Randomized Trial of Drainage, Irrigation and Fibrinolytic Therapy for Premature Infants with Posthemorrhagic Ventricular Dilatation: Developmental Outcome at 2 years

WHAT'S KNOWN ON THIS SUBJECT: Premature infants with PHVD have a high rate of severe cognitive and motor disabilities, but no intervention has been shown to improve outcome. Secondary cerebral injury may be caused by free radicals, inflammation, and pressure.

WHAT THIS STUDY ADDS: DRIFT, which lowers pressure and distortion and washes out free iron and cytokines, reduced death or severe disability, especially severe cognitive disability at 2 years, despite the risk of secondary intraventricular bleeding.

abstract

BACKGROUND: Preterm infants who develop posthemorrhagic ventricular dilatation (PHVD) have a high risk of cognitive and motor disability. No clinical intervention has been proven to reduce neurodevelopmental disability in such infants. We investigated whether drainage, irrigation, and fibrinolytic therapy (DRIFT), which aims to lower pressure, distortion, free iron, and cytokines, reduces death or severe disability in PHVD.

METHODS: We randomly assigned 77 preterm infants with PHVD to either DRIFT or standard treatment (ie tapping off cerebrospinal fluid to control excessive expansion). Severe disability was assessed at 2 years' corrected age and included severe sensorimotor disability and cognitive disability (<55 on the Bayley Mental Development Index).

RESULTS: Of 39 infants assigned to DRIFT, 21 (54%) died or were severely disabled versus 27 of 38 (71%) in the standard group (adjusted odds ratio 0.25 [95% confidence interval: 0.08–0.82]). Among the survivors, 11 of 35 (31%) in the DRIFT group had severe cognitive disability versus 19 of 32 (59%) in the standard group (adjusted odds ratio: 0.17 [95% confidence interval: 0.05–0.57]). Median Mental Development Index was 68 with DRIFT and <50 with standard care. Severe sensorimotor disability was not significantly reduced.

CONCLUSIONS: Despite an increase in secondary intraventricular bleeding, DRIFT reduced severe cognitive disability in survivors and overall death or severe disability. *Pediatrics* 2010;125:e852–e858

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KEY WORDS

intraventricular hemorrhage, hydrocephalus, treatment, cognitive function, premature infant

ABBREVIATIONS

IVH—intraventricular hemorrhage
PHVD—posthemorrhagic ventricular dilatation
MDI—Mental Development Index
PDI—Psychomotor Development Index
CSF—cerebrospinal fluid
DRIFT—drainage, irrigation, and fibrinolytic therapy
rTPA—recombinant tissue plasminogen activator
LP—lumbar puncture
OR—odds ratio
CI—confidence interval

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One of the most serious complications of preterm birth is hemorrhage into the cerebral ventricles with subsequent progressive enlargement. Despite improved survival rates and a reduction in the percentage of infants with intraventricular hemorrhage (IVH), posthemorrhagic ventricular dilatation (PHVD) persists as a serious condition with high risk of serious cognitive, motor, and sensory disability.[1] In the Neonatal Research Network, 33% of infants with birth weights of 401 to 1000 g developed IVH, and, of those, 10% required shunt surgery for hydrocephalus. Severe cognitive disability (Mental Development Index [MDI] $<$ 50) was found in 48% of infants with a grade 4 IVH and shunt.[1] No intervention has been shown to improve neurodevelopmental outcome in PHVD.

Multiple blood clots obstruct reabsorption of cerebrospinal fluid (CSF) initially but lead to a chronic arachnoiditis of the basal cisterns with deposition of extracellular matrix proteins.[2,3] Approximately half of the infants with PHVD have early hemorrhagic infarction of periventricular white matter, but over the following weeks, progressive injury to the immature cerebral hemispheres globally may result from pressure, distortion, free radical generation facilitated by free iron, and inflammation.[4–6]

Because of bloody CSF, small size, and instability of the patient, an early ventriculoperitoneal shunt is contraindicated, and various approaches have been used to treat infants with PHVD in the hope of reducing severe disability. Repeated tapping of lumbar or ventricular fluid has been tested in randomized trials and did not reduce any disability.[7] A randomized trial of reducing CSF production with acetazolamide and furosemide showed worse developmental outcome in the infants receiving the intervention.[8]

Standard treatment for PHVD varies. The standard arms of the ventriculomegaly trial and the PHVD drug trial both used selective tapping of CSF to control signs of pressure or excessive head enlargement.[8,9] Insertion of a ventricular access device such as an Ommaya or Rickham reservoir to facilitate repeated tapping of CSF is widely practiced without having been tested by randomized trial.[10]

We have piloted drainage, irrigation, and fibrinolytic therapy (DRIFT), a procedure that aims to decompress the distended ventricles early, reducing pressure and distortion and removing intraventricular blood, inflammatory cytokines, and iron, thereby reducing secondary injury to the cerebral hemispheres.[11]

We conducted this international randomized trial of DRIFT to study short- and long-term efficacy and safety in premature infants with PHVD. The short-term outcomes up to 6 months of age or discharge from hospital demonstrated that DRIFT did not reduce shunt surgery or death.[12] Because interim analysis showed there was no likelihood of shunt surgery or death being reduced and because of an excess of secondary intraventricular bleeding in the intervention group, recruitment to the study was stopped early on the recommendation of the data safety monitoring group. However, information on short-term outcomes was insufficient to assess the overall benefits and risks of neonatal interventions. The primary long-term aim of this study was to determine whether DRIFT altered the rate of death or severe neurodevelopmental disability at 24 months' corrected age.

METHODS

The study was approved by the research ethics board of each institution that took part: Southmead Hospital (Bristol, United Kingdom), Royal Hospital for Sick Children (Glasgow, United Kingdom), Medical University of Silesia (Katowice, Poland), and Haukeland Hospital (Bergen, Norway). Written informed consent was obtained from the mother of each infant.

Screening

In all 4 centers, preterm infants who required intensive care or showed neurologic abnormalities had daily cranial ultrasound scans for the first 3 days and then had scans at least weekly for 4 weeks. If IVH was diagnosed, ultrasound scanning was performed twice weekly. Ventricular measurements were made when there was any visible enlargement and head circumference was then measured daily. Cranial ultrasound continued twice weekly until resolution of ventricular enlargement and more frequently when enlargement was progressive.

Inclusion Criteria

Infants of $<$37 weeks' gestation were eligible if they had:

1. IVH documented on ultrasound scan
2. age no more than 28 days
3. progressive dilatation of both lateral ventricles with each side having

3a. ventricular width 4 mm over the 97th centile[13]

3b. all of the following:

- anterior horn diagonal 4 mm (1 mm over the 97th centile)
- thalamo-occipital distance 26 mm (1 mm over the 97th centile)
- third ventricle width 3 mm (1 mm over 97th centile)[14]

3c. If the infant had measurements above 3a or 3b on 1 side combined with obvious midline shift, this was accepted as a pressure effect, and the infant was eligible.

Exclusion criteria were prothrombin time $>$ 20 seconds, accelerated par-

tial thromboplastin time > 50 seconds or platelet count < 50 000/mL.

Randomization

A computer-generated randomization scheme was used to assign the infants to treatment groups in a 1:1 ratio. Randomization was stratified according to study center and in blocks of 8, 10, or 12. Each infant was allocated to sequentially numbered, double-opaque envelopes (1 envelope inside the other to ensure concealment of allocation) that each contained a "DRIFT" or "standard treatment" card.

Interventions

A detailed description of DRIFT has been published previously.[11] Under anesthesia, 2 ventricular catheters were inserted (right frontal and left occipital). Then, 0.5 mg/kg recombinant tissue plasminogen activator (rTPA) (Actilyse [Boehringer Ingelheim, Ingelheim am Rhein, Germany]) was injected intraventricularly. After 8 hours, artificial CSF with each 500 mL containing 10 mg of vancomycin and 5 mg intrathecal gentamicin was infused at 20 mL/kg per hour into the right frontal ventricular catheter with a pressure transducer on the in-going line. Simultaneously, fluid was allowed to drain from the left occipital ventricular catheter, the height of the drainage reservoir being adjusted to maintain intracranial pressure below 7 mm Hg and to achieve initial drainage volume of 60 to 100 mL/24 hours more than the infused volume. This reduced ventricular size considerably over 48 hours. Infusion was stopped when the drainage fluid became clear, and the catheters were removed after a median of 3 days (range: 2–7 days).

Standard treatment required no intervention unless there was excessive head enlargement or suspicion of raised intracranial pressure (irritability, apnea, persistent vomiting, reduced consciousness, bulging fontanelle, sun-setting, or loss of diastolic velocities on cerebral arteries). This policy was based on the standard arms of the 2 previous large trials.[8,9] Excessive head enlargement was defined as 2 mm/day. The standard intervention, if required, was lumbar puncture (LP) removing 10 mL/kg. Additional LPs depended on recurrence of the above-listed signs. If >2 LPs were required or if LP failed to drain enough to normalize head growth, a ventricular reservoir was indicated. Ten to 20 mL/kg was tapped at a frequency sufficient to limit head growth to <2 mm/day. If DRIFT was followed by persistent enlargement of ventricles and excessive head growth, standard treatment with LP and ventricular reservoir was used. Infants were not "crossed over" from standard treatment to DRIFT. Every infant in the intervention group received DRIFT, and no infant in the standard group received DRIFT. LP and reservoir were available, if needed, to both groups.

If an infant required repeated reservoir taps to control head growth, this was continued until weight reached 2500 g and CSF protein decreased to <1.5 g/L. Tapping was stopped and the head circumference was measured daily. If excessive head growth occurred (with expanding ventricles) at this stage, a ventriculoperitoneal shunt was indicated.

An external data safety monitoring group reviewed short-term outcomes after 50% of the target recruitment (based on the initial power calculation) and recommended that recruitment cease, by which time 70 infants had been recruited.

The recommendation was based on (1) the very low likelihood of continued recruitment achieving a statistically significant difference for the primary short-term outcome and (2) an excess of secondary intraventricular bleeding in the DRIFT group. After some discussion about the possibility of tightened vigilance reducing the risk of secondary bleeding, the Bristol center was allowed by the research ethics committee to resume recruitment. After 7 infants had been included, additional recruitment was stopped because 1 of the infants in the DRIFT group developed a secondary hemorrhage. These extra 7 infants had exactly the same entry criteria and were following exactly the same protocol as the other 70. The only differences were increased awareness of bleeding and motivation to follow the protocol in even greater detail.

Outcomes

The primary long-term outcome was severe cognitive or sensorimotor disability or death. All surviving infants were evaluated. At a mean corrected age of 25 months (SD: 1.7), each child was examined by a developmental assessor who was blind to the initial treatment allocation. The assessment included developmental history, neurologic assessment, classification of the degree and type of disability, and functional classification of hearing and visual ability. Development was assessed with the Bayley Scales of Infant Development (2nd edition).[15] We had prespecified that severe cognitive disability was indicated by an MDI score of <55, which is 3 SDs below the mean. Criteria for severe sensorimotor disability[16] were any 1 of:

(a) inability to walk without assistance,
(b) inability to sit without support,
(c) inability to control head without support,
(d) inability to use hands to feed self,
(e) blindness or only light perception,
(f) hearing loss uncorrected by hearing aid, or
(g) inability to communicate by speech.

In addition to the primary outcome, we prespecified 2 secondary outcomes: severe cognitive disability in survivors and severe sensorimotor disability in survivors.

Analysis was by intention to treat. Comparisons between the 2 treatment groups were made by using χ^2 tests or 2-tailed Fisher's exact test when frequencies were small. Logistic regression analyses were used to calculate adjusted odds ratios (ORs). A 5% level of significance was used throughout. In this group of seriously brain-injured infants, we considered that reduction in very severe disability was a more realistic objective, but we did carry out a secondary exploratory analysis of moderate cognitive impairment (MDI $<$ 70).

RESULTS

Recruitment started in Bristol in February 2003, paused in April 2006, restarted in July 2006, and finished at the end of December 2006. Seventy-seven infants were recruited in total: 54 in Bristol, 20 in Katowice, 2 in Glasgow, and 1 in Bergen. The great majority of infants recruited in Bristol and Katowice were transferred from other cities for neurosurgical assessment. Eighty-two infants were assessed for eligibility (Fig 1). One infant initially assessed was found to be ineligible because the gestation was $>$37 weeks and the cerebral injury was not a primary IVH. Seventy-seven of 81 parents of infants who met the trial criteria gave consent when asked, and none of the recruited infants were lost to follow-up. Sixty-three infants were eligible because they met both criteria 3a and 3b. Seven met criterion 3b alone, and 7 met criterion 3c alone. All 77 infants received the allocated treatment, and all were analyzed after 2 years.

Table 1 shows that the 2 groups were comparable at randomization except that children in the DRIFT group had a higher proportion of boys and parenchymal infarctions (grade 4 IVH)[17] and slightly lower birth weight and gestational age. Maternal socioeconomic backgrounds were similar between the 2 groups.

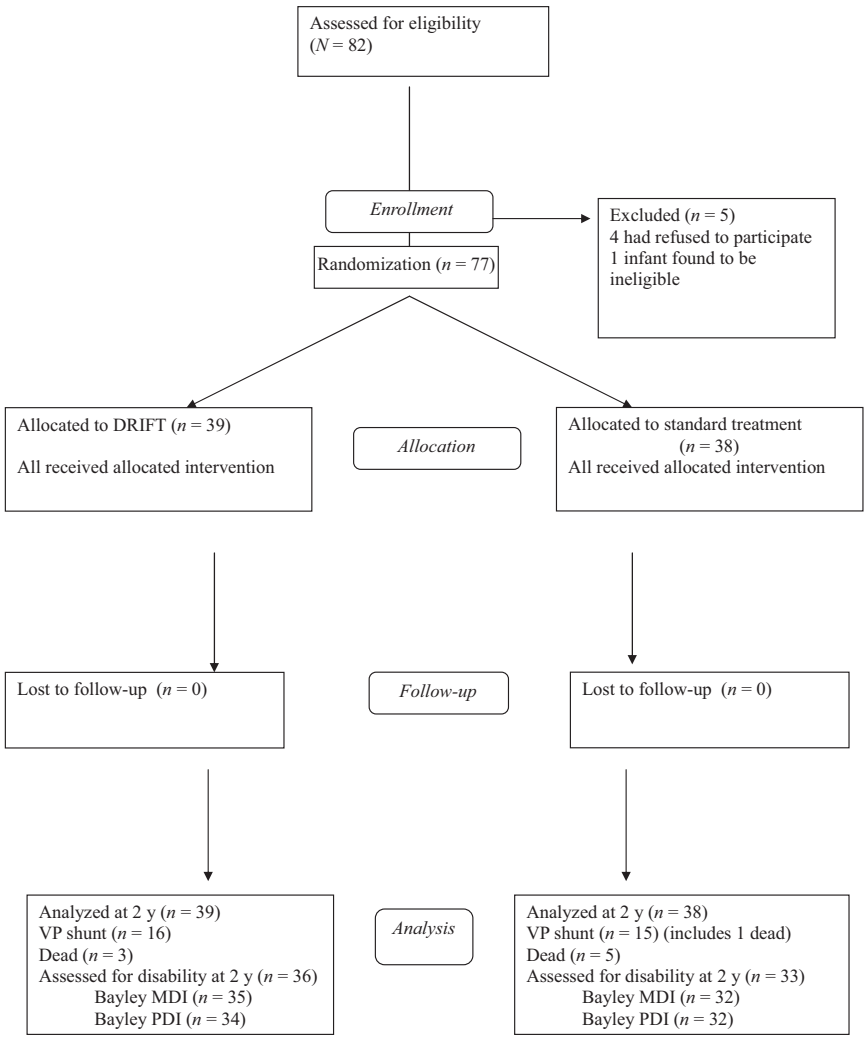

FIGURE 1
The DRIFT trial. VP indicates ventriculoperitoneal.

TABLE 1 Characteristics of Infants at Entry onto the DRIFT Trial

Characteristic	DRIFT (N = 39)	Standard (N = 38)
Bristol, *n*	27	27
Katowice, *n*	10	10
Glasgow, *n*	1	1
Bergen, *n*	1	0
Gestation, median (range), wk	27 (24–34)	28 (24–35)
Birth weight, median (range), wk	1050 (640–2100)	1130 (720–2755)
Male, *n* (%)	29 (74)	24 (63)
Parenchymal hemorrhagic infarction (grade 4 IVH), *n* (%)	20 (51)	18 (47)
Age at randomization, median (range), d	20 (7–28)	18 (9–28)
Ventricular width (mean of left/right) at entry, median (range), mm	16 (12–21)	18 (12–30)

Disability assessments were available for all 69 survivors and MDI for 67. One child had the MDI assessed but not the Psychomotor Development Index (PDI). Two children were assessed for the

above-listed components of disability but did not have Bayley Scales assessments and were not included in the analysis of Bayley scores.

Primary Outcome: Death or Severe Disability

The 7 extra Bristol recruits did not differ from the original 70, and combined results are reported. Five of 38 infants in the standard-treatment group died, and 3 of 39 in the DRIFT group died, leaving 69 survivors. According to the prespecified definitions of severe disability (cognitive and sensorimotor), 22 of the survivors in the standard-treatment group were severely disabled at 2 years, giving a combined total of 27 (71%) who were severely disabled or dead. In the DRIFT group, 18 of the survivors were severely disabled, giving a combined total of 21 (54%) dead or disabled (odds ratio [OR]: 0.48 [95% confidence interval (CI): 0.19–1.22]). The OR, adjusted for gender, birth weight, and grade of IVH was reduced to 0.25 (95% CI: 0.08–0.82).

Secondary Outcomes

Severe Cognitive Disability in Survivors

Eleven of 35 (31%) surviving children in the DRIFT group had severe cognitive disability as indicated by a Bayley MDI of <55, significantly fewer than 19 of 32 (59%) in the standard-treatment group (OR: 0.31 [95% CI: 0.11–0.86]) (Table 2). When adjusted for gender, birth weight, and grade of IVH, the OR fell to 0.17 (95% CI: 0.05–0.57). Risk difference was 0.279, and the number needed to treat was 4 (95% CI: 2–20). The median MDI in the DRIFT group was 68 compared with <50 in the standard-treatment group.

Severe Sensorimotor Disability in Survivors

Each of the components of severe disability in gait, sitting, hand control, head control, speech, vision, and hearing was less common in the DRIFT group than in the standard-treatment group but without reaching statistical significance (Table 3). The same trend applied to seizures.

TABLE 2 Effect of DRIFT on the Distribution of Bayley Developmental Indices

	Treatment		Severe Disability (<55)			
	DRIFT (N = 35/34),[a] n (%)	Standard (N = 32), n (%)	OR (95% CI)	P	OR (95% CI) Adjusted for Gender, Birth Weight, and Grade of IVH	P
MDI						
≥85	8 (23)	9 (28)	0.31 (0.11–0.86)	.024	0.17 (0.05–0.57)	.004
70–84	9 (26)	3 (9)				
55–69	7 (20)	1 (3)				
<55	11 (31)[b]	19 (59)[b]				
PDI						
≥85	4 (12)	5 (16)	0.54 (CI 0.20–1.45)	.22	0.21 (0.05–0.85)	.028
70–84	5 (15)	5 (16)				
55–69	11 (32)	4 (13)				
<55	14 (41)[b]	18 (56)[b]				

[a] One child had MDI assessed but not PDI.
[b] Severe disability.

Exploratory Analyses

In the DRIFT group, 14 of 34 infants had a psychomotor index of <55 (41%) compared with 18 of 32 (56%) in the standard-treatment group (unad-

TABLE 3 The Effect of DRIFT on the Components of Disability

	DRIFT, n (%)	Standard, n (%)	Comparison of Severe Disability vs the Rest, P
Total	36	33	
Gait normal	6 (17)	11 (33)	
Nonfluent gait	9 (25)	4 (12)	
Abnormal gait reduced mobility	5 (14)	1 (3)	
Unable to walk without assistance	16 (44)[a]	17 (52)[a]	.56
Sitting normal	22 (61)	20 (61)	
Sits unsupported but unstable	6 (17)	5 (15)	
Sits supported	4 (11)	1 (3)	
Unable to sit	4 (11)[a]	7 (21)[a]	.25
Hand use normal	18 (50)	15 (45)	
Some difficulty feeding with both hands	14 (39)	14 (42)	
Unable to use hands to feed	4 (11)[a]	4 (12)[a]	>.99[b]
Head control normal	31 (86)	24 (73)	
Unstable head control	4 (11)	5 (15)	
Needs support to control head	1 (3)[a]	4 (12)[a]	.19[b]
Speech normal	13 (36)	10 (30)	
Delayed speech	17 (47)	11 (33)	
No speech but using signing system	1 (3)[a]	3 (9)[a]	
No communication by speech or system	5 (14)[a]	9 (27)[a]	.06[b]
Vision normal	22 (61)	15 (45)	
Correctable vision	6 (17)	10 (30)	
Useful but not fully correctable	6 (17)	4 (12)	
Blind or perceives light only	2 (6)[a]	4 (12)[a]	.42[b]
Hearing normal	30 (83)	27 (82)	
Impaired but aid not needed	4 (11)	3 (9)	
Impaired corrected by aid	2 (6)	1 (3)	
Uncorrectable hearing loss	0 (0)[a]	2 (6)[a]	.23[b]
Seizures	4 (11)	5 (15)	.73[b]
Severe sensorimotor disability			
None	4 (11)	7 (21)	
Moderate	16 (44)	8 (24)	
Severe	16 (44)[a]	18 (55)[a]	.40

[a] Severe disability.
[b] Two-tailed Fisher's exact test.

justed OR: 0.54 [95% CI: 0.20–1.45]), but adjustment for gender, birth weight, and grade of IVH reduced the OR to 0.21 (95% CI: 0.05–0.85).

Only 8 of 27 boys surviving in the DRIFT group had an MDI of <55 (30%) compared with 14 of 20 in the standard-treatment group (70%) (OR: 0.18 [95% CI: 0.05–0.64]). In contrast, the proportion of girls with an MDI of <55 was almost identical, with 3 of 8 in the DRIFT group compared with 5 of 12 in the standard group. The effect difference, however, was not statistically significant ($P = .18$ for the interaction between the effects of male gender and DRIFT).

We found the expected increase in nearly all components of disability when grade 4 IVH (parenchymal hemorrhagic infarction) was compared with grade 3 IVH (Table 4). Among the infants surviving grade 3 IVH, 4 of 16 in the DRIFT group had an MDI of <55 vs 8 of 18 in the standard group. Among those surviving grade 4 IVH, 7 of 19 in the DRIFT group and 11 of 14 in the standard-treatment group had an MDI of <55.

When an MDI of <70 defined cognitive impairment, the difference between the 2 treatment groups was not statistically significant.

Secondary IVH within the DRIFT group did not increase disability. An MDI of <55 was found in 3 of 12 infants in the DRIFT group with secondary IVH (25%) and found in 8 of 23 infants in the DRIFT group without secondary IVH (35%). Severe sensorimotor disability was found in 6 of 12 (50%) infants in the DRIFT group with secondary IVH (50%) and 10 of 24 infants in the DRIFT group without secondary IVH (42%). These differences were not statistically significant. All but 1 of the secondary hemorrhages were asymptomatic, only diagnosed by daily scanning and hemoglobin values.

DISCUSSION

We performed this randomized trial because none of the previous treatments of PHVD have been shown to reduce disability. The intervention, DRIFT, is biologically plausible. First, raised pressure and distortion are present in PHVD.[4] Second, the CSF after IVH contains substances likely to be toxic to the immature brain.[5,6] Decompressing the brain early and washing out the ventricles has a rationale.

It is tempting to compare the rate of severe disability in the DRIFT trial with that in 2 previous PHVD studies with similar eligibility, although the ages and methods of assessment were different. In the ventriculomegaly trial, severe developmental delay was found in 30% of survivors, and 46% of entrants were dead or severely disabled.[9] In the PHVD drug trial, death, impairment or disability occurred in 77% of the infants.[8] It may be relevant that the infants in the DRIFT trial were lighter and less mature and had lower mortality rates.

We used an MDI of <55 as the definition of severe cognitive disability because this is the definition used in the large EPICURE study of extremely preterm infants[16] and is close to the definitions in the *International Classification of Diseases, 10 Edition*, and the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.[18,19] Many parents of children with MDIs of 55 to 69 who were able to walk and communicate did not consider their children to be severely disabled, but those parents with children who scored <55 did.

We previously reported that DRIFT did not reduce shunt surgery or death and was associated with an increase in secondary intraventricular bleeding.[12] In our study, the reduction in the primary long-term outcome, death or severe disability at 2 years in the DRIFT group reached statistical significance when adjusted for gender, birth weight, and grade of IVH. Severe cognitive disability was nearly halved and was statistically significant with or without adjustment. This benefit was more marked in boys than in girls. The reduction in severe sensorimotor disability with DRIFT did not reach statistical significance. The greater effect on cognitive than sensorimotor function might be explained by the fact that approximately half the infants already had parenchymal infarction in the periventricular white matter before entry to the trial, and one could not

TABLE 4 The Effect of DRIFT in Separate Grades of IVH

	Grade 3 IVH ($N = 39$)		Grade 4 IVH ($N = 38$)	
	DRIFT ($N = 19$)	Standard ($N = 20$)	DRIFT ($N = 20$)	Standard ($N = 18$)
Death, *n*	2	1	1	4
Components of severe disability among survivors, *N*	17	19	19	14
Unable to walk without assistance, *n* (%)	5 (29)	6 (32)	11 (58)	11 (79)
Unable to sit without support, *n* (%)	1 (6)	3 (16)	3 (16)	4 (29)
Unable to use hands to feed, *n* (%)	1 (6)	2 (11)	3 (16)	2 (14)
Needs support to control head, *n* (%)	0 (0)	3 (16)	1 (5)	1 (7)
No speech, *n* (%)	2 (12)	6 (32)	4 (21)	6 (43)
Blind or light response, *n* (%)	0 (0)	2 (11)	2 (11)	2 (14)
Uncorrectable hearing loss, *n* (%)	0 (0)	1 (5)	0 (0)	1 (7)
Severe sensorimotor disability, *n* (%)	5 (29)	7 (37)	11 (58)	11 (79)
Severe cognitive disability MDI < 55, *n*/*N* (%)	4/16 (25)	8/18 (44)	7 (37)	11 (79)
Moderate Cognitive impairment MDI < 70, *n*/*N* (%)	7/16 (44)	8/18 (44)	11 (58)	12 (86)
Overall outcome, death or severe disability, *n*/*N* (%)	9/19 (47)	10/20 (50)	12/20 (60)	17/18 (94)

expect DRIFT to repair a hole in the brain. Cognitive function is less localized in the brain than motor function. Decompression and washing out toxic substances should affect cerebral tissue globally. Thus, if DRIFT were to affect brain function, it would be more likely to affect cognitive than motor function.

Secondary bleeding with DRIFT is most likely to be caused by intraventricular rTPA. If DRIFT is used in the future, we would advocate not using rTPA routinely but restricting its use to clearing blocked ventricular catheters.

CONCLUSIONS

The results of this study raise a difficult dilemma in trial management. The data monitoring and safety group had responsibility for protecting the trial participants from avoidable harm, and few would have taken responsibility in 2007 for continuing to recruit to a treatment that increased intraventricular bleeding and did not reduce the need for shunts. Longer-term assessment showed a significant reduction in severe disability in the intervention group. The difference in MDI between the 2 treatment groups was >18 points, which most families and clinicians would rate as important. Children with cerebral palsy may manage their physical disability better with improved cognition. The results must be treated with caution, because trial recruitment was curtailed early and numbers were small.

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