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Effects of Serial Lumbar Puncture on Severe Intraventricular Hemorrhage of Neonates

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Abstract: Objective Hydrocephalus is one of the most common complications of neonatal intraventricular hemorrhage (IVH). In this study, the effect of serial lumbar puncture (LP) on severe neonatal IVH is evaluated. **Methods** The effects of serial LP on 30 neonates hospitalized with severe IVH at Xinhua hospital since 1993 was evaluated. Another 30 neonates with severe IVH who had not been treated for preventing post-IVH hydrocephalus were used as the control group. **Results** Of the 30 cases which received serial LP therapy, the cerebral ventricles of 25 cases stopped enlarging and shrank distinctly. The effective rate was 83.3%. The average age when serial LP therapy initiated was (15.0 ± 13.5) days, the average treatment course was (16.9 ± 12.9) days. The serial LP therapy was repeated (6.4 ± 4.7) times. The avarage interval of LP was (2.9 ± 2.7) days and the average CSF volume removed was (6.7 ± 1.6) ml. The average time of LP taking effect was (9.6 ± 5.5) days. Ten cases received diamox treatment during the course of serial LP. After 1 – 2 weeks' combined treatment, the enlarged ventricles of 8 cases returned to normal or remained steady. Eighteen of 25 ases were followed-up for (8.3 ± 1.9) months. Their physical and mental development were normal. Cranialcerebral ultrasound examination found that the shapes of cerebral ventricles of 14 cases were normal and the cerebral ventricles of another 4 cases enlarged slightly. The treatment with removed CSF >5 ml/time or with a shorter interval of LP (<2 d) acheived better effect (P <0.05 or 0.01). In the control group, the cerebral ventricles of 23 cases enlarged moderately or severely (6 of them complicated with hydrocephalus). **Conclusions** Serial LP is a safe and effective method for severe neonatal IVH in preventing post-IVH hydrocephalus.

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Key words: Intraventricular hemorrhage; Serial lumbar puncture; Hydrocephalus; Newborn

连续腰穿治疗新生儿重度脑室内出血的疗效评估

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[摘 要] 目的 重度脑室内出血常导致脑积水及其它后遗症,本文评估连续腰穿对新生儿重度脑室内出血(IVH)的疗效。**方法** 对我院1993年以来30例行连续腰穿(LP)治疗的严重脑室内出血(IVH)患儿进行疗效评估。并与30例未予任何防治IVH后脑积水措施的严重IVH进行对照。**结果** 经连续LP治疗的30例中,25例患儿的脑室停止扩张并明显缩小,有效率83.3%。初次LP日龄为(15.0±13.5) d,疗程(16.9±12.9) d,平均LP次数(6.4±4.7)次,平均LP间隔时间(2.9±2.7) d,平均每次脑脊液放液量(6.7±1.6) ml。LP治疗后起效时间为(9.6±5.5) d。10例在连续LP同时联用乙酰唑胺治疗,患儿增大的脑室在1–2周左右恢复正常或趋于稳定。25例中18例平均随访(8.3±1.9)月,体格、智能发育均正常,B超显示14例脑室形态正常,4例脑室轻度增大。每次脑脊液放液量>5 ml者及腰穿间隔时间<2 d者有效率明显较高(P <0.05或0.01)。对照组中23例脑室中重度扩张(其中6例并发脑积水),3例失访。**结论** 连续LP为治疗新生儿严重IVH的安全有效方法,可有效防止脑积水的发生发展。

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[关 键 词] 脑室内出血;连续腰穿;脑积水;新生儿

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Hydrocephalus is one of the most common complications of neonatal intraventricular hemorrhage (IVH). Its incidence in severe IVH survivals is higher than 50%[1]. Currently, serial lumbar puncture (LP) is the main effective method of treating and preventing hydrocephalus[2-4] secondary to IVH. The first successful serial LP therapy on a neonatal with hydrocephalus secondary to IVH was carried out in China in 1990 and since then the authors have performed the therapy on several neonatal IVH cases. These cases are reported in this paper.

Subjects and methods

Subjects

Since 1993, serial LP therapy has been performed on 30 severe neonatal IVH cases hospitalized in the Neonatal Division of Xinhua Hospital, Affiliated to the Shanghai Second Medical University. All these cases were diagnosed by trans-cranial type B ultrasound examination at an early stage and their cerebral ventricles enlarged progressively in a short time. Those cases which received serial LP treatment were the LP-treated group. During the same period, another 30 severe IVH cases did not receive any treatment for preventing post-IVH hydrocephalus because of discharging without permission and other relevant reasons. These cases formed the control group.

Methods

All cases in both groups received their first bedside trans-cranial ultrasound examination by special personnel within 3 days of admission. The examination was repeated every 3-7 days, while in the treated group it were repeated every 1-3 days depending on the situations. According to the Papile scale criterion, cases above grade III were considered as severe IVH[1]. Cases with progressive enlarged cerebral ventricles were diagnosed as post-IVH hydrocephalus. The degree of ventricular enlargement was determined by the vertical diameter of lateral cerebral ventricle detected through sagittal plane of ultrasound scan: greater than 5 mm was considered as mild cerebral ventricle enlargement, greater than 10 mm was moderate enlargement and greater than 15 mm was severe enlargement. If the triangular part or posterior horn of lateral ventricle enlarged compared with the previous examination, the case should also be diagnosed as cerebral ventricle enlargement.

Once the progressive enlargement of cerebral ventricles was diagnosed, serial LP therapy was carried out immediately. CSF samples were sent to the laboratory for routine examinations. If a LP injury influenced the normal treatment courses, diamox, a drug which could reduce CSF production, was administered.

Data analysis

The t Test and χ^2 test were used in the significance analysis of the data.

Results

Comparison of clinical data of the 2 groups

The scales of trans-cranial ultrasound in both groups were both grade III. In both groups, the difference of gestational age, birth weight, Apgar score, gender ratio, clinical severity degree (especially nervous system symptoms) and severity degree of cerebral ventricle enlargement was not significant ($P > 0.05$). Nervous system symptoms referred to convulsion, coma, apnea, irritation and muscular tension changes. See Table 1.

Table 1 Comparison of clinical data between 2 groups

Groups	Gestational age (week)	Birth weight (g)	1 min Apgar score	Male/Female	Incidence of nervous system symptom (%)	Ratio of severe cerebral ventricle enlargement (%)
Control group	35.2±3.4	2 400±670	7.9±2.3	21/9	13(43.3)	21(70.0)
LP group	36.4±3.9	2 700±800	6.9±3.2	19/11	14(46.7)	18(60.0)

The effects of serial LP treatment

The average age when the LP therapy initiated was (15.0 ± 13.5) days (3 - 60 days), the interval of LP was (2.9 ± 2.7) days (0 - 10.5 days), the removed CSF volume of each time was (6.7 ± 1.6) ml (2.3 - 10 ml). The serial LP was repeated (6.4 ± 4.7) times (2 - 21 times) and the duration was (16.9 ± 12.9) days (3 - 63 days).

After serial LP therapy, cerebral ventricles stopped enlarging and shrank significantly in 25 of the total 30 cases. The average time of LP taking effect was (9.6 ± 5.5) days (3 - 26 days). Among these 25 cases, cerebral ventricles of 16 cases returned to normal completely, in the other 9 cases (including 2 which received mechanic ventilation) the shape of the cerebral ventricle remained steady, although a little bit larger than normal. The cure rate of IVH patients who received serial LP therapy was 83.3%.

In the 5 cases which did not response to the LP therapy, the volume of CSF removed in 4 cases was relatively small (<5 ml) and the LP was carried out only twice. Moreover, the treatment courses were short (4 - 10 days) and with longer intervals (9 days in 1 case). The other case which did not respond was a tiny baby with severe asphyxia and HIE complications. High-frequency oscillation ventilation therapy was carried out 1 day after birth and continued for 19 days. Because of the progressively enlarged cerebral ventricle, serial LP therapy was carried out 10 days after birth and continuted for 34 days with the interval of 2.3 days. But the volume of CSF removed every time was very small (3.8 ml on average). Even with this treatment, cerebral ventricles of the patient enlarged progressively and further surgical drainage also failed.

During the initial phase of the treatment, the protein concentration in CSF was (1.8 ± 3.5) g/L. After LP treatment, the protein concentration decreased to (0.75 ± 0.55) g/L. In those 5 cases which did not respond to the LP treatment, the protein concentration in CSF of 4 cases at the initial phase of treatment was higher than 1.5 g/L. In the case which died the protein concentration rose as high as 20 g/L and it was still as high as 3 g/L after several LP's.

Of the 30 treated cases, 24 were discharged after cure, 2 died, 2 discharged without permission and 2 cases transferred to the surgical division for drainage treatment. The average hospitalization duration was (42.7 ± 17.6) days (8 - 73 days).

Among the 24 patients who were discharged after cure, 18 cases were followed up for (8.3 ± 1.9) months (5.5 - 11.5 months). Their physical and mental development were normal. Trans-cranial ultrasound examination indicated that cerebral ventricles of 4 cases were slightly larger than normal (the shape of cerebral ventricle remained steady), while the shapes of cerebral ventricles of the other 14 cases were normal. 6 cases were not followed up.

Some factors which influenced serial LP treatment

Generally speaking treatment was more effective when the volume of CSF removed greater than 5 ml and the LP interval less than 2 days. See Table 2.

Table 2 Relationship between LP effect and the removed CSF volume, LP interval

		number	Effective rate (%)	χ^2	P
The removed CSF volume	≤5 ml/time	8	3(37.5)	16.5	<0.01
	>5 ml/time	22	22(100)		
Interval	<2 d	13	13(100)	4.6	<0.05
	≥2 d	17	12(70.6)		

The effect of serial LP treatment in combination with diamox

Ten cases (4 male, 6 female) received diamox treatment during the course of serial LP. Among them were 5 premature neonates. Their average gestational age was (35.75 ± 4.6) weeks (29 - 40.6 weeks), the average birth weight was (2.5 ± 0.9) kilogrammes (0.95 - 3.5 kilogrammes) and the 1 min Apgar score was 7.0 ± 3.2 (2 - 10). The average age of those cases which received LP treatment

was (15 ± 7.6) days (5 – 23 days). In 6 cases the LP was postponed or the LP interval was prolonged because of LP injury. In 2 cases, LP treatment was suspended after 2 – 3 times of LP because of the parents' refusal. The other 2 cases received high-frequency oscillation ventilation treatment on the admission day. After LP treatment, their cerebral ventricles did not enlarge further. Diamox, with the dosage of 50 mg/kg each day was added to the above mentioned patients when they were 2 – 3 weeks old. The treatment of diamox continued for (18.4 ± 13.6) days (8 – 65 days) and the average LP treatment course was (19.7 ± 18.0) days (4 – 63 days). After 1 – 2 weeks of combined treatment, the enlarged ventricles of 8 cases returned to normal size or remained steady. During the treatment, the blood gas and electrolytes of all patients were normal. The follow-up of 1 – 3 months found that the cerebral ventricles of 4 cases were normal and that the cerebral ventricles of another 4 cases were slightly enlarged but remained steady. The combined treatment failed in 2 cases (diamox was used for only 8 – 10 days).

The outcome of the control group

In the control group, there were another 30 cases of severe IVH newborns who did not receive any treatment to prevent post-hemorrhagic hydrocephalus. The cerebral ventricle enlarged within 1 – 3 weeks after birth. The degree of ventricle enlargement of 23 cases was moderate to severe and 6 of them were transferred to the surgical division for cerebral ventricle drainage treatment 2 months after birth. Four cases discharged without permission 1 – 1.5 months after birth and 1 case died a half month after the discharge. The other 3 cases were not followed up. One case with moderate cerebral ventricle enlargement died of RDS and respiratory failure 18 days after birth.

Trans-cranial ultrasounds during the 1 – 3 months of follow-up found that the 4 cases with slightly enlarged ventricle had already developed to moderate enlargement; the ventricles of 9 cases enlarged slightly but their size remained steady. The ventricles of 6 cases returned completely to nomal. The rate of adverse outcome in IVH patients without serial LP treatment was as high as 50% (15/30).

Discussion

Compared with the 20 years before, the incidence of neonatal IVH has increased significantly, especially in the neonates of low birth weight, it reached 65%. This increase is closely related to the rapid development of diagnostic imageology techniques. The statistical data of 10 years' hospitalized premature infants in Xinhua hospital showed that the IVH incidence of hospitalized premature infants was 56.6%, of which 16.3% had severe IVH[7]. Another data investigation of neonates born in Xinhua hospital during the last 3 months showed the incidence of neonatal IVH and severe IVH were 15.8% and 3% respectively.

Post-hemorrhagic hydrocephalus is mainly related to the progressive enlargement of cerebral ventricle resulting from CSF absorption disorder, which compresses the periventricular tissues and causes ischemic necrosis. It has been reported that the incidence of hydrocephalus caused by grade III and IV of IVH were 40% and 70% respectively and that it usually happens within 15 – 70 days of hemorrhage. After the development of trans-cranial imageology techniques, early diagnosis of post-hemorrhagic hydrocephalus before the enlargement of head circumference has become possible. So corresponding measures can be carried out timely, which improved the adverse outcome significantly[1].

Serial LP therapy for treating post – hemorrhagic hydrocephalus appeared during 1980's. It was reported that through serial LP therapy, the success rate of controlling post-hemorrhagic hydrocephalus was 75% – 91%. Serial LP mainly solves the problem of CSF absorption. Serial LP therapy at an early stage, the accumulated blood, increased protein and excessive CSF can be removed. So, the blockage of CSF circulation route caused by clot and inflammatory adhesion are prevented and the ischemic damage of periventricular tissues induced by increasing intraventricular pressure are reduced. It can also gain time for compensatory changes of the CSF absorption route. So surgical drainage or permanent drainage whose effect is limited and often needs repeated surgery be-

cause of infection, blockage of the drainage tube or drainage failure can be avoided.

Since 1993, under the monitoring of trans-cranial ultrasound, the outhors have performed serial LP therapy for 30 cases of severe IVH, 83.3% (25/30) of them were successful. From these cases, it has been found that the success of serial LP therapy was related to the following factors.

The serial LP should be carried out as soon as possible. The patients with a rapid development of cerebral ventricles enlargement should receive LP therapy as early as possible. It was reported that the earliest LP treatment was from the 6th day after birth but was usually from the 2nd week after birth. In this paper the average initial time of LP was 13.7 days after birth.

The intervals of LP should be short. It is recommended that at the early stage of treatment, LP should be performed every day untill the cerebral ventricle stops enlarging or shrink[9]. In this paper, the 3 cases which did not respond to LP treatment all had prolonged intervals of 3 - 9 days during the early stage of treatment, which might be responsible for the failure of LP treatment.

The volume of CSF romoved should not be too small. Under the circumstances of ventricle enlargement, even if the pressure of CSF is not high, the amount of CSF removed each time should be between 8 - 10 ml and the most may reach 14 ml[1]. In this paper, the amount of CSF which was removed from 5 cases which failed was less than 5 ml, which indicates that the removal of an adequate volume of CSF is of great importance.

The course of LP treatment is usually within 1 month and the longest is less than 2 months and should be stopped only when the size of the cerebral ventricle remains stable. If the LP treatment is ended too early, cerebral ventricles will enlarge again because the CSF circulation route is still blocked or lateral circle has not yet formed.

LP treatment can only be guaranteed if there is no LP injury; LP injury should therefore be avoided but this is often not possible.

There are also some objective factors which result in the termination of serial LP. In this study 10 cases received diamox during the course of serial LP and the cerebral ventricles of 8 of these cases returned to normal after 1 - 2 weeks. It is suggested that when the efficacy of serial LP therapy is not satisfied that diamox shoud be used in combination with serial LP therapy. The recommended dosage of diamox is 40 - 100 mg/kg per day and blood gas and electrolytes should be measured during its administration. Because diamox only reduces the secretion of CSF, the cerebral ventricle enlarge again once the administration stops and so severe IVH should not be treated with diamox alone.

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