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Endoscopic third ventriculostomy in the management of hydrocephalus: Outcome analysis of 168 consecutive procedures

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ABSTRACT

Background: Endoscopic third ventriculostomy (ETV) is the treatment of choice for obstructive hydrocephalus, but the outcome is still controversial in terms of age and aetiology.
Methods: Between 1998 and 2011, 168 consecutive procedures were performed in 164 patients, primarily children (56% < 18 years of age and 35% < 2 years of age). The causes of obstructive hydrocephalus included tumoural pathology, Chiari malformation, congenital obstruction of the aqueduct, post-infectious and post-haemorrhagic membranes, and ventriculo-peritoneal shunt (VPS) malfunctions. Successful ETV was defined by the resolution of symptoms and the avoidance of a shunt.
Results: ETV was successful in 75.6% of patients, but 19% of the patients required VPS in the first month after ETV, and 5.4% required a VPS more than one month after ETV. Four patients were ultimately submitted for second ETVs. In this series, no major permanent morbidity or mortality was observed.
Conclusions: ETV is a safe procedure and an effective treatment for obstructive hydrocephalus even following the dysfunction of previous VPSs and in children younger than two years.

1. Background

The incidence of congenital hydrocephalus is estimated to be 0.7 cases per 1000 live births in developed countries [1], and the incidence of neonatal hydrocephalus is estimated to be 3–5 per 1000 live births and predominantly occurs in males [2,3].

Hydrocephalus is one of the most common developmental disorders in children; it is more common than Down syndrome and congenital deafness [4] and is the leading indication for brain surgery in children [5].

Currently, many patients with hydrocephalus are considered candidates for endoscopic third ventriculostomy (ETV). The idea of an intracranial non-prosthetic "internal shunt" to overcome the obstruction site to achieve cerebro-spinal fluid (CSF) circulation and avoid the use of ventricular-peritoneal or auricular prostheses has gained wider increasing acceptance in the last 20 years [6]. The endoscopic fenestration of the third ventricle floor has been used with increasing frequently since the early 1990s primarily because of technical improvements (e.g., lighting sources, magnification and image resolution) [7,8]. The surgical indications for this procedure include the following: stenosis of the aqueduct, idiopathic stenosis of the Magendie and Luschka foramina, some cases of Dandy–Walker malformations, and post-haemorrhagic hydrocephalus [9–17]. ETV may also be performed in selected cases of hydrocephalus that are caused by mass effect of tumours of the pineal gland; tectal plate or posterior fossa; some suprasellar, quadrigeminal cistern, or arachnoidal extra ventricular cysts; or even midline intra-ventricular cysts [9,10,18–25].

Higher success rates have been reported for patients with stenosis of the aqueduct [11,26–30]. Lower success rates have been

Abbreviations: CSF, cerebrospinal fluid; CT, computed tomography; ETV, endoscopic third ventriculostomy; MRI, magnetic resonance image; VPS, ventriculo peritoneal shunt.

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reported for patients with post-infectious hydrocephalus and for post-haemorrhagic patients with prior ventriculo-peritoneal shunt (VPS) failures [28,29,31–33]. This procedure is considered less effective in paediatric populations, although the minimum age for the procedure remains controversial [9,26,28,29,34–36].

In this retrospective study, the surgical indications, surgical techniques, nosocomial outcomes and results of 168 consecutive ETVs that were performed in 164 patients at the Centro Hospitalar de São João do Porto (CHSJ) over a period of 13 years beginning with the introduction of the technique (performed between December 1998 to December 31 2011) were reviewed.

2. Methods

2.1. Patient population

Between December 1998 and December 2011, 168 consecutive ETVs (77.1% of the neuroendoscopic procedures) were performed at the Centro Hospitalar de São João do Porto (CHSJ) in 164 patients with obstructive hydrocephalus who were followed until December 31, 2012. The patients were predominantly male (the male:female ratio was approximately 3:2). The average age was 22.1 years at the time of surgery (56% of the patients were paediatric and 20.8% were infants), and the age of the male group was slightly younger (19.6 vs. 25.7 years in the males and females, respectively). The average follow-up was 77.6 months (13–168 months). Magnetic resonance imaging (MRI) diagnostic considerations included T1 with thin reconstruction in three planes, T2, CISS, flair and cine-phase contrasts.

The proportion of paediatric patients (i.e., those below the age of 18 years) was 56%, 31.6% were younger than two years (mean 6.7 months), and the youngest patient was 6 days old. Among our patients, 19.0% were 2–10 years old (mean 5.8 years), 5.4% were between 10 and 18 years (mean 13.9 years) and 44% were adults (mean 45.6 years).

The selection of the 168 cases of ETV (of the total of 817 surgeries for hydrocephalus thus excluding 649 VPSs) was based on clinical and imaging (i.e., computed tomography (CT) and MRI) evidence for obstructive hydrocephalus. The group included 34 patients with previous VPSs.

Procedural success was defined by clinical improvements and VPS independence, and failures were divided in two groups, early failure (within one month of the procedure) and late failure (after one month).

2.2. Surgical technique

All patients were operated on under general anaesthesia, in the dorsal decubitus position, with their heads stabilised. In the introduction of the rigid endoscope (MINOP®; Aesculap, Tuttlingen, Germany) transcortically towards the Monro cavity, 0–30° optics were used, and the working channel length was 18 cm. We also used two cannulae; one had an external diameter of 4.6 mm (13 F) and its own channels for the optic and for irrigation and drainage, and another 6 mm (18 F) cannula with another channel (2.2-mm diameter) for the introduction of micro-endoscopy instruments. The most frequently used optic was the 0° viewing angle.

After identifying the thalamo-striate vein, the septal vein, and the choroid plexus at the level of the Monro foramen and avoiding the fornix, the endoscope was advanced to the third ventricle as identified by the thin membrane that forms its floor. This membrane is bluish in colour and is located before the mammillary bodies and posterior to the tuber cinereum. For the cannulation of this structure, a Fogarthy type balloon-tip catheter with a blunt tip was used (4 French) to achieve an opening diameter on the floor of the third ventricle of at least 5 mm. None of the cases had histories of prior coagulation of the third ventricle floor. The endoscope was then inserted through the cisternostomy to the pre-pontine cistern to allow for the identification of the basilar artery and confirmation of the existence of a flawless communication.

After removing the endoscope, duraplasty and biologic glue were used. The mean operative time was 75 min.

During the surgical procedure, continuous irrigation with Ringer's lactate (at 37 °C) was utilised to prevent ventricular collapse. Cisternostomies were achieved in all cases without resorting to stereotactic techniques, radiology or computerised neuronavigation (using the hands-free method).

Table 1
ETV failure adjusted for aetiology, gender, and age. The Aetiology distribution and logistic regression were used to compute odds ratios (ORs) and 95% confidence intervals (95% CIs).

	Adjusted OR (95% CI)
Aetiology	
Aqueductal stenosis	1
Chiari	3.26 (0.96–11.1)
Tumour	0.46 (0.14–1.48)
Others[a]	0.92 (0.33–2.57)
Age	0.97 (0.95–0.99)
Gender	
Female	2.00 (0.90–4.45)
Male	1

[a] Cysts (19), post-infectious (12), post-haemorrhage (12), Dandy–Walker malformation (4), occlusion of the basal cistern (4).

3. Results

ETV was effective in 75.6% of cases, 19.0% required the insertion of a VPS system in the first month post-ETV, and 5.4% required a later intervention (VPS or re-ETV). In all ineffective ETV cases, the patency of the stoma was verified before placing the VPS.

As shown in Table 1, the incidence of ETV failure varied significantly across the different age groups (Chi square test–$p = 0.012$); the ETV incidence decreased with age (p for the trend = 0.00) and was significantly greater when the aetiology was a Chiari malformation (OR = 3.4).

Among the ETV failure cases, 23.2% of the patients who underwent ETV required an additional procedure, and 1.2% required more than two procedures (due to clinical and radiological findings related to complex hydrocephalus).

The procedure had to be repeated in four patients, including two failures (10 months and 9 years after the first procedures) and two obstructions by fibrin (two months and four years after the first procedure). Three of these patients were children older than two years.

No deaths were directly related to the surgical procedures. One of the cases (with an underlying pathology of a Chiari malformation) experienced subsequent ETV failure (13 months after the procedure) and developed acute and fatal intracranial hypertension.

In 78 patients, post-procedure, nonspecific, self-limited fevers (38 °C) were diagnosed, and 80% of these patients were below the age of 18. In these cases, no microbial agents were isolated from blood or CSF samples.

One patient exhibited self-limited bleeding of the pontic artery during the stoma balloon dilatation and required and external ventricular drain (EVD) and posterior VPS.

The success of the procedure appeared to increase with age. Although the adults exhibited a higher ETV success rate, there difference between the adults and children did not reach significance ($p = 0.14$). The primary diagnosis in this series was congenital

Table 2
Aetiology distribution for the 164 patients.

Aetiology	*n*	%
Congenital malformations	74	45.1
Idiopathic aqueductal stenosis	39	23.8
Chiari malformation	22	13.4
Other[a]	13	7.9
Tumours	52	31.8
Cysts	15	9.1
Infections	12	7.3
Haemorrhage	11	6.7

[a] Other (congenital malformation) includes vascular malformations, Blake's pouch cyst, Dandy–Walker, and occlusion of the basal cistern.

malformation, particularly stenosis of the aqueduct, and this diagnosis was followed by cancer as shown in Tables 1 and 2.

The obstructions of the CSF predominantly occurred at the levels of the aqueduct level (63.1%) and the fourth ventricle (24.4%). Obstruction at Monro level (9.5%) and subarachnoid space and obstruction at more than one level (3.0%) were also observed.

Second procedures during the ETV were performed in 69.3% of the patients; 27.1% of the procedures were VPS removals, 27.1% were tumoural biopsies, 9.5% were intraventricular cyst fenestrations, 2.4% were septostomies, 1.8% were aqueductoplasties, and 1.4% (one patient) was an Ommaya introduction.

Hydrocephalus secondary to tumour was found in 52 cases (31.0%) that were predominantly male (2:1) and averaged 27.4 years of age (5 months to 77 years). In this oncologic group, 7.7% of the patients were below the age of 2 years, 32.7% were between two and 9 years, 7.7% were between 10 and 17 years and 51.9% were adults.

Among all tumours, 48.1% were located in the posterior third portion of the third ventricle, 46.1% in the posterior fossa, and 5.8% in the anterior two-thirds of the third ventricle. The mean follow-up time was 63.4 months (1–162).

Histological evaluations revealed malignant glial series (i.e., ependymoma, astrocytoma, oligodendroglioma and glioblastoma multiform) in 57.8% of the cases, embrionary cells (i.e., medulloblastoma, pineoblastoma, and PNET) in 26.9% of the cases and benign forms (i.e., meningioma, haemangioblastoma, granuloma, macroadenoma, neuroma, craniopharyngioma, and glioneuronal tumour rosette-forming) in 11.5% of the cases; 1.9% of the cases corresponded to metastasis, and 1.9% corresponded to lymphoma.

The success rate in this group was 88.5%. The technique was ineffective in 11.5% of the cases, and 7.7% required VPSs within the first post-ETV month.

There were 39 (23.2%) patients with stenosis of the Sylvian aqueduct (51.3% due to congenital malformations). The average age of these patients was 30.4 years at surgery, and they were followed-up for a median of 87.1 months (range: 3–167 months). There was a slight female predominance among this population (53.8%). The success and early failure rates of this group are described in Table 3.

Table 3
Success and early failure rates by age group among the patients with idiopathic aqueduct stenosis.

Age group	*n*	Success (%)	Early failure (%)
<2 years	8	3 (37.5)	3 (37.5)
≥2 years and <10 years	4	3 (75.0)	1 (25.0)
≥10 years and <18 years	3	3 (100.0)	0 (0.0)
≥18 years	24	21 (87.5)	2 (8.3)

In 23.1% of these patients VPSs was required, and 15.4% required VPS within the first month after ETV. Two of these patients required an additional ETV as shown in Table 4.

Chiari malformations were present in 13.1% of these cases (28.9% were due to congenital malformations). The average age of this group was 4.8 years, and the median follow-up time was 104.1 (18–164) months. Men predominated in this group (63.6%). Most of the patients (81.8%) were below the age of two years, and the overall success rate was 41.0% (50% for those older than two years and 38.5% for those in younger than two years). The early failure rates were 50% for those younger than two years and 25% for those older than two years. The patients below the age of 2 years presented with Chiari II malformations, and the remaining patients presented with type I. Fifty-nine per cent of the patients required VPSs, and half of these patients required VPSs within the first month following ETV.

There were no statistically significant differences in the outcomes ($p = 0.515$) between the patients with Chiari malformations who underwent primary ETVs (10 patients) and those who underwent ETV for prior VPS failure (8 patients).

ETV was performed in 34 patients with previous VPS failures (20.7% of the series) including 21 males and 13 females. Twenty-three of these cases had triventricular hydrocephalus, and eleven had tetraventricular hydrocephalus. Most of these patients were below the age of two years (n 19), nine were aged between two and 17 years, and six were 18 years old or older.

The obstructions in the patients with previous VPS malfunctions were at the aqueduct level in 21 patients, the fourth ventricle level in 11 patients, and the Monro level in two patients. Nineteen of these patients were younger than two years old (with obstruction at the Monro level: 1, aqueduct level: 8, and the fourth ventricle level: 10), nine were between two and 17 years (with obstructions at the aqueduct level: 8 and at the fourth ventricle level: 1), and six were adults (with obstructions at the Monro and aqueduct levels; 1 and 5, respectively).

Table 4
Data from the patients who were subjected to repeated ETVs.

Gender	Diagnosis	Age at first surgery	Time between surgeries	Reason for re-intervention	Current age	VPS			Current status
						Previous VPS	After first ETV	After second ETV	
F	Neonatal infection	6 years	10 months	Failure/closure	9 years	Yes	Yes	Yes	LWD
F	Idiopathic aqueductal stenosis	13 years	2 months	Obstruction by fibrin	13 years	Yes	No	No	AWD
F	Chiari	6 years	9 years	Failure/closure	15 years	Yes	Yes	Yes	LWD
F	Idiopathic aqueductal stenosis	71 years	4 years	Obstruction by fibrin	76 years	No	No	No	AWD

AWD, alive without disease; LWD, living with disease (i.e., shunt dependence).

The reasons for VPS failure were mechanical dysfunction in 28 (82.4%) patients, infection in five patients (14.7%), and a foreign body reaction in one patient.

The success rate in this group was 61.8%; 21 of the 34 patients became VPS independent (mean follow-up time of 96.8 months; range: 22–167 months). The VPSs were replaced in 38.2% of the patients (13 of 34), and the average time elapsed between the ETV and the new VPS placement was 8.6 days (2–18 days).

4. Discussion

Endoscopy is currently widely applied in neurosurgery either alone or in combination with other procedures. ETV is well established as a treatment option for obstructive hydrocephalus [37,38] and might also be useful in other circumstances, such as the VPS failure [39–41], as per our experience.

The success of ETV is generally defined by the clinical improvement and VPS independence, and success rates vary from 50 to 90% [42–44]. Beems and Grotenhuis [9] reported one of the largest series of patients (339) and achieved a success rate of 76%. The overall success rate in our series was 61.8%, which is slightly lower than that described in the reviewed literature. We defined ETV failure as the reappearance of symptoms of intracranial hypertension followed by CT or MRI confirmation whenever possible. After a successful ETV, the size of the ventricular system can require a few months to stabilise [45–47], and the presence of a flow void appears to correlate with clinical success, as the absence of flow void correlates with clinical failure [48]. However, as Buxton et al. [49] noted, we considered that "clinical outcome is the most important guide to success or failure as reduction in ventricular size is by no means guaranteed, and radiological outcomes alone may be misleading, and the reliance on them should be avoided". However, it is important to consider that our patient population was a heterogeneous group in terms of age, gender, and underlying pathologies. All of the failures (i.e., those within the first month after the procedure) required the placement of a VPS as described in the literature.

Age was a predictor of ETV failure in our series as evidenced by the statistically significant difference in procedure failure rate according to age. However, the underlying pathology should be taken into account.

Regarding morbidity and mortality, a review [50] 2884 patients who had undergone ETV has been published. In this review, the permanent morbidity was 2.38%, and the rate of permanent neurological complications (e.g., hemiparesis, gaze palsy, memory disorders, and altered sensorium) was 1.44%. The overall complication rate was 8.5%. The other complications related to ETV included intraoperative haemorrhage from the ependymal veins, choroid plexus or basilar artery and its branches (3.7%), permanent diabetes insipidus, weight gain, and precocious puberty. The early postoperative mortality rate due to sepsis and haemorrhage was 0.21%. Within the first month following the ETV, the reported complications included CSF leakage, ventriculitis, subdural fluid collection, and re-stenosis of the stoma.

It is widely accepted that the complication rate is related to the experiences of each centre and each individual surgeon [51]. In the present study, a single neurosurgeon (Josué Pereira, one of the authors) performed all neuroendoscopies, was present for all neuroendoscopic procedures (more than 250 in same period and more than 200 for hypophyseal pathologies) Only recently has another neurosurgeon in our clinical reached autonomy regarding neuroendoscopic procedures and has remained under the supervision of the head neuroendoscopy neurosurgeon. Bouras and Sgourus [51] recently performed a meta-analysis, and the overall complication rate was found to be 8.5%. Warf [52–54] reported a greater success rate for endoscopic third ventriculostomy with choroid plexus cauterisation (ETV-CPC) than for ETV alone even in infants. Recently Kulkarni et al. [55] concluded that "early North American multicentre experience with ETV-CPC in infants demonstrates that the procedure has reasonable safety in selected cases. The degree of CPC achieved might be associated with a surgeon's learning curve and appears to affect success, suggesting that surgeon training might improve results". We did not perform this technique as most European (literature evidence is increasing, but still scarce – e.g., approximately 30 articles related to the issue on Pubmed). In our series, we observed no mortality and a very low rate of major morbidity. Most of our morbidity was related to post-procedure unspecific and self-limited fevers (peaking a 38 °C) in 78 patients (46.4%); most of these patients were children, no agents were isolated from the blood or CSF samples, and no antibiotic treatments were required. We observed no sepsis. One patient (0.6%) exhibited self-limited pontic artery bleeding during the procedure. We observed no hypothalamic dysfunction.

The role of age in predicting the success of ETV remains controversial in the literature. Several authors have reported similar results in children and adults and did not consider age as a limiting factor for the indication of ETV even for in new-borns as described by Spennato et al. [56] and several other authors [9,11,57–59]. Other works, such as those of Buxton et al. [60], Kadrian et al. [61] and Koch-Wiewrodt et al. [62] as referred to in Spennato et al. [56], reported the opposite extreme of success rates below 30% in infants and considered an age under one year to be a contraindication for ETV.

The majority of authors have described intermediate results with success rates of approximately 50% [52,56,58,63,64] and continue to advocate ETV as the first-line treatment for children and infants with obstructive hydrocephalus. We concur with this opinion. Obstructive hydrocephalus is typically defined based on the mean ratio between the sizes (as defined by the maximum cross-sectional surface) of the third and fourth ventricles, which is typically approximately 0.5 [65]. Our radiological criteria for the definition of obstructive hydrocephalus included an increase in this value in addition to the presence of enlarged of temporal horns, transependymal oedema in the lateral ventricles, outward bowing of lateral the walls, inferior bowing of the floor of third ventricle [66] and the absence of flow voids at the level of the aqueduct [67]. Post-infectious (12) and post-haemorrhagic (11) cases were included in this series and categorised as obstructive hydrocephalus because these cases fulfilled our classification criteria. Such cases represented less than 5% of the post-infectious and post-haemorrhagic cases in our centre. Our success rate was 50% in infants, which overlaps with that reported in the literature. The reduced success rate among infants (particularly those below the age of six months) is likely due to (1) the fact that these patients exhibit a greater tendency to form new arachnoid membranes that lead to the obstruction of the stoma [68] and (2) to deficits in the reabsorption of CSF due to the immaturity of the arachnoid villi [59,69].

In both congenital and acquired stenosis of the aqueduct, Jones et al. [13,29] and, more recently, Mugamba and Stagno [13,29] reported high success rates that were related to the acquired type, the age at symptom onset and the surgical procedure [13,70,71]. Similarly, in our series, we found a success rate among adults of 87.5%, which is similar to that reported in more recent studies [13,56].

The exact cause of hydrocephalus associated with Chiari malformation is not clear. It is believed that the blockade of the CSF in the foramen magnum region (at the foramina of Luschka and Magendie or at the peri-cervicomedular level due to a herniated amygdala [72]) is the cause as described by Milhorat [73] in one of the largest series in the literature. It is also agreed that

hydrocephalus associated with myelomeningocele is due to an obstruction of the exit area of the fourth ventricle resulting from an associated Chiari malformation [74].

Several authors [37,75–77] have reported that hydrocephalus in Chiari patients can be treated with ETV and that the success rate of this treatment can be as high as 50%. The success rate in our series was 40%, which is within the range of rates that have been described in international series. In our opinion, the success of ETV in these patients further supports the utilisation of this procedure for selected patients with Chiari, although the numbers of patients with this condition in our series was low.

The role of ETV is well established, and its success in the treatment of obstructive hydrocephalus due to intracranial tumours is recognised both in paediatric patients (as described in recent articles by Wong et al. [78], Di Rocco et al. [79], and other authors [21,80–82]) and adults [83,84].

In the above referenced series, the success rates for the restoration of CSF flow were high, and we observed a similar result in our series (88.5%). Only four patients required VPSs in the early stage, and two required VPSs at later times. The lesions of 19 cases were submitted to endoscopic biopsies that allowed for histological diagnoses for these patients. This procedure is indicated primarily for lesions in the quadrigeminal plate and the posterior third of the third ventricle as described by Wong et al. [83], Morgenstern and Souweidane [84], Pople et al. [21] and Depreitere et al. [85]. Histological diagnoses were achieved in all biopsied cases.

VPS failures are relatively common and have been defined by Mugamba and Stagno in terms of indications for endoscopic third ventriculostomy [13] as "any revision performed on the prosthesis after being implemented, a phenomenon being directly related to time which seems to be more frequent in children". This definition is supported by Bilginer et al. [86] and Marton et al. [87]. In our series we also observed that 28 of the 34 patients with previous VPSs were children. ETV is a safe and effective procedure for the treatment of appropriately selected patients with VP shunt failure, and MRI evidence regarding flow obstruction is essential for these cases. As described by Baldauf et al. [70], the success rates for such cases are approximately 70% [88–90]. The occurrence of VPS malfunctions does not influence the incidence of ETV failure [13,91,92] because the majority of failures tend to occur at an earlier stage.

The closure of the ETV stoma has always been recognised as a cause of failure of the procedure, and a new ETV procedure has been described as an alternative to VPS by several authors, including Peretta et al. [93], Siomin et al. [94], Wagner and Koch [68]. These authors have reported success rates between 65 and 75% but have also reported worse outcomes for children particularly those below the age of two years. In their series, Mahapatra et al. [95] reported a stoma closure rate of 9% and a re-ETV success rate of 93.2%; the majority of the latter patients experienced late failures. According to Fukuhara et al. [31,96] and Cinalli et al. [11], the performance of an additional ETV due to the failure of the primary procedure should be considered based on intracranial hypertension and the absence of flow in MRI cine phase-contrast images.

We had four cases of stoma closure; these cases exhibited signs of intracranial hypertension and flow obstruction on MRI cine-phase-contrast images. All of these cases were female, two exhibited closure of the stoma, and the other two exhibited occlusion by fibrin. Closure of new ETV occurred in two patients within one year of the procedure, and these two cases required VPSs. The data for the patients who were subjected to repeated ETVs are presented in Table 4.

Based on the above discussion, ETV represents a feasible alternative to VPS in the treatment of hydrocephalus. A large number of children might benefit from ETV, which is a simpler treatment option that does not require the placement of prosthetic material (i.e., a VPS), has a lower rate of associated complications [97–100] and, we believe, requires less frequent follow-ups and thus reduces the socio-economic effects on the families and the patients themselves [101,102]. Even in cases of VPS dysfunction, ETV is an alternative for the treatment of appropriately selected cases due to its good success rate and the absence of other associated complications.

5. Conclusions

Endoscopic surgery is experiencing increasingly widespread use in the treatment of obstructive hydrocephalus. This technique is associated with lower medium-to-long-term costs than the use of CSF shunt devices and avoids the complications associated with shunt dependency. This technique is considered to be the first choice treatment even for latent cases because it is possible to avoid the use of VPSs and of the complications related to VPS use. In our series, the use of a VPS was permanently avoided in 134 cases, including 31 of the 53 total cases who were below the age of two years.

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