Hydrocephalus is extremely common in the developing world. It has been estimated that in sub-Saharan Africa alone, there are more than 100,000 new infant cases per year with an estimated annual economic burden of up to $56 billion US dollars. With an estimated 1 neurosurgeon per 10 million people in East Africa, most hydrocephalus patients have a level of access to care that makes shunt dependence more problematic. For this reason, more than half of the patients treated for hydrocephalus at CURE Children’s Hospital of Uganda (CCHU) are successfully treated using endoscopic methods. Although reasonably acceptable rates of shunt infection in children have been reported from Kenya (9.1%) and Uganda (9.7%), shunt infection and failure remain major causes of morbidity and mortality for shunt-dependent patients.

One strategy for reducing shunt infections in the developed world is the implantation of antibiotic-impregnated shunt catheters. Bactiseal (Codman, Johnson & Johnson) shunt components were designed to reduce the risk of infection by releasing antibiotics around the catheter site. However, antibiotic-impregnated shunts have yet to find widespread use in the developing world, largely due to cost. Given potential differences in the microbial spectrum, their effectiveness in preventing shunt infection for populations in low-income countries may differ and has not been demonstrated. This study is the first to compare the efficacy of a Bactiseal shunt system with a non–antibiotic-impregnated system in a developing country.

Object. Antibiotic-impregnated shunts have yet to find widespread use in the developing world, largely due to cost. Given potential differences in the microbial spectrum, their effectiveness in preventing shunt infection for populations in low-income countries may differ and has not been demonstrated. This study is the first to compare the efficacy of a Bactiseal shunt system with a non–antibiotic-impregnated system in a developing country.

Methods. The Bactiseal Universal Shunt (BUS) was placed in 80 consecutive Ugandan children who required a shunt. In this retrospective cohort study, the outcome for that group was compared with the outcome for the immediately preceding 80 consecutive children in whom a Chhabra shunt had been placed. The primary end points were shunt failure, shunt infection, and death. Shunt survival was analyzed using the Kaplan-Meier method. Significance of differences between groups was tested using the log-rank test, chi-square analysis, Fisher’s exact test, and t-test.

Results. There was no difference between groups in regard to age, sex, or etiology of hydrocephalus. Mean follow-up for cases of nonfailure was 7.6 months (median 7.8 months, interquartile range 6.5–9.5 months). There was no significant difference between groups for any end point. The BUS group had fewer infections (4 vs 11), but the difference was not significant (p = 0.086, log-rank test). Gram-positive cocci were the most common culturable pathogens in the Chhabra group, while the only positive culture in the BUS group was a gram-negative rod.

Conclusions. These results provide equipoise for a randomized controlled trial in the same population and this has been initiated. It is possible that the observed trends may become significant in a larger study. The more complex task will involve determining not only the efficacy, but also the cost-effectiveness of using antibiotic-impregnated shunt components in limited-resource settings.

Key Words • ventriculoperitoneal shunt • infection • Bactiseal • Uganda • global surgery • hydrocephalus
postoperative shunt infections by using catheters impregnated with 0.15% clindamycin and 0.54% rifampicin to protect against bacterial colonization in the 1st month following implantation. Data from the United Kingdom Shunt Registry demonstrated a significant reduction (p = 0.04) in shunt infections with 16 infections in 715 patients receiving Bactiseal shunts and 31 in 715 non-Bactiseal control shunts.7 Other smaller studies have not demonstrated significantly decreased infection rates. One non-randomized sequential series of 80 non-Bactiseal shunts versus 80 Bactiseal shunts had infection rates of 8.8% versus 5% (p = 0.53).8 A meta-analysis of 9 retrospective studies totaling 1649 pediatric patients found that antibiotic-impregnated shunts were associated with a significant decrease in shunt infections (5.0% vs 11.2%; OR 0.421, p < 0.0001).9 However, the authors concluded that a prospective, randomized controlled trial was necessary to confirm these findings.

Antibiotic-impregnated shunts have yet to find widespread use in the developing world, mostly due to cost. The total cost for an uncomplicated, initial shunt implantation at CCHU in 2005 was determined to be $470 when using the inexpensive Chhabra shunt (G. Surgiwear).10 However, in the same setting, the cost of a shunt operation complicated by infection—treated by shunt removal, insertion of an external ventricular drain, 2 weeks of intravenous antibiotics, and subsequent insertion of a new Chhabra shunt—approximately quadruples the cost of treatment. Taking into consideration the morbidity and mortality caused by shunt infection, Bactiseal shunts might be more cost-effective—even in limited-resource settings—if shown to sufficiently reduce the rate of shunt infection to offset the additional cost of the initial shunt product.

It is yet to be determined if antibiotic-impregnated shunts designed for the developed world will result in a significant reduction in shunt infections in limited-resource countries. While Staphylococcus epidermidis and Staphylococcus aureus are the most common pathogens in most reported series from developed countries, this may not be the case for other regions, such as sub-Saharan Africa, where bacteriological data in regard to shunt infection are very sparse. Staphylococcus aureus was reportedly a common organism in studies from Kenya and Nigeria.11 But in Uganda, where neonatal ventriculitis is the most common cause of infant hydrocephalus,11 we recently found evidence for a high prevalence of enteric organisms, especially Acinetobacter species, in the CSF of these infants, as well as in their home environments.3 While clindamycin and rifampicin are effective against staphylococcal species, this is not true for gram-negative and enteric organisms. With the potential for a different spectrum of pathogens, and without a prior study of Bactiseal shunts in a limited-resource setting, the efficacy of these shunts in reducing the risk of shunt infection in Uganda was unknown. This study was intended to gauge the value of this innovation in that context.

Methods

The majority of shunts implanted at CCHU are Chhabra shunts, which are donated by the International Federation for Spina Bifida and Hydrocephalus. These shunts are very low cost (< $40 US) and were previously shown not to be associated with an increased risk of shunt infection or malfunction when compared with a standard shunt commonly used in North America that was 20 times more expensive.9 Despite this, a larger and more recent retrospective study of 900 consecutive shunt placements at CCHU found that the total failure rate within 6 months of placement was 25.7%, and the rate of infection was 11.7%.14 The Codman company (a subsidiary of Johnson & Johnson), which manufactures Bactiseal products, donated a supply of Bactiseal Universal Shunts (BUS) to CCHU in 2011. This shunt was designed with lower-income countries in mind, and the cost is currently on the order of $400–$500 US. The BUS utilizes a distal slit valve and Bactiseal components. From October 10, 2011, to February 15, 2012, the BUS was placed in 82 consecutive patients who required a ventriculoperitoneal shunt at CCHU. We stopped using the BUS once the supply was exhausted. In the summer of 2012, after the last of the BUS implants had achieved 6 months of follow-up and with approval from the institutional review board at both Boston Children’s Hospital and CCHU, we initiated a retrospective cohort study to compare the outcomes for these patients with a cohort of consecutive patients treated prior to October 10, 2011, who had received the Chhabra shunt.

We excluded patients who lived outside of Uganda because of difficulties with follow-up. This criterion excluded only 2 patients in the Bactiseal group (1 patient lived in Kenya and the other in the Democratic Republic of the Congo). The 80 consecutive patients living in Uganda who received Chhabra shunts immediately treated prior to October 10, 2011, were chosen as the control group.

The primary negative outcome for the analysis was shunt failure, which was defined as death or neurosurgical intervention to revise, replace, or remove the shunt. A second analysis was performed for which the outcome was shunt infection, as confirmed by clinical presentation and CSF analysis. Children presenting with fever, irritability, vomiting, poor feeding, obvious soft-tissue inflammation along the shunt tract, wound breakdown, or exposed hardware typically underwent a shunt tap to obtain CSF for analysis. In this context, patients with more than 5 white blood cells/μl, protein greater than 100 mg/dl, glucose less than 40 mg/dl, or a positive bacterial culture were considered to have a shunt infection. All patients with the diagnosis of shunt infection met these criteria. The medical records for patients in the study were reviewed to determine whether an operative intervention for shunt failure or infection occurred prior to 6 months after the original shunt placement or if there was evidence of a postoperative appointment with a member of the staff that determined the shunt was functioning at least 6 months after surgery. If there was not significant evidence of shunt failure or success in the medical record, then the guardians of the patient were contacted to determine the outcome. This initially consisted of attempting to contact the family at the mobile phone number provided in the medical record. If contact was made with
a family member who had direct access to the patient, then the outcome was determined by confirming the patient’s current condition and whether any neurosurgical intervention had occurred since the original shunt placement. The CCHU social work staff performed home visits to patients throughout the country for whom outcomes could not be determined by phone or medical record.

The 2 groups were evaluated for significant differences in age at surgery (t-test) and sex (Fisher’s exact test), as well as circumstances of surgery (primary shunt placement, aborted or failed endoscopic third ventriculostomy, or replacement shunt) and etiology of hydrocephalus (chi-square analysis). Kaplan-Meier survival analysis was conducted using SPSS (version 20, IBM) for the outcome of all causes of shunt failure and of shunt infection.

Results

The patient characteristics for the 2 groups are shown in Table 1. Although the groups comprised consecutive patients treated at CCHU and were not intentionally age or etiology matched, there was not a significant difference in age at shunt insertion (p = 0.25), sex (p = 0.21), the distribution of hydrocephalus etiologies (p = 0.90), or surgery type (p = 0.59).

Outcome results are summarized in Table 2. Shunt failure, defined as any death or subsequent shunt operation, was known to occur at some point in 47 patients, with failure occurring by 6 months in 42 (26.2%). The mean follow-up time for the 113 patients who were not known to have had shunt failure was 7.6 months (median 7.8 months, interquartile range 6.5–9.5 months). The duration of follow-up was less than 6 months for only 18 patients. Follow-up data of at least 1 month were available for 105 (92.9%) of those with no known shunt malfunction. Death due to any cause occurred by 6 months in 15 (9.4%) of the 160 patients in the study, with 6 of these having received the Chhabra shunt and 9 having received the BUS.

Kaplan-Meier survival analysis for all causes of shunt failure in the 2 groups (inclusive of infections) was performed (Fig. 1). While there appeared to be a trend toward increased shunt survival for the BUS, the difference was not significant (p = 0.447, log-rank test).

Shunt infection survival analysis is shown in Fig. 2. The BUS group trended toward reduced shunt infections, with the Chhabra group having nearly 3 times the number of infections (11 compared with 4); however, the difference was not significant (p = 0.086, log-rank test). In addition, the clinical presentation in 2 patients, both having received a Chhabra shunt, was of exposed shunt hardware. This raises the possibility that the real primary shunt infection rate for this group could be even lower (11.3%), and the chance of meaningful difference between groups even less. The culture results for all of the infected shunts are provided in Table 3. The Chhabra group had 4 patients with CSF cultures that grew gram-positive cocci and 2 with gram-negative rods. One of the patients in the BUS cohort developed infection with gram-negative rods, and there were no instances of cultures growing gram-positive cocci. The remaining patients had clinical and CSF profile evidence for shunt infection, but no bacteria grew in culture.

Discussion

This is the first study of which we are aware in which a

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**TABLE 1: Patient characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>BUS</th>
<th>Chhabra Shunt</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>160</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>hydrocephalus etiology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIH</td>
<td>118 (73.8)</td>
<td>60 (75.0)</td>
<td>58 (72.5)</td>
</tr>
<tr>
<td>myelomeningocele</td>
<td>18 (11.2)</td>
<td>9 (11.2)</td>
<td>9 (11.2)</td>
</tr>
<tr>
<td>other</td>
<td>24 (15.0)</td>
<td>11 (13.8)</td>
<td>13 (16.2)</td>
</tr>
<tr>
<td>surgery type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>abandoned ETV</td>
<td>79 (49.4)</td>
<td>40 (50.0)</td>
<td>39 (48.8)</td>
</tr>
<tr>
<td>failed ETV</td>
<td>28 (17.5)</td>
<td>15 (18.8)</td>
<td>13 (16.2)</td>
</tr>
<tr>
<td>primary shunt placement</td>
<td>15 (9.4)</td>
<td>5 (6.2)</td>
<td>10 (12.5)</td>
</tr>
<tr>
<td>shunt replacement</td>
<td>38 (23.8)</td>
<td>20 (25.0)</td>
<td>18 (22.5)</td>
</tr>
<tr>
<td>mean age at VPS placement (mos) ± SD</td>
<td>11.3 ± 17.7</td>
<td>9.7 ± 17.1</td>
<td>12.9 ± 18.1</td>
</tr>
<tr>
<td>male sex</td>
<td>83 (51.9)</td>
<td>46 (57.5)</td>
<td>37 (46.2)</td>
</tr>
</tbody>
</table>

*ETV = endoscopic third ventriculostomy; PIH = postinfectious hydrocephalus; VPS = ventriculoperitoneal shunt.
†Values are number of patients (%) unless noted otherwise.

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**TABLE 2: Patient outcomes at 6 months**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Total (%)</th>
<th>BUS (%)</th>
<th>Chhabra Shunt (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>160</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>shunt failure, total</td>
<td>42 (26.2)</td>
<td>19 (23.8)</td>
<td>23 (28.8)</td>
</tr>
<tr>
<td>shunt infection</td>
<td>15 (9.4)</td>
<td>4 (5.0)</td>
<td>11 (13.8)</td>
</tr>
<tr>
<td>died, total</td>
<td>15 (9.4)</td>
<td>9 (11.2)</td>
<td>6 (7.5)</td>
</tr>
<tr>
<td>follow-up &lt;6 mos</td>
<td>18 (11.2)</td>
<td>11 (13.8)</td>
<td>7 (8.8)</td>
</tr>
<tr>
<td>successful shunt at 6 mos</td>
<td>100 (62.5)</td>
<td>50 (62.5)</td>
<td>50 (62.5)</td>
</tr>
</tbody>
</table>
Bactiseal shunt system is directly compared with a non–antibiotic-impregnated shunt in a developing country. While the effectiveness of Bactiseal components in reducing the risk of shunt infection has not yet been proven through randomized controlled trials, they are becoming widely used throughout the developed world. However, the efficacy of a shunt designed to reduce infections in one setting may not prove effective in another. In Uganda, as in other largely rural populations in sub-Saharan Africa, the microbial environment may differ from that in other parts of the world. Gram-negative bacteria have been readily cultured from rural domestic sites in Uganda. Furthermore, in contrast to more developed countries, neonatal ventriculitis is the predominant cause of infant hydrocephalus in Uganda, and evidence suggests enteric organisms may play an important role. The value of Bactiseal shunt components in preventing shunt infection in this context has not been previously tested. In this retrospective cohort study comparing the BUS with the non–antibiotic-impregnated Chhabra shunt, we found no significant difference in the number of patients who developed shunt failure or infection, although there was a trend toward fewer infections with the BUS. It is notable that the 5% infection rate for the BUS group we report in the present study is identical to that reported in 2 North American retrospective studies, and that the infection rate of 13.8% for the Chhabra shunt group is similar to the 8.8% and 11.2% infection rates reported for the non–antibiotic-impregnated shunts in those same studies. Assuming an infection rate of 12% for the Chhabra shunt group and 6% for the BUS group, 356 patients per study group (712 patients) would be required for a power of 80% and a p value of 0.05. A study with 80 patients per group would be adequately powered for detecting a significant difference between infection rates of 20% and 5%, respectively. The decrease in infection risk possibly afforded by using the Bactiseal product appears to be on an order that would require a much larger study to detect statistical significance. Similar to other studies from North America, our data suggest a possible reduction in infections but fall short of distinguishing between a true benefit and no benefit at all.

As in previous studies, the results reported here suggest the need for a randomized prospective trial in a much larger population. This study in Uganda provides equipoise for such a trial in this population, excluding economic factors. But, if a similar difference in infection rate were found to be statistically significant in a larger study, the more complex question would be whether use of the more expensive product were justifiable in a limited-resource environment. Such a determination would necessarily consider factors beyond the immediate costs of treatment, such as the long-term consequences of morbidity from shunt infection. This study also demonstrated that the BUS performed at least as well as the Chhabra shunt in regard to other causes of failure in the initial months following implantation.

It is of interest that the only organism cultured in the BUS group was a gram-negative rod; whereas, 4 of 6 positive cultures in the Chhabra group were of gram-positive cocci, with the remainder being gram-negative rods. This might suggest that, as expected, the Bactiseal product’s effectiveness against Staphylococcus species was responsible for the trend toward lowering the infection rate, although the number of positive cultures was too small to draw any conclusions.

**Limitations of the Study**

An obvious limitation of this study is that, as with those from more developed countries, it was a retrospect-
Bactiseal shunt effectiveness in Uganda

tive cohort study and not a randomized prospective trial. We have previously shown that the incidence of postinfectious hydrocephalus is tied to rainfall patterns in Uganda with the largest number of infections leading to postinfectious hydrocephalus occurring during periods of intermediate rainfall. Furthermore, the spectrum of pathogens in the CSF of infants with postinfectious hydrocephalus also appears to change with the rain cycle. Hence, although we found no significant demographic or etiological differences between the 2 groups, studying 2 cohorts that differ by epoch might introduce a time-sensitive variable in the spectrum of pathogens that would be eliminated in a randomized controlled trial.

Another limitation is the lack of a bacterial culture result in several cases. This may be due in part to the limitations within our own microbiology laboratory; however, we have previously demonstrated that organism detection with optimal conventional methods often fails in children presenting with postinfectious hydrocephalus in Uganda. Given these realities, the diagnosis of shunt infection in the absence of a positive culture had to be made on clinical grounds, and the practice standards were the same for both groups. Needless to say, strict, predetermined parameters to define shunt infection would be used in a prospective study.

Finally, 2 patients with infections in the Chhabra group presented with exposed shunt hardware. It is impossible to know whether primary infection led to skin breakdown or vice versa in this situation. Discounting primary infections in these 2 cases brings the infection rate in the Chhabra group to 11.3%, reducing further the likelihood of a significant difference between the 2 groups.

Conclusions

The relative infection risks for non–antibiotic-impregnated shunts and Bactiseal shunts previously reported in North America are very similar in this population of Ugandan children. The lack of evidence for a significant decrease in shunt infections or malfunctions in this study provides equipoise for a randomized controlled trial in the same population. It is possible that the observed trends may become significant in a larger study. Given the suggested level of protection from infection, the more complex question will be whether use of the more expensive product is appropriate in a limited-resource environment.

Acknowledgment

We would like to acknowledge the social work staff of CURE Children’s Hospital of Uganda for their tireless efforts.

Disclosure

Codman donated the Bactiseal Universal Shunts for use at CCHU, and the International Federation of Spina Bifida and Hydrocephalus kindly provided the Chhabra shunts. The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Warf. Acquisition of data: Lane, Mugamba, Ssenyonga. Analysis and interpretation of data: Warf, Lane. Drafting the article: Warf, Lane. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Warf. Statistical analysis: Warf, Lane. Administrative/technical/material support: Warf, Mugamba, Ssenyonga. Study supervision: Warf.

References