Application of the Ommaya Reservoir in the Treatment of Hydrocephalus in Prematurely Born Children: Correlation with Animal Results

Miljan Mihajlović[1], Milan Mrdak[1], Vladimir Radlović[1], Igor Nikolić[2,3], Miodrag Rakić[2,3], Nikola Repac[2], Vaso Antunović[2,3], Aleksandar Janićijević[2], Vuk Šćepanović[2], Goran Tasić[2,3], Siniša Dučić[1]

[1]University Children's Hospital, Belgrade, Serbia;
[2]Neurosurgical Clinic, Clinical Center of Serbia, Belgrade, Serbia;
[3]School of Medicine, University of Belgrade, Belgrade, Serbia

SUMMARY

Introduction Intraventricular hemorrhage occurs in almost one fifth of prematurely born children. Due to present complications, such as hydrocephalus and neurological deficit, it endangers the child's life, therefore there is the need for understanding and prevent risk factors as well as the need for finding most optimal methods of treatment.

Objective The aim of the study was to point out the current therapeutic modalities of the treatment of posthemorrhagic hydrocephalus in prematurely born children.

Methods The study included 60 patients divided into two groups of 30 patients treated at the University Children's Hospital of Belgrade in the period 2003–2008.

Results Treatment outcome of the control group of patients treated by standard methods was influenced by gestational age (p=0.024), head circumference on birth (p=0.043), body mass on birth (p=0.006), Apgar score on birth (p<0.001), peripartum asphyxia (p<0.001), cardiorespiratory arrest (p<0.001), respiratory distress (p=0.002) and intraventricular hemorrhagic grade (p<0.001). As statistically significant predictors of the poor treatment outcome of the experimental group of patients treated by using Ommaya reservoir were identified: low body mass on birth (p<0.05), low Apgar score (p<0.05), prolonged number of days on assisted ventilation (p<0.05), presence of peripartum asphyxia (p<0.05) and cardiorespiratory arrest (p<0.05).

Conclusion No statistically significant difference was detected in the outcome between the patients treated by the standard method and those with installed Ommaya reservoir. However, the difference of 10% in mortality between the two groups may be clinically significant so that further studies of larger samples are necessary.

Keywords: prematurely born child; intraventricular hemorrhage; hydrocephalus; treatment

INTRODUCTION

Posthemorrhagic hydrocephalus (PHH) represents a serious complication in prematurely born children due to its association with a high degree of mortality and morbidity. Due to the continuous progress of intensive care in the last 20 years there has been a progressive decrease of the incidence of intraventricular hemorrhage in prematurely born children, so that it is now estimated to be 15–25% as compared with 39–49% in the late seventies [1, 2]. In a significant number of newborns intraventricular hemorrhage (IVH) is complicated by hydrocephalus which is considered to occur as the consequence of the obstruction of cerebrospinal fluid drainage by multiple small blood clots and cerebrospinal fluid paths and arachnoidal uvulas. The final outcome of chronic arachnoiditis involves the development of permanent hydrocephalus with destruction of paraventricular white matter and poor prognosis of psychomotor development [3].

There is still no agreement on the protocol for the treatment of newborns with posthemorrhagic ventricular dilation. For the time being, attempts with medication treatment with diuretics (acetazolamide and furosemide) have not shown to be effective in decreasing mortality, and may lead to complications such as electrolytic disbalance and nephrocalcinosis [4, 5]. Repeated lumbar punctures represent the first and most frequently applied neurosurgical procedure in these patients, although there are different opinions about its efficacy [6, 7, 8]. Another option represents the repetition of ventricular puncture but which may lead to complications such as bleedings and infections and thus it cannot be recommended as a long-term solution [9].

The subcutaneous Ommaya reservoir was initially used in 1960 for intraventricular application of medicaments in adults. However, since 1980 it has been used for evacuation of the cerebrospinal fluid in prematurely born children with PHH [9, 10]. This method also has its advocates as well as opponents stating that there are no advantages in comparison to other methods of treatment [11].

OBJECTIVE

The aim of this study was to point out to the current therapeutic modalities of treatment of posthemorrhagic hydrocephalus in prematurely born children.

Correspondence to:

Igor NIKOLIĆ
Neurosurgical Clinic
Clinical Center of Serbia
Višegradska 26, 11000 Belgrade
Serbia
i.m.nikolic@gmail.com

METHODS

The study was designed as partly retrospective (control group, classical treatment methods) and partly prospective (experimental group where the Ommaya reservoir was installed). The first group – control, consisted of 30 patients who were treated medicamentously by repeated lumbar or ventricular punctures or by insertion of ventriculoperitoneal (VP) shunts in the period from 2003-2005 at the University Children's Hospital of Belgrade. The second group – experimental consisted of 30 patients treated by subcutaneous placement of the Ommaya reservoir in the period from 2006-2008 in the University Children's Hospital in Belgrade. The criteria for inclusion into the study were the diagnosis of posthemorrhagic hydrocephalus diagnosed by ultrasound examination (US). In the experimental group of patients the Ommaya reservoir (Meditronic Co.) was installed in the operation theater and connected to ventricular catheter placed in the right frontal horn of the lateral ventricle. Regulating hydrocephalus means puncturing the reservoir and removing the cerebrospinal fluid. The frequency of puncturing the Ommaya reservoir, as well as the quantity of the evacuated cerebrospinal fluid depended on the clinical picture and the size of ventricles.

Statistical methods used in the data analysis included the Student T test for numerical variables, while attributive variables were tested by Chi-square (χ^2) test. The method of the univariate and multivariate logistic regression analysis was used for distinguishing statistically significant and independent factors that influenced the outcome in each group of patients independently and jointly. Comparison of treatment results between the two studied groups of patients was done by using the Chi-square (χ^2) test.

RESULTS

The study included 60 patients with IVH treated at the University Children's Hospital of Belgrade and at the Institute for Neonatology in the period from 2003-2008. The patients were divided into control and experimental groups of 30 patients each.

The average gestational age in the experimental group was 29.27±3.33 months, and in the control group 29.63±2.91 months, without statistically significant difference in the average gestational age (t=0.472; p>0.05), as well as in the representation of gender between the studied groups (χ^2=0.268; p>0.05).

Between the control and experimental groups there was no statistically significant difference at the time of VP shunt placement (Z=0.809; p>0.05), the average head circumference (cm) at the time of VP shunt placement (t=0.853; p>0.05) and the average body mass (g) at the time of VP shunt placement (t=0.107; p>0.05). In the control group, the outcome was influenced by the following factors: gestational age (t=2.323; p=0.024), head circumference on birth (t=2.072; p=0.043), body mass on birth (t=2.832; p=0.006), Apgar score on birth (t=5.026; p<0.01), peripartum asphyxia (χ^2=17.376; p<0.01), cardiorespiratory arrest χ^2=24.914; p<0.01), respiratory distress (χ^2=9.176; p=0.002) and IVH grade (Z=6.202; p<0.01) (Table 1).

In the experimental group, by using the univariant logistic regression analysis, the following factors were identified as significant predictors of poor treatment outcome: low body mass on birth (p<0.05), low Apgar score (p<0.05), prolonged number of days on assisted ventilation (p<0.05), presence of peripartum asphyxia (p<0.05) and cardiorespiratory arrest (p<0.05).

By using the multivariant logistic regression analysis, the prolonged number of days on assisted ventilation was identified as the most significant predictor of the poor treatment outcome (p<0.05) (Table 2).

There was no statistically significant difference in representation of poor (χ^2=0.271; p>0.05) and lethal outcome (χ^2=0.659; p>0.05) between the studied groups (Table 3). However, the experimental group had by 10% lower mortality than the control group, which may be clinically

Table 1. Predictors of poor treatment outcome in the control group of patients (using univariant and multivariate logistic regression analysis)

Examined characteristic	Univariate analysis			Multivariate analysis		
	p	RR	95%CI	p	RR	95%CI
Gestational age	0.030	0.804	0.606–0.979	/	/	/
Body mass on birth (g)	0.012	0.998	0.996–1.000	/	/	/
Head circumference on birth (cm)	0.050	0.803	0.645–1.000	/	/	/
Apgar score	<0.001	0.517	0.368–0.726	/	/	/
Number of days on assisted ventilation	<0.001	1.215	1.099–1.343	0.005	1.160	1.046–1.285
Grade IVH	<0.001	149.930	15.724–1429.636	0.007	43.757	2.744–697.788
Peripartum asphyxia	<0.001	11.667	3.384–40.220	/	/	/
Cardio-respiratory arrest	<0.001	52.800	6.209–449.033	/	/	/

p – significance; RR – relative risk; CI – confidence interval

Table 2. Predictors of poor outcome of the treatment in the experimental group of patients (using univariate and multivariate logistic regression analysis)

Examined characteristic	Univariate analysis			Multivariate analysis		
	p	RR	95%CI	p	RR	95%CI
Body mass at birth (g)	0.033	0.997	0.995–1.000	/	/	/
Apgar score	0.014	0.543	0.334–0.883	/	/	/
Number of days on assisted ventilation	0.013	1.218	1.042–1.424	0.013	1.218	1.042–1.424
Peripartum asphyxia	0.008	22.000	2.274–212.860	/	/	/
Cardio-respiratory arrest	0.003	34.000	3.253–355.409	/	/	/

Table 3. Distribution of newborns according to represented treatment outcome

Examined characteristic		Control group (n=30)		Experimental group (n=30)	
		N	%	N	%
Treatment outcome	Poor	14	46.7	12	40.0
	Good/excellent	16	53.3	18	60.0
Treatment outcome – survival	Exitus	12	40.0	9	30.0
	Survived	18	60.0	21	70.0

N – number of patients

significant difference, however the size of the examined sample was insufficient for the statistical test to be sufficiently powerful to show the significance of the presented difference.

DISCUSSION

Treatment of congenital hydrocephalus is based on the decrease of the production of the cerebrospinal fluid [12]. Oral administration of prednisone and acetazolamide may lead to improvement in individual cases, but a long-term medicamentous therapy does not lead to curing [13, 14]. Surgical treatment of hydrocephalus is the only choice if there is no improvement after a two-week application of medicamentous therapy [15, 16]. A ventriculoperitoneal shunt has routine application in the treatment of hydrocephalus in human population as well as in the treatment of hydrocephalus in dogs and cats [14, 17, 18, 19]. Installation of VP shunt in cats with hydrocephalus as the consequence of dilation of the fourth brain ventricle due to syringomielia have shown excellent results that are almost equal to the results in the treatment of hydrocephalus of the same genesis in human population [19, 20, 21]. The ventriculoperitoneal shunt is the method of choice in resolving hydrocephalus in dogs in 75% of cases, but although there is evident clinical improvement, the diameter of the lateral ventricles never returns to its normal values [15, 22].

Experimental studies indicate that the reconstruction of the cerebral hemispheres after drainage of hydrocephalus in animals develops only on the level of white matter [15]. Principal complications caused by the ventriculoperitoneal shunt are infection, excessive drainage and hypofunction of the system for cerebrospinal fluid drainage due to poor functioning of the ventricular or peritoneal catheter [14, 15, 20]. Ultrasonography is the method of choice for diagnosing and follow-up of hydrocephalus. Taga et al. [18] emphasize that magnetic resonance is doubtlessly the superior diagnostic method for hydrocephalus in the animal population, but its limitation is dependence on the periprocedural application of anesthesia [13].

Intraventricular hemorrhage (IVH) is the leading cause of the occurrence of serious neurologic deficit in prematurely born children, and in over 50% of cases it leads to the development of ventriculomegalia [23, 24]. IVH most often occurs in the period within 72 hours after birth. Liu et al. [25] point out that the antenatal application of corticoster-

oids and vitamin K in women who have just given birth decreases the incidence of peri-intra-ventricular hemorrhage.

Blood present in the cisterna magna leads to the development of fibrous glial tissue which impedes normal resorption of the cerebrospinal fluid, which further leads to chronic arachnitis and extravasation of the protein matrix that blocks the apertures of the fourth brain ventricle and causes obstructive hydrocephalus [26, 27, 28]. Posthemorrhagic hydrocephalus (PHH) occurs in 35% of patients with IVH, and 15% requires urgent installation of the ventriculoperitoneal shunt [2]. PHH is defined as a fast and progressive dilation of the brain ventricles followed by increase of head circumference for more than 2 cm weekly [29]. In prematurely born children and children born with low body mass the frequency of IVH and PHH ranges from 30–40% [30, 31, 32]. These children have a high risk for the onset of severe neurological deficit, epilepsy, decreased IQ and visual problems [3, 33, 34]. Experimental studies on animals indicate that PHH damages the white matter of the brain, initially seizing oligodendrocytes and later also axones of the nerve cells causing ischemia of the tissue due to mechanical pressure on the drainage veins [35, 36]. Currently, it is difficult to choose a uniform attitude on the treatment of posthemorrhagic hydrocephalus. The ventriculoperitoneal shunt is followed by a high risk for the occurrence of complications. Pikus et al. [37] have presented a series of 52 patients with PHH treated by the ventriculoperitoneal shunt. The total mortality during 18 years of follow-up amounted to 60%, together with the registered deficit of mental functions in 78% of cases. Boynton et al. [33] presented a series of 50 prematurely born children with PHH. The rate of mortality during the follow-up period up to 10 years amounted to 7%, with the average of 4 performed revisions of the vetriculoperitoneal shunt per patient during the follow-up period. Lee et al. [38] emphasized that in the group of patients with installed ventriculoperitoneal shunt, during the treatment period of PHH, had a generally worse treatment outcome and a more serious neurological deficit than the group of analyzed patients who did not have installed the system for continuous drainage of the cerebrospinal fluid. This group of authors finds explanation in the fact that the group of patients who had the ventriculoperitoneal shunt installed was in a more serious clinical condition initially and that they were additionally burdened by the risks of the shunt itself (poor function, infection). The treatment outcome of patients in our series with the ventriculoperitoneal shunt installed is influenced by gestational age (t=2.323; p=0.024), head circumference on birth (t=2.072; p=0.043), body mass on birth (t=2.832; p=0.006), Apgar score on birth (t=5.026; p<0.001), peripartum asphyxia (χ^2=17.376; p<0.001), cardiorespiratory arrest χ^2=24.914; p<0.001), respiratory distress (χ^2=9.176; p=0.002) and IVH grade (Z=6.202; p<0.001).

The current neurosurgical attitude on indications for the installation of the ventriculoperitoneal shunt in the treatment of PHH implies that the prematurely born child's weight is over 1500 g and the protein level of the cerebrospinal fluid under 200 mg/dl, with the use of a low-pressure valve [39]. In further course, depending on the ultrasound

findings of the ventricular system, the low-pressure valve should be replaced with a high-pressure valve in order to avoid the possibility of excessive drainage. Application of programmable valves is disputable.

The alternative for the ventriculoperitoneal shunt is the installation of the Ommaya reservoar and ventriculostomy of the third brain ventricle [40]. The risk of infection upon installing the Ommaya reservoir is 12–24%, and the main agent is coagulase negative staphylococcus. Direct installation of the Ommaya reservoir is recommended without previous lumbar punctures in order to decrease the risk of additional infection [41]. Successful solving of PHH by using the Ommaya reservoir amounted to 35%, and ventriculostomy was successful in two from three children. In 2007 Peretta et al. [40] showed a series of 18 cases of PHH treated with the Ommaya reservoir. During the two-year follow-up one child died, and 59% of children became shunt independent. It was concluded that the application of the Ommaya reservoir significantly decreased the need for a shunt. When using the Ommaya reservoir, the results of our study identified the following predictors of poor treatment outcome: prolonged number of days on assisted ventilation and high grade IVH.

CONCLUSION

Results achieved by the analysis of the current therapeutic modalities are in accordance with results published in the world literature and do not yield a statistically significant proof on the improvement of outcome in prematurely born children with posthemorrhagic hydrocephalus after the application of the subcutaneous reservoir. Factors that stand out as predictors of poor outcome clearly point out the fact that, beside the intensity of intracranial bleeding and neurologic consequences, a significant role is played by the general condition of the patient and the time spent on artificial ventilation, which stands out as an independent factor that had influence on the outcome in both groups, as well as in the entire investigated population. Although the decrease of mortality in 10% of patients with installed Ommaya reservoir is not statistically significant, it is encouraging and requires further work on the application and improvement of this method, with good prospects that it may contribute significantly to the improvement of treatment outcome in patients with this disease.

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Примена Омајиног резервоара у лечењу хидроцефалуса код превремено рођене деце: поређење с резултатима истраживања на животињама

Миљан Михајловић[1], Милан Мрдак[1], Владимир Радловић[1], Игор Николић[2,3], Миодраг Ракић[2,3], Никола Репац[2], Васо Антуновић[2,3], Александар Јанићијевић[2], Вук Шћепановић[2], Горан Тасић[2,3], Синиша Дучић[1]

[1]Универзитетска дечја клиника, Београд, Србија;
[2]Клиника за неурохирургију, Клинички центар Србије, Београд, Србија;
[3]Медицински факултет, Универзитет у Београду, Београд, Србија

КРАТАК САДРЖАЈ

Увод Интравентрикуларна хеморагија се јавља код скоро петине превремено рођене деце. Због компликација у виду хидроцефалуса и неуролошког дефицита, угрожен је живот детета, па се намеће потреба за спознајом и превенцијом фактора ризика и налажења оптималних метода лечења.

Циљ рада Циљ овог рада је био да се укаже на актуелне терапијске модалитете лечења постхеморагијског хидроцефалуса код превремено рођене деце.

Методе рада У испитивање је укључено 60 деце (сврстане у две групе од по 30) која су лечена у Универзитетској дечјој клиници у Београду од 2003. до 2008. године.

Резултати На исход лечења болесника контролне групе, код којих је примењена стандардна метода лечења, утицали су: гестациони узраст (p=0,024), обим главе на рођењу (p=0,043), телесна маса на рођењу (p=0,006), Апгар скор (p<0,001), перипартална асфиксија (p<0,001), кардиореспи-

раторни застој (p<0,001), респираторни дистрес (p=0,002) и степен интравентрикуларне хеморагије (p<0,001). Статистички значајни предиктори лошег исхода лечења испитаника експерименталне групе, код којих је примењен Омајин (*Ommaya*) резервоар, били су: мала телесна маса на рођењу (p<0,05), низак Апгар скор (p<0,05), продужен број дана на вештачким плућима (p<0,05), постојање перипарталне асфиксије (p<0,05) и кардиореспираторни застој (p<0,05).

Закључак Није утврђена статистички значајна разлика у исходу лечења превремено рођене деце с хидроцефалусом код које је коришћена стандардна метода лечења и деце с уграђеним Омајиним резервоаром, али разлика од 10% у стопи смртности између ове две групе болесника може бити клинички значајна, те су потребна даља истраживања на већем броју испитаника.

Кључне речи: превремено рођено дете; интравентрикуларна хеморагија; хидроцефалус; лечење