Original Article

Should Not Children with Ventriculoatrial Shunts Be Taking Aspirin? An Update: 0% Distal Malfunction

Suhas Udayakumaran[1] Shine Kumar[2]

[1] Division of Paediatric Neurosurgery, Department of Neurosurgery, Amrita Institute of Medical Sciences and Research Centre, Kochi, India
[2] Department of Pediatric Cardiology, Amrita Institute of Medical Sciences and Research Centre, Kochi, India

Address for correspondence Suhas Udayakumaran, MCh, Amrita Institute of Medical Sciences and Research Centre, Kochi, Kerala 682041, India (e-mail: dr.suhas@gmail.com).

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Abstract

Background Ventriculoatrial (VA) shunts have the potential to preserve life in the event of failure of ventriculoperitoneal (VP) shunts. Contrary to VP shunts, they are susceptible to consequences, particularly cardiac problems. There are no established guidelines for screening patients following VA shunt placement regarding prevention, anticoagulant treatment, or risk factor screening.

Objective We aim to investigate aspirin's potential function and effectiveness in enhancing shunt survival and preventing secondary morbidity from distal thrombosis in children with VA shunts.

Materials and Methods The study's design is prospective and observational. It began in 2011 and is ongoing. Before inclusion in the study, we obtained clearance from the hospital ethics board and consent from the family. All patients with VA shunts were given a once-a-day antiplatelet dose of 5 mg/kg of aspirin from the first postoperative day. The study's primary end points include: (1) Major distal end malfunction documented on echocardiography or (2) any cardiac complications directly associated with the VA shunt.

Results Since March 2011, 13 patients have been followed up. So far, no cardiac complications have been ascribed to VA shunts in any of the patients. The current follow-up period is 28 to 170 months. Patient follow-up is continuing.

Conclusion Our observations regarding the efficacy and safety of aspirin in VA shunts are encouraging. However, sufficient time would be needed to establish its effectiveness in chronic sequelae such as pulmonary hypertension.

Keywords
- silicone
- complications
- thromboprophylaxis

Introduction

In many clinical situations, the ventriculoatrial (VA) shunt is better than the ventriculoperitoneal (VP) shunt. Even while they can save lives when VP shunts fail, they come with a risk of unique problems, most notably cardiac issues.[1–8] The literature contained reports of cardiovascular problems related to the VA shunt, such as atrial and great vein thrombosis, pulmonary embolism, pulmonary hypertension, and cor pulmonale.[4,7,9–16] An essential worry with VA shunts is cardiopulmonary morbidity. At times, several of these situations may be lethal.[17–20]

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The risk of thrombus formation and its consequences are primarily responsible for all distal catheter complications. Despite the substantial contribution of thrombus formation, its effect, and awareness of complications, there are *currently no standard recommendations regarding screening for risk factors, prevention, or anticoagulation treatment in patients following VA shunt placement*.[7,8]

The author of this article provides support for the use of aspirin in a VA shunt in the form of results from an *ongoing prospective study*. This research is an update on a prospective study regarding aspirin's importance and efficacy in enhancing shunt survival, avoiding secondary morbidity in children with VA,[21] and being safe.

Objective

This study aimed to investigate prospectively the effectiveness of aspirin in preventing morbidity and increasing shunt survival in children with VA shunts.

Materials and Methods

It is a prospective study design. The study commenced in 2011 and is now in progress. Before the study, approval from the hospital ethics board and family consent were obtained.

Indications for VA Shunt

All patients who had VA shunts had several failed VP shunt attempts and were therefore deemed unsuitable for VP shunts (►**Table 1**).

Inclusion Criteria

The inclusion criteria are as follows:

- Primary or revision VA shunt.
- Willingness to participate.

Exclusion Criteria

The exclusion criteria are as follows:

- Any coagulopathy.
- Any underlying cardiac and pulmonary abnormalities which may confound the end points or where the VA shunt may add additional risk to the patient.
- Using other medications that interfere with the study outcome (rivaroxaban, clopidogrel, warfarin, active malignancy, etc.).

Table 1 Details of the patient included in the study

Patient	Age/sex (mo)	Indication for VA shunt	Indication for CSF diversion	Follow-up (mo)	Complications noted till date
1	21/F	Peritoneal adhesions with multiple failures of VP shunts	Myelomeningocele with hydrocephalus	120	None
2	5/M	Peritoneal adhesions with multiple failures of VP shunts	Occipital encephalocele	46	None
3	16/M	Peritoneal adhesions with multiple failures of VP shunts	Postinfective hydrocephalus	170	None
4	4/M	Peritoneal adhesions with multiple failures of VP shunts	Multiloculated hydrocephalus, ventriculitis	46	None
5	10/M	Peritoneal adhesions with multiple failures of VP shunts	Postinfective hydrocephalus, prematurity	106	None
6	8/M	Peritoneal adhesions with multiple failures of VP shunts	Prematurity, posthemorrhagic hydrocephalus	88	None
7	12/M	OPG, ascites	OPG, shunt ascites	39	None
8	17/M	Peritoneal ascites, hypoproteinemia	Posthemorrhagic hydrocephalus	Expired due to unrelated bacterial sepsis	None
9	78/M	Peritoneal adhesions	Aqueductal stenosis	70	None
10	36/M	OPG, ascites	OPG	46	None
11	24/M	Ascites	Postinfective hydrocephalus	34	None
12	216/M	Peritoneal adhesion, pseudocyst/adhesions	Postinfective hydrocephalus	28	None
13	11/M	Shunt ascites	OPG	36	None

Abbreviations: CSF, cerebrospinal fluid; OPG, optochiasmatic glioma; VA, ventriculoatrial; VP, ventriculoperitoneal.

Table 2 Complications of VA shunt secondary to thrombogenicity

Complications	Morbidity	Comment
Complications secondary to catheter thrombogenicity	• Catheter thrombus[43,48] • Mural and deep vein thrombus[7,16,18] • Pulmonary hypertension[1,4,10,11,43–47] • Fatal cardiopulmonary complications[17–20] • Cor pulmonale and fatal cardiopulmonary complication[6,17–20]	The majority of distal and cardiac complications are related to the thrombogenicity of the catheter

Abbreviation: VA, ventriculoatrial.

- No intention of participating or noncompliant for successful completion of the follow-up.

Primary End Points of the Study

The primary end points of the study are as follows:

1. Major distal end malfunction.
2. Any cardiac complications directly attributable to the VA shunt.

Technique and Dosing of Aspirin

The distal end is inserted using the Seldinger technique. Technical success was defined as correctly positioning the catheter tip at the cavoatrial junction, confirmed by a plain chest radiograph and a water-soluble contrast study. Aspirin (5 mg/kg/d) is started the next morning and continued.[22–28]

Follow-up Protocol

1. Baseline echocardiography was done at discharge to ascertain the position of the tip of the distal catheter and as a baseline for future reference.
2. For the study, the patients were followed up clinically by echocardiography every 6 months. An experienced operator (S.K., second author) performed all the echocardiography studies using an IE 33 echocardiographic machine (Philips, Bothell, United States) with 5 to 12 MHz transducers. The imaging confirmed that the catheter tip was in the right atrium and showed evidence of thrombus, pulmonary hypertension secondary to chronic thromboembolism to the lungs, and other significant new findings.
3. A plain chest radiograph was also done to monitor the location of the shunt and its distal tip.

Results

Since March 2011, we have had 13 consecutive patients being followed up. None of the shunts had distal malfunction until the reporting. None of the patients reported any cardiac issues, as confirmed on echocardiography. The present follow-up ranges from 28 to 170 months. The details are summarized in ►**Table 1**.

The patient follow-up is being continued, with no patient dropouts. One patient died due to systemic sepsis and associated morbidity (unrelated). All the study participants strictly complied with aspirin and the follow-up protocol.

None of the study participants has had any aspirin-related side effects to date.

Discussion

In hydrocephalus, when the VP shunt is unsuitable for various reasons, VA shunts are utilized as an alternative cerebrospinal fluid (CSF) diversion method (►**Table 1**). Shunt-specific problems following VA shunting may be more severe than those following VP shunting.[18,29] The literature has documented the following complications associated with VA shunts: mechanical failure of shunt systems, atrial or major venous thrombosis, pulmonary embolism, pulmonary hypertension, cor pulmonale, arrhythmia, septicemia, and shunt nephritis.[1,4,7,9–20,30–47] Thus, cardiovascular morbidity is a significant concern in the context of VA shunts. A thrombus and its consequences account for most VA distal catheter problems (►**Table 2**).

Thrombogenicity of the Distal Catheter of the VA Shunt and the Resulting Complications

1. *VA distal catheter malfunction*: The significant and most prevalent morbidity associated with a VA shunt and shunt dysfunction is a distal catheter thrombus. Patients who present with thrombi frequently exhibit a documented record of prior shunt infections. Clinical manifestation of thromboembolic problems in patients undergoing VA shunts occurs in 0.3% of the cases; however, autopsy series data indicate a significantly greater incidence rate of 60%.[43,48,49]
2. *Mural and great vein thrombus*: A distal catheter may lead to atrial thrombus formation[7,18] and thrombosis of the superior vena cava and the internal jugular vein.[7,16,18,50,51]
3. *Pulmonary hypertension*: Significant pulmonary emboli have been reported in 3.2 to 8% of patients with VA shunts,[10,11,46] forming a risk factor for developing chronic thromboembolic pulmonary hypertension.[1,4,10,11,17,43–46,49] The rate reported postmortem has been as high as 50 to 100% of patients.[47] Potential mechanisms have been suggested, such as a reaction of the pulmonary endothelium to specific components of CSF, such as brain thromboplastin, or a shunt infection (which may or may not induce persistent activation of clotting factors accompanied by recurrent thromboembolism.[43] Patients who have VA shunts frequently experience isolated, minor microembolization. In light of this significant morbidity, Kluge et al proposed that individuals undergoing VA shunt should undergo lifelong follow-up consisting of echocardiography and pulmonary function tests that assess

Table 3 Literature review and timeline of cardiac complications

Complication	Incidence (%)	Timeline (y)	Comments
Distal thrombus[43,48]	20% of patients after indwelling catheters 2 y 67% if the catheter was left in for up to 6 y 85% if it was left for up to 14 y	2–14	Management • Long-term anticoagulation • Removal of the catheter (if possible), or continued anticoagulation therapy • Removal of the VA shunt may not be an option in all patients
Mural and intracavitary thrombus (SVC, IVC, RA, RV)[7,16,18,50,51]	34%	2–14	As children mature and grow into adulthood, the tip of the catheter may move out of the atrium and into the great vessels, increasing the risk of thrombosis. Ensuring that the tip of VA catheters is implanted into the vessel at an adequate length—despite its relatively narrow diameter—and monitoring it during a patient's growth will help ensure it remains mobile distally, decreasing the risk of this complication[50]
Pulmonary thromboembolism[10,11,17,46]	3.2–100%	2–10	100% in postmortem
Pulmonary hypertension[1,4,10,11,43–47]	0.3–8%	9–27 (median 16.5)	• Early detection of pulmonary hypertension may be of limited value; by the time pulmonary hypertension occurs, there has already been obstruction of 60% of the pulmonary vascular bed • Prognosis is serious and often life-threatening, even with the removal of the shunt and adequate therapy, which may end in lung or heart–lung transplantation • In untreated patients with pulmonary hypertension, the median survival rate was only 2.8 y[52]
Cor pulmonale[4,6,17–20]	3% (5–10%)	1–8	Antibiotics, anticoagulants, antifibrinolytics, management of cardiac failure, alternate diversion

Abbreviations: IVC, inferior vena cava; RA, right atrium; RV, right ventricle; SVC, superior vena cava; VA, ventriculoatrial; VP, ventriculoperitoneal.

single-breath diffusion capacity for carbon monoxide every 12 months (►**Table 3**).[10,11]

Even with the removal of the shunt and appropriate treatment, the prognosis for pulmonary hypertension is dire and frequently life-threatening once the condition is diagnosed. Early identification of pulmonary hypertension may have little utility, given that occlusion of 60% of the pulmonary vascular bed has already occurred by the time the condition is detected, necessitating lung or heart–lung transplantation. In a sizable cohort of untreated individuals with pulmonary hypertension, the median survival rate was a mere 2.8 years.[11,52]

4. *Fatal cardiopulmonary complication*: The progression of time has revealed certain instances involving critical or lethal cardiopulmonary problems.[4,6,17–20,49]

Potentially hazardous problems related to VA shunts are reversible with prompt and appropriate evaluation and treatment. Catheter-associated pulmonary and distal thrombi necessitate the use of prolonged anticoagulant therapy. The suggested course of action is to administer anticoagulation therapy for 3 months to catheter-related thrombosis, after which the catheter should be removed (if feasible), or anticoagulation therapy should be continued.[53–55]

The removal of the VA shunt may not be an option in all patients. Even the possibility of open surgery has been explored. Thus, such complications need to be regarded as highly relevant. A life-long follow-up that includes echocardiography and pulmonary function tests may be mandatory.[10] *Ironically, despite awareness of such morbidity associated with the thromboembolic effects of VA shunts, currently, there are no formal recommendations concerning screening for risk factors, prevention, and/or anticoagulation treatment in patients after VA shunt placement.*[7,8]

Mechanism of Thrombogenicity in a VA Shunt and the Role of Aspirin

Potentially, shunt catheters remain inserted into people for years. The material characteristics of the catheter have the potential to exert a substantial impact on consequences, such as thrombosis, which includes mural thrombi and total venous blockage (about 6%).[51]

Platelet depletion occurs on any foreign substance that enters the circulatory system. Silicone (SiO) has been used in the construction of shunt catheters because of its hypoallergenic characteristics. Moreover, SiO possesses hydrophilic characteristics that are advantageous for intravascular applications. Nevertheless, SiO catheters have been unable to

substantially reduce the occurrence of thrombotic events. The VA catheter is positioned in the right atrium, a slow-flow system contributing to its thrombogenicity.[56] Further potential contributors to deep venous thrombosis include catheter length, diverse levels of roughness, reduced diameter of the superior vena cava, and modifications in venous blood circulation.[56]

Platelet deposition accompanied by adhesion is the initial pivotal stage in the coagulation cascade. A multitude of coagulation factors are encapsulated within the platelet in addition to those that are absorbed on its surface. After platelets attach, they undergo contraction and intracellular granule depletion, which initiates a release reaction that results in more platelet aggregation and the formation of a platelet plug. As the thrombus develops, fibrin is deposited, and a coagulum of red and white cells forms at its tip.

Aspirin at low doses can effectively prevent platelet aggregation without significantly interfering with prostacyclin generation by endothelial cells. This is because the nucleated platelet storage is incapable of producing COX-1. Aspirin possesses the distinctive characteristic of irreversibly acetylating platelet COX-1, impeding the synthesis of thromboxane and explaining its antiplatelet characteristics.[57]

Aspirin is the most commonly prescribed medication in cerebrovascular disorders and cardiology, where thrombosis is a critical pathogenetic mechanism. Thromboembolic risk reduction techniques often concentrate on extracardiac or intracardiac shunts, foreign surfaces, and flow disturbances. Compared with the majority of other pediatric acute ischemic stroke etiologies, congenital and acquired cardiac disease thromboprophylaxis strategies have undergone more rigorous evaluation. Preventive approaches for congenital and acquired cardiac disease vary according to the historical and perceived risk of thromboembolism.[58–62]

Interestingly, thromboprophylaxis for VA shunt has not been practiced in the neurosurgical literature. An isolated work by Kuffer described prophylactic anticoagulants acenocoumarol (Sintrom); the authors concluded that distal catheter complications were twice as frequent in the group not receiving anticoagulant therapy.[63] *Drawing parallels with surgery for congenital heart disease, the risk of conduit thrombosis is high in early and late postoperative periods—conduit-related thromboses may occur decades later, and thromboembolic risk increases with delays in prophylactic anticoagulation initiation.*[61]

An Overview of Usage and Choice of Dosing, Resistance, and Complications

Low-dose aspirin (3–5 mg/kg/once daily) has been used in many conditions.[23–26] In two instances in children where aspirin has been used long term, viz. in Kawasaki's disease and congenital heart disease, it is considered helpful for its antiplatelet action with no significant side effects.[23,24,27,61] Many adverse reactions following the ingestion of aspirin are dose-related and/or occur upon long-term use. High-dose aspirin has been documented to have a higher risk of side effects, including dose-dependent minor bleeding and gastric injuries.[62] Much literature has supported equal efficacy with increased safety of lower doses of aspirin versus higher doses.[22,25,64,65] The long-term use of lower aspirin doses (e.g., cardiocoronary prevention) is considered safe with a favorable benefit/risk ratio. Caution is exercised in people at an increased risk of adverse reactions. Bleeding and other adverse reactions are of concern in particular life situations, such as late pregnancy and advanced age. In short, the safety profile of aspirin has been well established and is well known. It is a remarkably safe drug considering the benefit versus the risk.[66]

Another critical issue is aspirin resistance. The incidence of aspirin resistance (or high on-treatment platelet reactivity) using conventional platelet inhibition thresholds has not been validated in children and is widely variable. Therefore, aspirin resistance should be considered as a possible complication when using it for antithrombotic prophylaxis.[61] These pertinent issues have been discussed in many other specialties where the therapeutic benefits of aspirin have been exercised.

In a nutshell, aspirin is an effective noninferior anticoagulant in preventing venous thrombosis with low bleeding risks compared with other anticoagulants due to its safety, ease of use, low price, and good patient compliance profiles, as indicated by many studies on posttotal knee arthroplasty and pediatric cardiology anticoagulant choices[61,67] (►**Table 3**).

Limitations

A lack of appropriate outcome measures and an excessive reliance on data from similar scenarios with few high-quality investigations impede our ability to comprehend VA shunt distal thrombosis and its impact on children, which are obstacles shared by other uncommon pediatric diseases and outcomes.

Our research has apparent limitations. To ensure the validity and reliability of our conclusion, we must initially augment our sample size. Proof of the efficacy and benefit of aspirin in the presence of a VA shunt necessitates a multicenter effort due to the inherent difficulties in amassing sufficient data and randomization. Moreover, the occurrence of certain complications, such as pulmonary hypertension, necessitates an extended period of observation beyond what we have currently allocated.

As there is substantial morbidity associated with the thromboembolic phenomenon, it is evident that awaiting the identification of complications is not warranted, given the available evidence regarding the safety of aspirin usage. While no literature report exists regarding the use of aspirin in conjunction with a VA shunt, our published brief communication is the only exception.[21] *Strong surrogate evidential association exists for the etiopathogenesis of thrombosis and the need for prophylactic use of aspirin for thromboprophylaxis in many nonneurosurgical subspecialties.*[23–26,61,67] *The evidence supporting its choice, dosing, benefit, and safety versus other anticoagulants is building up.*

Concerns regarding the role of aspirin-independent platelet reactivity, the effect on normal hemostasis resistance, the lack of clarity regarding the utility of aspirin monitoring, and the absence of solid evidence for efficacy are the strongest

arguments against optimizing our understanding of aspirin use in pediatric VA shunts with high-quality research.[61]

Conclusion

Our preliminary observation and follow-up of the use of aspirin in VA shunt are promising along with being safe.

1. We have demonstrated 0% distal malfunction to date.
2. The prime open question remains: whether we can prevent pulmonary hypertension, which we believe requires even longer follow-up than we have.
3. The optimal thromboprophylaxis for a VA shunt is still being determined due to the need for more relevant literature. Given the severe complications that may arise due to the thrombogenic nature of the catheter, our identification of early thromboprophylaxis commences a potentially beneficial course of action.

Note

This study was previously presented as a platform presentation at ISPN 2023, held at Vina de la Mer, Chile.

Authors' Contributions

S.U. contributed to the concept, study design, statistics, drafting, and final revision. S.K. contributed to the concept and final revision.

Ethical Approval

This study protocol was reviewed and approved by the Institutional Ethics Committee, AIMS, approval number IECAIMS 22200-2019.

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None.

Conflict of Interest

None declared.

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