Childs Nerv Syst (2007) 23:1111–1118
DOI 10.1007/s00381-007-0324-7

ORIGINAL PAPER

Hydrocephalus in children born in 1999–2002: epidemiology, outcome and ophthalmological findings

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Received: 23 October 2006 / Revised: 1 February 2007 / Published online: 12 April 2007

Abstract
Objective The purpose of this study was to monitor incidence and outcome in children with hydrocephalus.
Materials and methods This is a population-based prospective study of all the children with hydrocephalus born in western Sweden in 1999–2002. Etiological and clinical information was collected from records, neuroimaging and ophthalmological examinations. Comparisons with 208 children born in 1989–1998 were made.
Results The incidence was 0.66 per 1,000 live births, 0.48 for infantile hydrocephalus and 0.18 for hydrocephalus associated with myelomeningocele. The corresponding rates for 1989–1998 were 0.82, 0.49 and 0.33. Ventriculoperitoneal shunt treatment was used in 42 of the 54 children and endoscopic third ventriculostomy in 12. Revisions were performed in 33 (61%). Neurological impairments were present in 63%, and they were more common in children born preterm than in those born at term. The radiological extent of parenchymal lesions correlated significantly with outcome. Ophthalmological abnormalities were found in 80%, including visual impairment in one third.
Conclusion The incidence of post-haemorrhagic hydrocephalus in children born extremely preterm increased; a group running a high risk of neurological sequelae. Ophthalmological abnormalities were frequent and need to be assessed in all children with hydrocephalus. The high rate of morbidity and complications necessitates the further development of preventive and treatment methods.

Keywords Epidemiology · Hydrocephalus · Myelomeningocele · Disability · Ophthalmology · Neuroradiology

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Introduction

Incidence and outcome in subgroups of hydrocephalus in children have been continuously monitored in western Sweden for almost 40 years [15, 20, 40]. The incidence of hydrocephalus has decreased during the last two decades mainly because of a decreasing trend in children with hydrocephalus associated with myelomeningocele (MMC) [21]. In Sweden, this is mainly due to improved prenatal diagnosis leading to the termination of MMC pregnancies [9]. This decrease has been counterbalanced by an increase in the number of children born very preterm, with a high risk of developing post-haemorrhagic hydrocephalus [20, 22, 41]. Improved neurosurgical techniques have increased the prevalence of hydrocephalus, as most children who are treated now survive. The mortality rate was about 50% in the pre-shunting era in 1940–1950 [24], while it is currently 5–10% [15, 40]. Complications such as obstruction, disconnection and infection of the shunt system are, however, common, and there is a need for surgical revisions

in about half the children [7]. This has resulted in the development of alternative treatment methods such as endoscopic third ventriculostomy (ETV), introduced back in 1923 by Mixter [35] but rarely used until the last few decades, in parallel with improved neurosurgical and neuroradiological techniques [36, 47]. The more sophisticated neuroimaging investigations have also improved the opportunity to clarify etiology and make predictions about outcome [25, 32].

The aim of this study was to calculate the incidence of infantile hydrocephalus and hydrocephalus associated with MMC during the birth year period 1999–2002 and to relate it to earlier epidemiological studies from the same region. Another objective was to analyse whether modern neurosurgery has reduced morbidity and mortality and whether etiology, treatment, complications and neuroradiological findings correlate with outcome. The ophthalmological consequences of hydrocephalus and their relationship to etiology and brain lesion patterns were also investigated.

Materials and methods

This prospective study was population-based, and the study area was the western part of Sweden during the birth year period 1999–2002, an area with 2.06 million inhabitants constituting 23% of the total population of 8.9 million in Sweden. The study population was the 82,016 live-born children in the region during the period. All children fulfilling the criteria for hydrocephalus (see below) and requiring surgical treatment during their first year of life, who were born in the area, were included in the study.

Two main groups were identified, children with infantile hydrocephalus, not associated with a spinal lesion or malignant intracranial tumour [15], and children with hydrocephalus associated with MMC.

The children were followed prospectively from birth up to 2.5–6.5 years of age (median 4 years and 3 months). Information about etiology, treatment, complications and outcome was gathered consecutively from clinical records from paediatric, neurosurgical and rehabilitation departments. Ophthalmological abnormalities were investigated at the ages of 1 year and 10 months to 6 years and 5 months (median 4 years and 4 months). The best corrected binocular (monocular if possible) visual acuity (VA) [51] was tested with a letter chart for visual acuity testing [26], Kay's charts [30] at a distance of 3 m and, in the youngest children, with the Cardiff chart [1] at a distance of 1 m. Refraction was measured in cycloplegia. To detect strabismus, cover and uncover tests were performed for near and distance fixation. The anterior segments were examined with a slit lamp. Indirect ophthalmoscopy was performed after pupil dilatation.

The neuroradiological examination before the first surgical intervention and that after the latest revision were evaluated by a neuroradiologist (L-M W.). The findings were categorised as no parenchymal lesion, I: small/moderate periventricular leukomalacia, II: extensive white matter loss, III: focal white matter loss with grey matter lesion and IV: generalised severe white and grey matter pathology.

Definitions Hydrocephalus was defined as ventricular expansion due to elevated intraventricular pressure, with an increased amount of intraventricular cerebrospinal fluid manifested during the first year of life. Prenatal referred to the period before the onset of labour, perinatal to the period from the onset of labour resulting in delivery to the 28th day of life and post-neonatal to the period from day 29 up to the age of 1 year. Children born at term were those born after 36 completed weeks of gestation, moderately preterm comprised those born between 32 and 36 weeks of gestation, very preterm those born between 28 and 32 weeks and extremely preterm those born before 28 completed weeks of gestation. Cerebral palsy was defined according to the criteria proposed by Mutch et al. [37], epilepsy was defined as two or more unprovoked epileptic seizures, and learning disability was defined as an IQ measured or estimated to be less than 70.

Significant refractive errors were defined as a spherical equivalent of myopia ≥0.5 dioptres (D), hyperopia ≥2.0 D, astigmatism >0.75 D and anisometropia of ≥1.0 D for children of 4 years of age and above [39]. For children less than 4 years of age, significant refractive errors were defined as a spherical equivalent of myopia ≥5.0 D, hyperopia ≥ 4.5 D, astigmatism >3.0 D and anisometropia of ≥1.5 D [2, 3]. Strabismus was defined as heterotropia manifested intermittently or constantly.

Statistical analysis For comparisons between two groups, the Mann–Whitney U test was used for ordered and continuous variables. Fisher's exact test and χ^2 test were used for fourfold tables. A p value of <0.05 was considered significant.

Ethics This study was approved by the Research Ethics Committee at Göteborg University.

Results

Fifty-four children with hydrocephalus were identified, 39 with infantile hydrocephalus and 15 with MMC, from the 82,016 children born during the period. The overall incidence was 0.66 per 1,000 live births, 0.48 per 1,000 live births for those with infantile hydrocephalus and 0.18 for children with MMC. These findings, combined with the results from the period 1989–1998, are shown in Fig. 1.

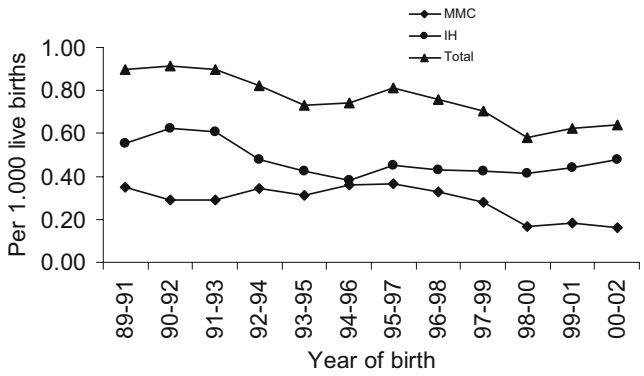

Fig. 1 The incidence of hydrocephalus per 1,000 live births in western Sweden in children with infantile hydrocephalus (IH) and hydrocephalus associated with myelomeningocele (MMC; birth years 1989–2002; 3-year moving average)

The gestational age-specific incidence for children with infantile hydrocephalus was 0.26 per 1,000 in children born at term, 0.96 per 1,000 in those born moderately preterm, 8.5 per 1,000 in those born very preterm and 23.1 per 1,000 in children born extremely preterm. The gestational age-specific incidence in children with infantile hydrocephalus born extremely preterm in relation to the perinatal mortality is shown in Fig. 2. The incidence in these children increased from 13 per 1,000 live births in 1997–1999 to 45 in 2000–2002 ($p<0.0005$). During the same period, the perinatal mortality in this gestational age group decreased from 24 to 15 per 1,000 live births.

Twenty-two (56%) of the 39 children with infantile hydrocephalus were born at term and 17 preterm. Of the 17 children born preterm, seven were born extremely preterm. The majority, or 11 of 15 children with MMC, were born at term, and the remaining four were born moderately preterm.

There was a gender difference among children with infantile hydrocephalus, with almost twice as many boys ($n=25$) as girls ($n=14$). The difference was even more pronounced among those born very preterm, ten boys and three girls. Among children with MMC, there were nine boys and six girls.

Based on clinical and neuroradiological findings, the etiology was considered to be malformations in 19 of 39 (49%) children with infantile hydrocephalus, in three of them in the form of an aqueductal stenosis. The distribution of etiology by gestational age groups is shown in Table 1. Cerebral haemorrhage was the cause in 16 (41%), prenatal in two, perinatal in 13 and postnatal in one child. In all seven children born extremely preterm, the etiology was a cerebral haemorrhage.

Treatment The first surgical intervention was performed during the first month in 19 children, in 15 of 33 (45%) children born at term, whereas no child born extremely preterm was treated during the first month. The ages at the initial surgical intervention by gestational age are shown in Fig. 3. Forty-two children were initially treated with a ventriculo-peritoneal shunt and 12 with an ETV. In 33 of the 54 children (61%), at least one revision was performed, and in all, there were 81 revisions. In children with infantile hydrocephalus, 23 of 39 (59%) had at least one revision compared with 10 of 15 (67%) in children with MMC. The mean rate of revisions in children with infantile hydrocephalus was 1.6 (range 0–8) and 1.3 (range 0–4) in children with MMC. In children with a ventriculo-peritoneal shunt, 17 of 42 (40%) did not need any revision compared with 4 of 12 with an ETV. In six cases, the revision was done in the form of an ETV, and further revisions were needed in five of these cases. There were no differences in the rate of revision between the various gestational age groups.

In five children, the first revision was performed during the first month after the initial intervention, in 14 during the second and third month, in three between 4 and 6 months and in 11 after 6 months or more. The most common cause of revision was mechanical ($n=45$), in the form of obstruction in 29, disconnection in six, leakage in four, catheter problems in five and not specified in one case. The second most common cause was infection, which occurred in 20 cases. In 14, the infection occurred within

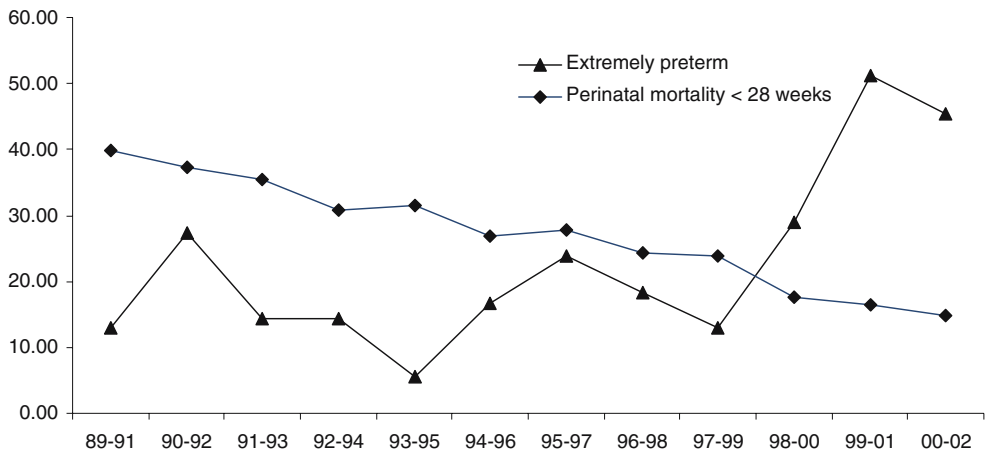

Fig. 2 The gestational age-specific incidence in children with hydrocephalus born extremely preterm (<28 weeks of gestation) in western Sweden in relation to perinatal mortality (birth years 1989–2002; 3-year moving average)

Table 1 Etiology in relation to gestational age in 54 children with infantile hydrocephalus and hydrocephalus associated with myelomeningocele (MMC)

	Extremely preterm $n=7$	Very preterm $n=6$	Moderately preterm $n=8$	Term $n=33$	Total $N=54$
MMC	0	0	4	11	15
Malformations other than MMC[a]	0	1	2	13	16
Aqueductal stenosis	0	1	0	2	3
Benign congenital tumors[b]	0	0	0	2	2
Infection	0	0	0	2	2
Cerebral haemorrhage	7	4	2	3	16

[a] Arachnoidalcyst, Goldenhaar syndrome, encephalocele, holoprosencephaly
[b] Papilloma of the plexus, low grade glioma

6 months after the initial surgical intervention, in seven of them within the first month, constituting seven of 135 surgical procedures (5%), defined here as a surgery-related infection. In ten cases, the reason for revision was a non-functioning ETV, in four the need for fenestration, over-drainage in one and treatment of a haematoma in one case.

Outcome Six children (11%) died during the follow-up period, four with infantile hydrocephalus and two with MMC. In five children, death was caused by multiple major malformations and not by the hydrocephalus. In one child, the hydrocephalus, in combination with the consequences of a cerebral haemorrhage, was considered to be the cause of death.

Of 16 surviving children with infantile hydrocephalus born preterm, 13 had learning disabilities compared with 7 of 19 born at term ($p<0.05$). The corresponding proportions for cerebral palsy were 12 of 16 and five of 19, respectively ($p<0.01$). In children with MMC, 3 of 13 had learning disabilities, and none had cerebral palsy. Of children with infantile hydrocephalus, 24 of 35 (69%) had some neurological impairment compared with 4 of 13 children with MMC ($p<0.05$), except for the consequences of the spinal lesion. The rates of neuroimpairment in the form of learning disabilities, epilepsy and cerebral palsy by gestational age in children with infantile hydrocephalus or MMC are shown in Table 2.

Half the children who needed no or one revision had some neuroimpairment compared with 13 of 18 children who had two or more revisions (Fig. 4).

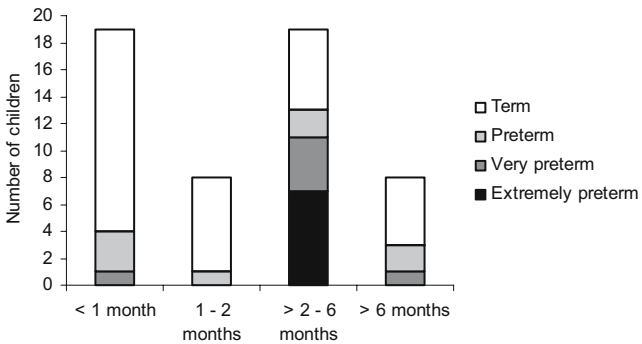

Fig. 3 Age at the initial surgical intervention by gestational age in 54 children with infantile hydrocephalus or hydrocephalus associated with myelomeningocele

Ophthalmological findings Of the 48 surviving children, 40 were examined ophthalmologically. Some children were unable to cooperate in all the examinations. In 32 (80%) children, ophthalmological abnormalities were revealed. There was no significant difference in outcome between different etiologies of the hydrocephalus or between children born at term and those born preterm.

For visual acuity, 26 of the 40 children were able to cooperate in visual testing with a letter or picture chart. Ten more were only able to fixate a penlight, and another three did not fixate at all. One child was not tested. Thirteen of the 39 (33%) children were visually impaired (VA<0.3). A low visual acuity (VA<0.8) was significantly more common among children with optic atrophy, learning disability, cerebral palsy and epilepsy ($p<0.001$, $p=0.01$, $p<0.05$ and $p=0.05$, respectively). There was no correlation between the number of revisions and visual acuity.

For refraction, ocular motility and morphology, the majority of the children, 21 of 34 (62%), had refractive errors, most commonly hyperopia in 14 of 34 (41%) and astigmatism in 13 of 34 (38%), while one child was myopic. Strabismus was present in 19 of 36 (53%) children, with esotropia in 14 and exotropia in five. During indirect ophthalmoscopy, optic atrophy was noted in 8 of 37 children (22%), while one child had optic disc oedema. Of the eight children with optic atrophy, all had learning disabilities, six had epilepsy, and seven had cerebral palsy.

Neuroradiology Magnetic resonance imaging had been performed in 30 and computed tomography in 24 of the 54 children. Six of them had no parenchymal lesions apart from the ventricular dilatation, five had small or moderate

Table 2 Outcome in 54 children with infantile hydrocephalus (IH) and hydrocephalus associated with myelomeningocele (MMC) by gestational age groups

	IH								MMC		IH + MMC	
	Extremely preterm		Very preterm		Moderately preterm		Term		Total IH			
	$n=7$	Percentage	$n=6$	Percentage	$n=4$	Percentage	$n=22$	Percentage	$n=39$	Percentage	$n=15$	Percentage	Total $n=54$	Percentage
Learning disabilities	4	57	5	83	4	100	7	32	20	51	3	20	23	43
Cerebral palsy	5	71	3	50	4	100	5	23	17	44	0	0	17	31
Epilepsy	3	43	2	33	2	50	8	36	13	33	1	7	16	30
Deaths	0	0	1	17	0	0	3	14	4	10	2	13	6	11
No impairment	2	29	0	0	0	0	9	41	11	28	9	60	20	37

leukomalacia, 13 had extensive white matter loss, 18 focal white matter loss combined with grey matter lesions, and 12 children had generalised severe white and grey matter pathology. None of the six children with normal imaging findings had any neurological impairment compared with 11 with these impairments among the 12 children with generalised lesions. Epilepsy was present in 14 of 25 (56%) children with cortical involvement (type III–IV) compared with 2 of 23 children with normal findings or isolated white matter lesions (type I–II; $p<0.01$). The corresponding numbers for children with cerebral palsy were 13 of 25 and 4 of 23, respectively ($p<0.05$). The correlation between neuroimaging findings and neurological impairments is shown in Table 3. Visual acuity did not differ between the neuroimaging patterns, apart from the finding that no child with normal imaging was visually impaired. Optic atrophy was present in 7 of 20 children with grey matter involvement compared with 1 of 17 without such lesions.

Discussion

This study was population-based, and it was possible to compare the results with those previously reported from the same region [15, 17, 19, 40]. The decreasing trend continued, from 0.82 per 1,000 live births in 1989–1998 to 0.66 in 1999–2002, but no further decrease was noted during the latest study period. On the contrary, there was an increasing trend from 0.50 per 1,000 in the last year of the previous period to 0.76 in the last year of the present study mainly because of an increase in the survival of children born extremely preterm with a high risk of developing hydrocephalus after cerebral haemorrhage, combined with a stable incidence of hydrocephalus associated with MMC. Ventriculo-peritoneal shunting was the most common form of treatment, and the revision rate remained high. As in previous studies, children with infantile hydrocephalus born preterm more frequently had neuroimpairments in the form of learning disabilities, cerebral palsy and epilepsy than children born at term [17] and those with MMC [6, 27].

The more sophisticated neonatal intensive care has increased the survival of children born extremely preterm, a group that runs a high risk of developing intraventricular haemorrhage resulting in hydrocephalus [22, 45, 50]. The same phenomenon was noted in the 1980s by Fernell et al. [18], but at that time, for the group born very preterm, children that were then the "new survivors". Compared with the study in western Sweden of the 1989–1998 birth cohort [40], the prevalence of hydrocephalus in combination with MMC had decreased from 0.33 per 1,000 to almost half, and was now 0.18. The explanation for this decrease was the increased use and quality of early

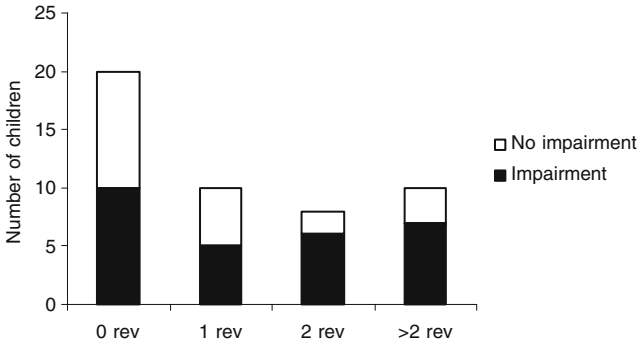

Fig. 4 The rate of revision in relation to associated neuroimpairments in 54 children with infantile hydrocephalus or hydrocephalus associated with myelomeningocele

ultrasound in pregnancy, leading to the termination of the pregnancy in many cases of neural tube defects [9]. Honein et al. [29] reported a reduction in the incidence of neural tube defects of about 20% after the introduction of folic acid enrichment in the USA. A further decrease of the same magnitude can also be expected in Sweden when such enrichment is introduced.

During the past decade, there has been a discussion about the optimal treatment for hydrocephalus of different etiologies and the appropriate age for intervention [33, 46]. The most common neurosurgical treatment is still ventriculo-peritoneal shunting. Ventriculo-atrial shunts were introduced in the 1960s, followed some years later by ventriculo-peritoneal [11]. The further development of adjustable and gravitational valves and shunts [12] has improved the situation, but the rate of shunt malfunction is still very high, and there is a need to develop alternative treatment methods. One such method is ETV, which is being used with increasing frequency around the world [14, 23]. The most common indication for ETV is aqueductal stenosis of malformative, inflammatory or neoplastic etiology [5, 28]. ETV has also been used to treat aqueductal stenosis in young children, and several studies have reported good results [5, 11]. Some argue that there is an age limit for its use in children [38, 43], but others claim that even children less than 1 year of age should be treated with ETV as the first intervention and that it is the etiology and not the age that is important [8]. It was recently suggested by Siomin et al. [44] that ETV is preferable when revising a malfunctioning shunt even in children with hydrocephalus caused by an infection or by cerebral haemorrhage. In this study, the revision rate was as high after ETV as after ventriculo-peritoneal shunt treatment, but the often most troublesome complication, i.e. infection, necessitating external drainage, did not occur after ETV.

The time for the first surgical intervention varied between the gestational age groups and was mainly dependent on etiology. Children born at term often have overt hydrocephalus already at birth [16] or develop hydrocephalus during their first weeks of life as a result of a prenatal malformation, and they have their first surgical intervention early, often during their first month of life. Children born very or extremely preterm, on the other hand, most frequently have an intraventricular haemorrhage with hydrocephalus developing successively over several weeks or months, with the first intervention often between the ages of 2 to 6 months. In a study by de Vries et al. [49], early external drainage as the first intervention in this group reduced the need for subsequent shunt insertion.

There was a need for revision in about 60% of the children, and the most common cause was obstruction followed by infection. An infection during the first 6 months after surgery occurred in about 10%. This can be compared with other surveys where the incidence of such infections varies from 1 to 19% [10, 13, 31, 48]. In this study, a surgery-related infection was defined as an infection occurring within 1 month after surgery, and this was the case in 5%. Neuroimpairments were found to be more common after two or more revisions. This difference was not statistically significant, due perhaps to the small numbers, as a significant correlation was found in an earlier study by Persson et al. [40] based on a larger group of children from the same region. However, Lumenta and Skotarczak [34] and Riva [42] did not find that the number of revisions had any impact on the prognosis, and Futagi et al. [22] found no correlation between the rate of revisions

Table 3 Outcome in 54 children with infantile hydrocephalus and hydrocephalus associated with myelomeningocele in relation to neuroradiological findings

	Normal $n=6$	I $n=5$	II $n=13$	III $n=18$	IV $n=12$	Total $n=54$
Learning disabilities	0	3	5	8	7	23
Cerebral palsy	0	1	3	6	7	17
Epilepsy	0	0	2	9	5	16
Deaths 0	1	0	1	4	6	
No impairment	6	0	8	5	1	20

Normal No parenchymal lesion, *I* small/moderate periventricular leukomalacia, *II* extensive white matter loss, *III* focal white matter loss with grey matter lesion, *IV* generalised severe white and grey matter pathology

and associated neuroimpairments. He stated that it was the extension of parenchymal destruction after a haemorrhage that was important for outcome rather than the hydrocephalic process. This was corroborated in this study by the finding of neuroimpairments in almost all the children with cerebral haemorrhages as the cause of their hydrocephalus.

Neuroimpairments such as learning disabilities, cerebral palsy and epilepsy were found to be more common among children with infantile hydrocephalus born preterm than in children born at term or with MMC. Learning disabilities, for example, were more than twice as common in children born preterm as in those born at term, and in the total group of children with infantile hydrocephalus, more than two thirds had some impairment compared with half the children with MMC; this was also found by Heinsbergen et al. [27].

The majority of the children had visual function deficits, which was well in accordance with earlier studies [4] regarding visual acuity, optic atrophy, strabismus and refractive errors. The finding of visual impairment in one third of the children was, however, even more frequent than the 15% reported by Andersson et al. [4] and the 13% reported by Heinsbergen et al. [27]. Optic atrophy in about one fifth of the children was also more common than previously reported [4]. These two findings may be explained in part by the large proportion of children with post-haemorrhagic hydrocephalus born extremely preterm in this study.

In this study, the severity and extension of the parenchymal lesion in the brain were important for outcome; none of the children with normal neuroimaging had any associated impairment, which was, on the other hand, present in almost all the children with generalised parenchymal lesions. There was also a tendency towards a correlation between the severity of visual impairment and the neuroimaging findings and with decreasing gestational age, although this was not significant, probably due to the limited number of children in this study.

Conclusion

The decreasing incidence of hydrocephalus during the birth year period 1989–1998 continued in 1999–2002, but no further decrease was noted during this period, mainly because of an increase in the survival of children with post-haemorrhagic hydrocephalus born extremely preterm. A decreasing trend for hydrocephalus associated with MMC has been seen during the last few decades, and a further decrease can be anticipated if folic acid enrichment is introduced. Neurological impairments were present in almost two thirds of the children and were most frequent in those born preterm. Ophthalmological abnormalities were very common, and all children with hydrocephalus need to be carefully assessed in terms of visual function. Neuroimaging was useful for etiological, prognostic and treatment considerations. The high rates of impairment and shunt-related complication necessitate the further development of preventive and treatment measures.

Acknowledgements This study was supported by grants from the Folke Bernadotte Foundation and the Scientific Council, Province of Halland.

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