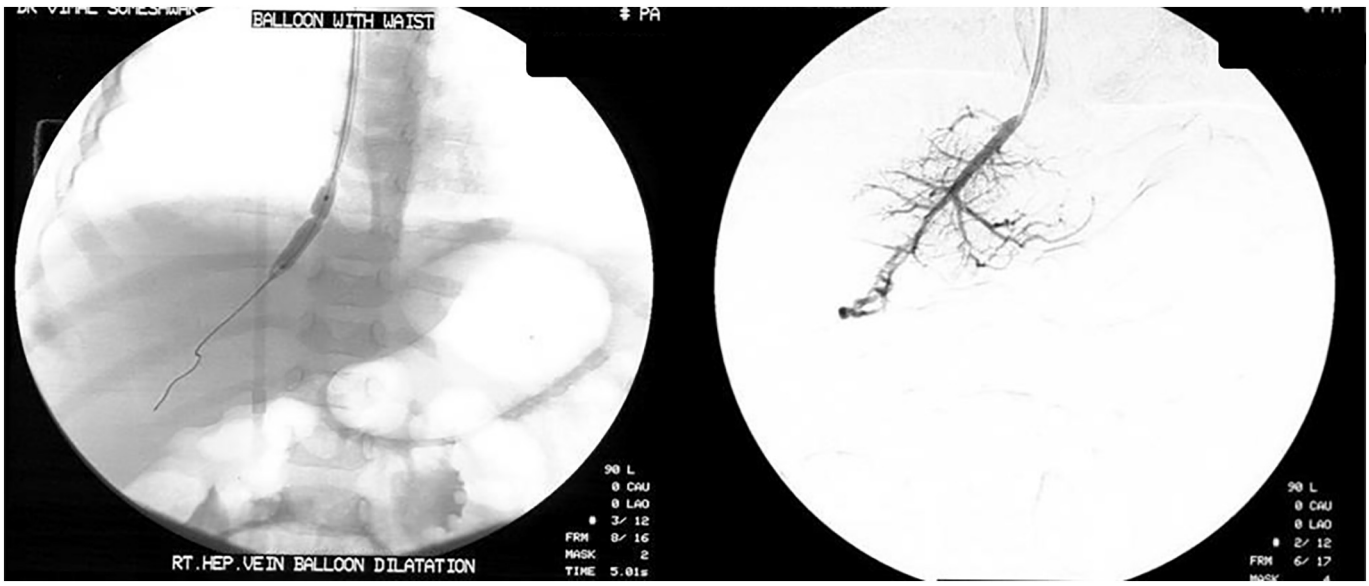

Fig. 1. Balloon venoplasty pre and post balloon dilatation.

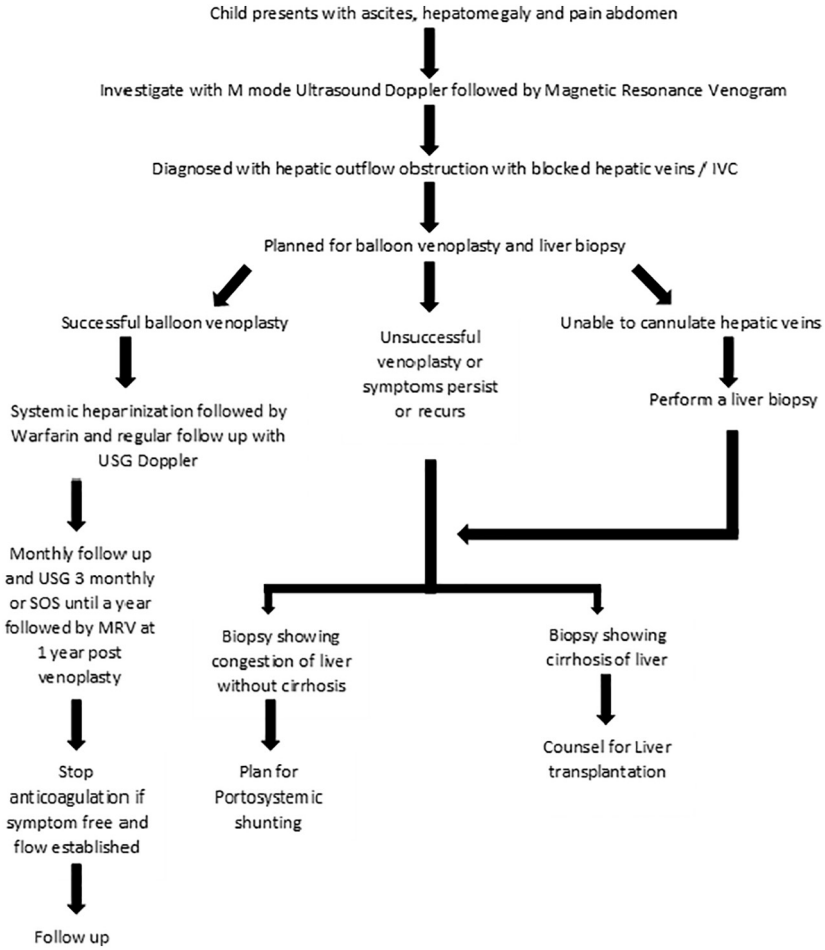

Fig. 2. Algorithm for management of pediatric Budd–Chiari syndrome.

4. Conclusion

Budd–Chiari syndrome is a rare condition affecting children. Timely diagnosis and prompt management will improve outcomes of these children. Balloon venoplasty as a primary modality of treatment for BCS is a promising option for management in children. Early and aggressive use of radiological intervention can help achieve recanalization in children. Protocolized follow up of these children will identify cases that may require further management in the form of portosystemic shunting or liver transplant.

References

[1] Sidonio R. Vanderbilt pediatric hematolgy anticoagulation guidance protocol n.d. http://www.vuneo.org/Heparin and enoxaparin guidance_8.2.12_final.pdf. [Accessed 29 July 2019].
[2] Valla DC. Budd–Chiari syndrome/hepatic venous outflow tract obstruction. Hepatol Int. 2018;12:168–80. https://doi.org/10.1007/s12072-017-9810-5.
[3] Misra V, Varma K, Singh DK, et al. The Budd–Chiari syndrome in a child: a case report and review of the literature. J Clin Diagnostic Res. 2012;6:1783–5. https://doi.org/10.7860/JCDR/2012/4525.2613.
[4] Ferral H, Behrens G, Lopera J. Budd–Chiari syndrome. Am J Roentgenol. 2012;199:737–45. https://doi.org/10.2214/AJR.12.9098.
[5] Cauchi JA, Oliff S, Baumann U, et al. The Budd–Chiari syndrome in children: the spectrum of management. J Pediatr Surg. 2006;41:1919–23. https://doi.org/10.1016/j.jpedsurg.2006.06.045.
[6] Correa Gaviria S, Ramírez AC, Espinoza Herrera YP. Restrepo Gutiérrez JC. A review of Budd–Chiari syndrome. Rev Colomb Gastroenterol. 2016;31:242–52. https://doi.org/10.22516/25007440.97.
[7] Cauchi JA, Oliff S, Baumann U, et al. The Budd–Chiari syndrome in children: the spectrum of management. J Pediatr Surg. 2006;41:1919–23. https://doi.org/10.1016/j.jpedsurg.2006.06.045.
[8] De Franchis R. Evaluation and follow-up of patients with cirrhosis and oesophageal varices. J Hepatol. 2003;38:361–3. https://doi.org/10.1016/S0.
[9] Saleh Y, Eldeen FZ, Kamel Y, et al. Liver transplant in Budd–Chiari syndrome: a single-center experience in Saudi Arabia. Exp Clin Transplant. 2014;12:52–4. https://doi.org/10.6002/ect.2013.0153.
[10] Nagral A, Hasija RP, Marar S, et al. Budd–Chiari syndrome in children: experience with therapeutic radiological intervention. J Pediatr Gastroenterol Nutr. 2010;50:74–8. https://doi.org/10.1097/MPG.0b013e3181aecb63.
[11] Kathuria R, Srivastava A, Yachha SK, et al. Budd–Chiari syndrome in children. Eur J Gastroenterol Hepatol. 2014;26:1030–8. https://doi.org/10.1097/meg.0000000000000144.
[12] Redkar R, Bangar A, Hathiramani V, et al. Pediatric Budd–Chiari syndrome: a case series. Indian Pediatr. 2018;55:871–4.
[13] Seijo S, Plessier A, Hoekstra J, et al. Good long-term outcome of Budd–Chiari syndrome with a step-wise management. Hepatology. 2013;57:1962–8. https://doi.org/10.1002/hep.26306.