Determining the Best Cerebrospinal Fluid Shunt Valve Design: The Pediatric Valve Design Trial

Myriad cerebrospinal fluid shunt valve designs are available (17, 18). None has ever been shown to be superior to another, although claims by neurosurgeons and shunt manufacturers of the merits of particular designs are numerous. Such is the case with two recent shunt valve designs, the Orbis-Sigma valve (Cordis Corporation, Miami, FL) and the Delta valve (PS Medical, Goletta, CA). Both reduce the siphoning effect when the patient is in the upright position by different mechanisms. Reports of reduced complication rates in uncontrolled series have been attributed to diminished shunt overdrainage (13, 19, 20, 22).

Aside from the problems of interpreting uncontrolled series, there are reasons why these shunts might be inferior to the standard differential pressure valves, which have been used for more than 3 decades. The Orbis-Sigma valve is a high-resistance system with a narrow orifice that might be easily occluded. The flexible membrane of the siphon control portion of the Delta valve may increase the ventricular pressure when the patient is in the upright position or become blocked by encasing scar tissue (4, 6). Therefore, a randomized trial with a standard differential pressure valve used as the control is required, to determine efficacy. Such a trial has been commenced, with accrual of the necessary 345 patients nearly completed. Patients will be observed for a minimum of 1 year to determine whether any design provides a 50% reduction in failure rate, which is defined as shunt obstruction, loculated ventricles, shunt overdrainage, or shunt infection. The details of the rationale and protocol for the trial will subsequently be published.

Shunt valve designs

Standard valves

The original cerebrospinal fluid shunt valves were introduced 40 years ago (18). They operate as differential pressure devices allowing one-way flow (10, 23). When less than a threshold pressure difference across the valve, they remain closed, and when more than the threshold pressure difference, they open (the opening pressure). There are a number of different valve mechanisms, including silicone rubber slit valves, silicone rubber diaphragm valves, silicone rubber miter valves, and metallic spring ball valves (5, 17). They all achieve essentially the same pressure/flow characteristics. A representative spring ball valve is shown in *Figure 1*. Once the valves are open, they provide very little resistance to flow. When the patient is in the upright position, because of the column of water in the shunt and the effects of gravity, a large pressure differential exists between the head and the abdomen so that the shunt flows at a high rate until the pressure in the head is excessively negative (siphoning [2, 11]). This is the presumed explanation of the complications of shunt overdrainage, including subdural hematoma (12), slit ventricle syndrome (7, 14), craniostenosis, and intracranial hypotension (8).

The standard valves usually are supplied by the manufacturers as low-, medium-, and high-pressure valves (and in some cases, very low- or very high-). Unfortunately, there are no uniform standards for these designations, and the manner in which this pressure is measured is also variable (5). In general, the pressure designation refers to the opening pressure, either just at the beginning of flow or at a low flow rate, such as 5 ml per hour. Low, medium, and high pressures in this scenario refer to pressures of approximately 5, 10, and 15 cm of H_2O pressure, respectively. The opening pressure differences are overwhelmed by the pressure effects when the patient assumes the upright position, as discussed above. A number of series using different combinations of standard valve designs have reported failure rates that are very similar (1, 15, 16, 21). Therefore, considering all standard valves to be equivalent for the purposes of the trial seems to be reasonable.

Cordis Orbis-Sigma valve

The Orbis-Sigma valve has quite different flow/pressure characteristics from those of a standard valve (20) (*Fig. 1*). A flexible diaphragm moves along a piston of variable diameter, basically resulting in three pressure/flow stages. In Stage 1, the valve functions in the same way as a standard differential pressure diaphragm valve, with an opening pressure and a low resistance to flow. In Stage 2, as the ventricular pressure increases, the diaphragm descends along the piston, whose diameter gets progressive larger. This reduces the flow orifice, dramatically increasing the resistance to flow. This results in very little increase in flow rate despite a progressive increase in pressure and effectively results in a flow limit. Stage 3 is a high-pressure 'safety' release mechanism. When the pressure in the ventricular catheter reaches a high level, ~40 cm H_2O, the diaphragm moves beyond the end of the piston, where the resistance is very low, resulting in a gush of fluid and limiting the pressure buildup. The transition between stages is not exact, so the pressure curve is sigmoid in shape (and thus the name Sigma).

PS Medical Delta valve

The Delta valve is a standard valve (silicone diaphragm mechanism) with an additional modified antisiphon device (13) (*Fig. 1*). The flexible membrane of the siphon control portion moves against the orifice, increasing the resistance to flow, as the patient assumes the upright posture and siphoning starts to occur. This antisiphon effect reduces the tendency to overdrainage in the upright position; however, the pressure required to maintain the same flow rate actually slightly increases (*Fig. 1*). To properly function, the diaphragm must be freely mobile and the pressure outside the membrane must be atmospheric (3). The position of the siphon control device along the distal column of fluid is also important (9). The lower the device is placed along the shunt path, relative to the ventricles, the greater the negative

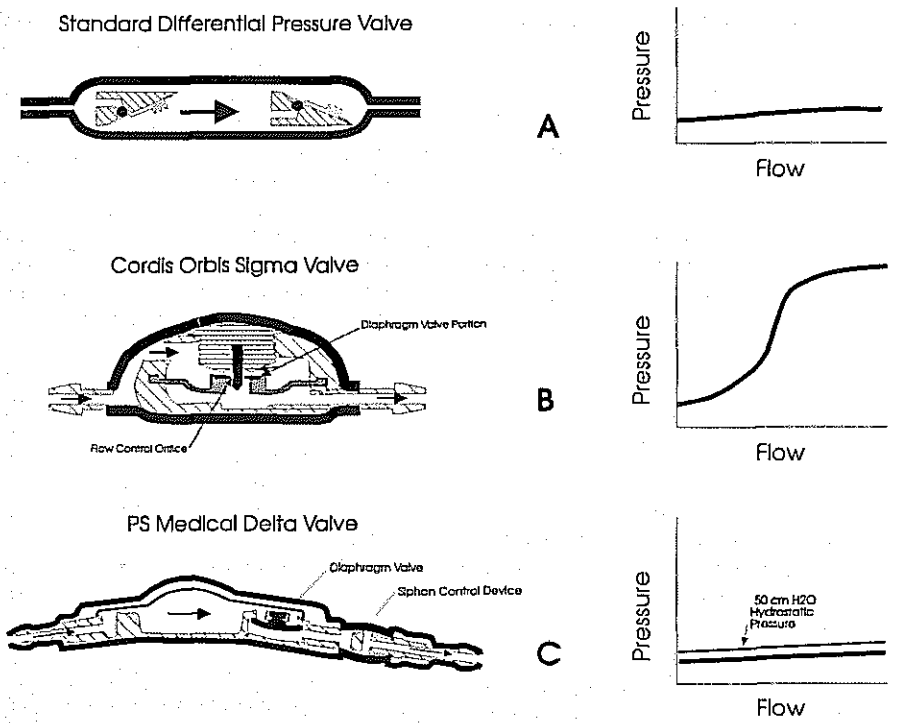

FIGURE 1. Valve design and pressure/flow measurements for the three valves involved in the trial. *A*, standard differential pressure valve illustrated by the Cordis Hakim spring ball valve. The valve is either open or closed. Once open, the resistance to flow is very low, so there is very little pressure increase for increased flow rates, as shown in the pressure/flow curve. Accordingly, large flow rates are possible, as when the patient assumes the upright position, leading to siphoning. *B*, Cordis Orbis-Sigma valve. As the flexible diaphragm moves along the increased diameter of the piston, the resistance rapidly increases, effectively producing a flow limit and reducing overdrainage. If the pressure becomes too high, the diaphragm moves beyond the narrow portion, which is a safety release mechanism. *C*, PS Medical Delta siphon control valve. Distal to the standard diaphragm valve is the siphon control portion. When the patient assumes the upright position and the pressure in the ventricle and shunt system becomes negative, the membranes close on the orifice, increasing the resistance. The effects of this are shown in the accompanying graph, in which, with 50 cm H_2O of negative hydrostatic pressure (as by dropping the distal catheter tip 50 cm below the valve), there is a slight increase in pressure at every flow rate.

pressure that will occur in the ventricles. In the limiting case, in which the device is placed at the level of the abdomen (or as in a lumboperitoneal shunt), the siphon control portion would never be active and the valve would function exactly like a differential pressure valve. The valve is available in three opening pressure levels (1, 1.5, and 2), which have successively higher opening pressures. The antisiphon portion functions in the same way.

Shunt valve failure

Several retrospective reviews have shown remarkably similar failure rates for standard valves. In a combined series of 1700 patients, the 1-year shunt failure rate was 40% (21). A similar study from Portland, OR, had a 1-year failure rate of 35% (16). A prospective series comparing frontal versus parietal shunt placement had a combined 1-year failure rate of 30% (1). Failure rates after the 1st year have been much lower, averaging ~5%.

The Cordis Orbis-Sigma valve has been reported to have a 1-year failure rate of 20% (19), which is much lower than that of standard valves. The PS Medical Delta valve has also been reported to have improved results (13). In 68 patients observed for 15 months after Delta valve insertion, only nine valves had failed (Wallstedt, Karolinska Institute, personal communication). As these are uncontrolled series, the mechanism for the improved results is not known and confounding factors such as excellence of surgical technique play an unknown role. The cerebral ventricles are maintained larger on average with the Cordis Orbis-Sigma valve than with standard valves. The proportion of slit, normal, and large ventricles with the Orbis-Sigma valve was 8.2, 36.5, and 55.3%, respectively, as compared with 30.9, 21.3, and 47.8% with standard valves (19). A higher number and proportion of proximal obstructions occurred with the standard valves, suggesting that coaptation of the small ventricles and the ventricular catheter may predispose to plugging of the catheter holes with adjacent tissue. The proportion of valve failures was higher with the Cordis Orbis-Sigma valve, which was possibly related to the small orifice, although the overall failure rate was much less.

Trial design

We designed the trial to detect a 50% reduction in the 1-year shunt failure rate (from 40 to 20%) comparing a standard shunt of the surgeon's choice, the Cordis Orbis-Sigma valve, and the Delta valve. Patients newborn to 18 years of age undergoing their first ventriculoperitoneal shunt insertions are eligible and are randomized to receive one of the three valves at the time of surgery. The configuration of the equipment (i.e., one piece versus several pieces) or the technique (i.e., with the aid of a ventriculoscope) are decided by the individual surgeon but are recorded. Exclusion criteria include premature patients whose skin is too thin to accept any of the shunts, patients who have active infections, patients with predisposition to shunt obstruction (blood-filled ventricles), or patients with Dandy-Walker malformations. Patients will receive follow-up for a minimum of 1 year. Shunt failure is subdivided into shunt obstruction, loculated ventricles, shunt overdrainage, and shunt infection. Patients need to satisfy a series of clinical, radiological, or surgical criteria to reach the

endpoint. All patients' eligibility and outcome will be reviewed by a blinded adjudication committee. The calculated sample size using an alpha type error of 0.017 (0.05 divided by 3) and a beta type error of 0.2 (power, 80%) is 345 patients (115 per group).

Trial limitations

There are several obvious limitations with this trial. It involves only pediatric patients, and neither the surgeons nor the patients are blinded to the study protocol. A separate pediatric trial is reasonable given the specific diseases that occur during this age. However, other adult trials to study normal-pressure hydrocephalus, for example, may be necessary. Blinding surgeons and patients to the study protocol is impossible, given the readily identifiable characteristics of the shunt equipment before and after implantation. However, there are specific definitions in terms of clinical symptoms and signs and there are diagnostic tests for each subset of the primary outcome measure, shunt failure, which must be met. In addition, an independent adjudication committee blinded to shunt type will determine whether each patient has reached the outcome measure.

Likely benefits of the trial

The results of this trial should allow surgeons to rationally choose a shunt design for use in their pediatric patients. A reduction of 50% in the 1-year shunt failure rate would dramatically affect the lives of thousands of patients with shunts as well as create significant savings for the health care system. Even a negative result would be helpful in that it would suggest that the most inexpensive shunt is adequate and that efforts should be focused in other areas, such as surgical technique, shunt material, etc. Finally, we think that this trial will establish a standard regarding claims of improved efficacy for new shunt devices. These claims will need to be backed up by sound scientific evidence.

Trial organization and progress

The multicenter cerebrospinal fluid shunt design trial commenced patient accrual in October 1993. Patient accrual concluded in October 1995. The results of the trial should be available in the spring of 1997. The primary authors of this communication are the coprincipal investigators. The trial Data Center is in Vancouver, Canada. Participating centers and surgeons are listed in the Appendix.

ACKNOWLEDGMENTS

The trial is funded by the British Columbia Health Development Fund, Technology Assessment, the Spina Bifida Association of Canada, the Spina Bifida Association of British Columbia, British Columbia Medical Services Foundation, P.A. Woodward Foundation, British Columbia Children's Hospital Telethon, and by Cordis Corporation and PS Medical. The Pediatric Hydrocephalus Treatment Evaluation Group, in addition to the primary authors, includes Dr. Frederick A. Boop, Little Rock, AR; Dr. David D. Cochrane, Vancouver, Canada; Dr. Stephen J. Haines, Minneapolis, MN; Dr. Christian Sainte-Rose, Paris, France; Dr. Steven J. Schiff, Washington D.C.; and Dr. Paul Steinbok, Vancouver, Canada.

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REFERENCES

1. Bierbauer KS, Storrs BB, McLone DG, Tomita T, Dauser R: A prospective, randomized study of shunt function and infections as a function of shunt placement. **Pediatr Neurosurg** 16:287–291, 1990.
2. Chapman PH, Cosman ER, Arnold MA: The relationship between ventricular fluid pressure and body position in normal subjects and subjects with shunts: A telemetric study. **Neurosurgery** 26:181–189, 1990.
3. da Silva MC, Drake J: Effect of subcutaneous implantation of anti-siphon devices on CSF shunt function. **Pediatr Neurosurg** 16:197–202, 1990.
4. da Silva MC, Drake JM: Complications of cerebrospinal fluid shunt antisiphon devices. **Pediatr Neurosurg** 17:304–309, 1991.
5. Drake JM, Sainte-Rose C: *The Shunt Book*. New York, Blackwell Scientific, 1995.
6. Drake JM, da Silva MC, Rutka JT: Functional obstruction of an antisiphon device by raised tissue capsule pressure. **Neurosurgery** 32:137–139, 1993.
7. Epstein F, Lapras C, Wisoff JH: 'Slit-ventricle syndrome': Etiology and treatment. **Pediatr Neurosci** 14:5–10, 1988.
8. Foltz EL, Blanks J: Symptomatic low intracranial pressure in shunted hydrocephalus. **J Neurosurg** 68:401–408, 1988.
9. Foltz EL, Blanks J, Meyer R: Hydrocephalus: The zero ICP ventricle shunt (ZIPS) to control gravity shunt flow—A clinical study in 56 patients. **Childs Nerv Syst** 10:43–48, 1994.
10. Fox JL, McCullough DC, Green RC: Cerebrospinal fluid shunts: An experimental comparison of flow rates and pressure values in various commercial systems. **J Neurosurg** 37:700–705, 1972.
11. Fox JL, McCullough DC, Green RC: Effect of cerebrospinal fluid shunts on intracranial pressure and on cerebrospinal fluid dynamics: 2—A new technique of pressure measurements: Results and concepts—3: A concept of hydrocephalus. **J Neurol Neurosurg Psychiatry** 36:302–312, 1973.
12. Hoppe-Hirsch E, Sainte-Rose C, Renier D, Hirsch JF: Pericerebral collections after shunting. **Childs Nerv Syst** 3:97–102, 1987.
13. Horton D, Pollay M: Fluid flow performance of a new siphon-control device for ventricular shunts. **J Neurosurg** 72:926–932, 1990.
14. Kiekens R, Mortier W, Pothmann R, Bock WJ, Seibert H: The slit-ventricle syndrome after shunting in hydrocephalic children. **Neuropediatrics** 13:190–194, 1982.
15. Liptak GS, Masiulis BS, McDonald JV: Ventricular shunt survival in children with neural tube defects. **Acta Neurochir (Wien)** 74:113–117, 1985.
16. Piatt JHJ, Carlson CV: A search for determinants of cerebrospinal fluid shunt survival: Retrospective analysis of a 14-year institutional experience. **Pediatr Neurosurg** 19:233–241, 1993.
17. Post EM: Currently available shunt systems: A review. **Neurosurgery** 16:257–260, 1985.
18. Pudenz RH: The surgical treatment of hydrocephalus: An historical review. **Surg Neurol** 15:15–26, 1981.
19. Sainte-Rose C: Shunt obstruction: A preventable complication? **Pediatr Neurosurg** 19:156–164, 1993.

20. Sainte-Rose C, Hooven MD, Hirsch JF: A new approach to the treatment of hydrocephalus. **J Neurosurg** 66:213–226, 1987.
21. Sainte-Rose C, Piatt JH, Renier D, Pierre-Kahn A, Hirsch JF, Hoffman HJ, Humphreys RP, Hendrick EB: Mechanical complications in shunts. **Pediatr Neurosurg** 17:2–9, 1991.
22. Tokoro K, Chiba Y, Abe H, Tanaka N, Yamataki A, Kanno H: Importance of anti-siphon devices in the treatment of pediatric hydrocephalus. **Childs Nerv Syst** 10:236–238, 1994.

23. Watts C, Keith HD: Testing the hydrocephalus shunt valve. **Childs Brain** 10: 217–228, 1983.

Appendix

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