



Evaluation of Neonates with Ventriculitis

Ventrikülit Tanısı Alan Yenidoğan Bebeklerin Değerlendirilmesi

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ABSTRACT

Purpose: Neonatal meningitis and ventriculitis still remain a problem with high mortality in spite of systemic and intraventricular antibiotics. Ventriculitis due to repeated taps is a serious problem of posthemorrhagic hydrocephalus in preterm infants.

Materials and Methods: In this study, we evaluated 16 infants with ventriculitis followed at Cukurova University Faculty of Medicine Neonatal Intensive Care Unit between January 1999-December 2004.

Results: Mean gestational week was 33 ± 5 (25-40) weeks and mean birth weight was 2096 ± 912 (980-3500) grams. Ventriculitis was diagnosed at 38 ± 22 days. Eleven of the infants had intraventricular hemorrhage and 15 had hydrocephalus, 5 of whom had congenital hydrocephalus. Drainage of CSF was performed by taps in 13 infants. Gram negative microorganisms (Klebsiella pneumonia, Pseudomonas aeruginosa) were predominating in cultures. Both intravenous and intraventricular antibiotic treatment was performed according to the cerebrospinal fluid cultures. Vancomycine and amicasine as intraventricular therapy were performed for 28 ± 17 days. Cerebrospinal fluid protein levels increased significantly at 8 infant during intraventricular therapy. Mean cerebrospinal fluid protein at the beginning of intraventricular treatment was 624.1 ± 429.1 (109-1330) mg/dl while on 14th day of treatment it was 993.7 ± 582.2 (89-1750) mg/dl. Seven of the infants were ventriculoperitoneal shunted 6 of them were reinfected. Seven of the infants were died during treatment, 1 infant with ventriculoperitoneal shunt was treated and 8 infants were discharged during treatment because of parents' refusal of therapy.

Conclusion: Despite the new treatment regimens, the ventriculitis still remains a problem because of nonstandardized practice in neonatal care.

Key Words: Ventricülitis, neonate.

ÖZET

Amaç: Neonatal menenjit ve ventrikülit, sistemik ve intraventriküler antibiyotik tedavilerine rağmen hala yüksek mortalite oranlarına sahip problemlerdir. Preterm infantlarda posthemorajik hidrosefali ciddi bir problem olmakla beraber tekrarlanan ventriküler girişimlerde ventrikülit oluşumuna neden olmaktadır.

Materyal ve Metod: Çalışmamızda Çukurova Üniversitesi Tıp Fakültesi yeni doğan yoğun bakım ünitesinde Ocak 1999-Aralık 2004 tarihleri arasında takip edilen ve ventrikülit tanısı konulmuş 16 yenidoğan değerlendirilmiştir.

Bulgular: Ortalama gebelik haftası 33 ± 5 (25-40) hafta ve ortalama doğum ağırlığı ise 2090 ± 912 (980-3500) gramdı. Ventrikülit tanısı yaklaşık 38 ± 22 günlerde konuldu. 11 infantta intraventriküler hemoraj ve 15 infantta hidrosefali vardı ki bunların 5 tanesi konjenital hidrosefalidir. 13 infantta serebrospinal sıvı (BOS) taps ile drene edildi. Kültürü yapılan sıvıda GR(-) bakteriler (klebsiella pnömoni, Pseudomonas auroginasa) baskın olarak bulundu. BOS kültür sonuçlarına göre intraventriküler ve intravenöz tedavi yöntemi uygulandı. 28 ± 17 gün intraventriküler olarak vankomisin ve amikasin tedavisi uygulandı. İntraventriküler tedavi sırasında 8 infantta ait BOS proteinleri seviyelerinde artışlar görülmüştür. İntraventriküler tedaviye başlarken BOS protein miktarı ortalama $624,1 \pm 429,1$ (109-1330) mg/dl iken tedavinin 14. günü bu oran $993,7 \pm 582,2$ (89-1750) mg/dl olmuştur. Ventriküloperitoneal şantı olan 7 infanttan 6 sında enfeksiyon tekrarı gözlenmiştir. Infantların 7 si tedavi sırasında yaşamını yitirmiştir, ventriküloperitoneal şantı olan 1 infant tedavi edilirken, ailesi tedaviyi reddeden 8 infant taburcu edilmiştir.

Sonuç: Yeni tedavi metodlarının geliştirilmesine rağmen, ventrikülit neonatal bakımda belirli bir standardizasyon olmamasında ötürü halen önemli bir problemdir.

Anahtar Kelimeler: Ventrikülit, neonatal

INTRODUCTION

Neonatal meningitis and ventriculitis still remain a problem with high mortality in spite of systemic and intraventricular antibiotics. Ventriculitis especially due to repeated tap or external drainages is a serious complication of posthemorrhagic hydrocephalus in preterm infants. Multiple ventricular obstructions, may isolate portions of lateral ventricles or the fourth ventricle, cause disproportionate, severe dilatation of affected ventricle and produce a difficult therapeutic problem¹. In these cases, drainage has to remain in place until physiological cerebrospinal fluid (CSF) circulation is restored or an internal shunt can be inserted. On the other hand hematogeneously born bacteria localize first in choroid plexus, cause choroids plexitis with subsequent entrance of bacteria into ventricular space. Ventricle may be major reservoir for bacterial infection. Treatment of ventriculitis remains controversial^{2,3,4,5,6}. The relationship between intraventricular therapy and prognosis has been investigated by many researchers^{7,8,9}. However few studies have examined the prognosis of ventriculitis in neonates^{9,10,11}. Although considerable research has been devoted to intraventricular therapy in adulthood especially after neurosurgical operations, rather less attention has been paid to neonates^{4,12,13}. This retrospective study was designed to evaluate the infants with ventriculitis and intraventricular treatment for ventriculitis in Newborn Intensive Care Unit.

MATERIAL and METHODS

The medical records of all newborn infants admitted to the Neonatal Intensive Care Unit (NICU), Çukurova University Faculty of Medicine, between January 1999 and January 2005 who developed ventriculitis were reviewed. Data pertaining to maternal history, ante partum events,

gestational age, birth weight, gender, Apgar scores, use of antenatal betamethasone, presence of mechanical ventilation therapy, intraventricular hemorrhage, hydrocephalus, and time of the diagnosis of intraventricular hemorrhage, hydrocephaly and ventriculitis, empirical antibiotic usage at the time of diagnosis of ventriculitis, intraventricular antibiotic therapy, results of cerebrospinal fluid (CSF) cultures, antibiotics used for ventriculitis, biochemical analysis of CSF at the time of diagnosis of ventriculitis and at 14th day of treatment, duration of intravenous and intraventricular antibiotic therapy, time of reservoir implanting, and ventriculoperitoneal shunts and outcomes of patients were collected retrospectively. Intraventricular hemorrhage was graded as suggested by Papile et al¹⁴.

Repeated lumbar punctures (LP) were performed for communicating hydrocephaly; and ventricular tap, external drainage or reservoirs were performed for noncommunicating hydrocephaly. Ventriculitis was diagnosed if there was persistence of infection in lumbar CSF after 4 days of appropriate treatment or clinical deterioration or failure of clinical improvement, even with improvement of CSF pleocytosis and CSF sterilization¹.

Ventriculostomy, usually through reservoir was indicated when the ventricular tap demonstrates purulent fluid with persistent infections. Intraventricular antibiotic treatment was started when the CSF pleocytosis and high protein levels continue after 4 days of appropriate intravenous antibiotic treatment. The dose of intraventricular vancomycine was 20 mg/day for once⁶, amicasine 10 mg/day twice² and tobramycine 5 mg/kg/day¹⁵. Intraventricular antibiotics continued until pleocytosis disappeared.

Statistical analysis: Data was analysed by using the SPSS-X 11 for Windows. Results are given as mean \pm standard deviation.

RESULTS

Of 3852 patients hospitalized in NICU 58 were diagnosed hydrocephalus and in this study 16 infants with ventriculitis were evaluated. Thirteen of the infants were male. Mean gestational age was 33 ± 5 (25-40) weeks and mean birth weight was 2096 ± 912 (980-3500) grams, 11 of the infants were premature; 7 were very low birth weight (VLBW) infant. Mean Apgar scores at 1st and 5th minutes were 5.1 ± 1.2 (3-6) and 7.4 ± 1.4 (5-9). Twelve infants had mechanical ventilatory therapy. Eleven preterm babies had IVH and posthemorrhagic hydrocephaly was diagnosed at 23 ± 10 (6-23) days. Two of the term infants had noncommunicating hydrocephaly and 3 of them had communicating hydrocephaly. Drainage of CSF was performed by ventricular taps in 13 infants. All of the infants were having empirical or culture dependent antibiotics during diagnosis of ventriculitis. Ventriculitis was diagnosed at 38.5 ± 22.8 (13-90) days of hospitalization. Gram negative microorganisms (*Klebsiella pneumoniae*, *Pseudomonas aeruginosa*) were predominating in CSF cultures. Both intravenous and intraventricular

antibiotic treatment were performed after the diagnosis of ventriculitis. Vancomycine and amicasine as intraventricular therapy were performed for 28 ± 17 days. Intraventricular tobramycine and gentamycine were used only in two patients who had persistence of ventriculitis in spite of intraventricular vancomycine and amicasine treatment. Mean cerebrospinal fluid protein at the beginning of intraventricular treatment was 624.1 ± 429.1 (109-1330) mg/dl while on 14th day of treatment it was 993.7 ± 582.2 (89-1750) mg/dl. Cerebrospinal fluid protein levels increased significantly at 8 infant during intraventricular therapy. But increased protein was not significantly correlated with mortality and morbidity ($p > 0.05$). Ventriculoperitoneal shunt was performed to seven of the infants and six of them were reinfected at 4.2 ± 1.2 days of operation and one infant with non-reinfected ventriculoperitoneal shunt was treated. Reinfected 6 infants had appropriate intravenous antibiotic treatment. Seven of the infants died, and eight infants were discharged during treatment because of parents refusal of therapy.

Table 1: Properties and CSF findings of the patient

patient s	gender	GA (weeks)	BW (gr)	IVH	Time of diagnosis of ventriculitis (days)	At the time of ventriculitis diagnosed		At 14th day of ventriculitis treatment		Duration of intraventricular treatment (days)	V-P shunt application
						CSF protein (gr/dl)	CSF cells (WBC/mm ³)	CSF protein (gr/dl)	CSF cells (WBC/mm ³)		
1	f	38	2270	absent		129	100	134	40		present
2	m	40	3160	absent	35	105	1000			5	present
3	m	29	1420	absent	37	1186	250	1750	80	40	present
4	m	34	3120	absent	29	709	1000	951	1000	32	present
5	m	29	1200	present	16	806	1000	1253	1000	66	absent
6	m	40	2980	present	13	82	100				absent
7	m	40	3060	absent	27	353	0	555	200	23	absent
8	m	25	1190	present		79	100	89	0	14	absent
9	f	36	1960	present	35	2469	0	1024	0	28	absent
10	m	29	1380	present	51	1330	160	1457	180	20	absent
11	f	38	3500	absent	43	228	20	368	40	20	present
12	m	30	1340	present	21	618	1100	646	180	60	absent
13	m	41	3180	present	90	206	30	137	40	20	present
14	m	28	980	present	31	109	1000	673	50	38	absent
15	m	32	1530	present	28	300	150	1527	80	22	absent
16	m	28	1270	present	84	597	1000	300	40	12	present

DISCUSSION

High risk for intraventricular hemorrhage in preterm infants predisposes ventriculitis in this age group as these infants mostly need ventricular drainage for hydrocephaly. Either ventricular tap, lumbar puncture or external ventricular drainage of CSF have been indicated in acute hydrocephaly after intraventricular bleeding or infection and risk of bacterial meningitis and ventriculitis increased¹⁶. In this study group most of the patients (11/16), predominately preterm infants, had ventriculitis after posthemorrhagic hydrocephalus during CSF drainage with tap or LP. Also in other reports preterm infants were forming the study group^{8,13}.

The pathogenesis of ventriculitis is discussed on the basis of the histomorphological structure ependyma, the subependymal tissue and the glycogen rich choroid plexus at the first few weeks after birth. It seems that this structure facilitates local bacterial growth and act as bacterial reservoir, relatively resistant to antimicrobial therapy⁹. High glycogen content of neonatal choroid plexus is an excellent medium for bacteria. This can be the cause of resistance to therapy.

Clinician has to suspect ventriculitis if poor clinical and laboratory results responding to usual therapy exist, critically ill patient with convulsion and bulging fontanel, and growth of unusual microorganisms in culture. Also CSF from ventricular puncture with more than 150 WBC, glucose less than 50 mg/dl and protein more than 200 mg/dl doubt for ventriculitis¹⁷. Infants in this study had increased CSF protein and wbc, clinical deterioration like apnea and convulsions. The diagnosis of ventriculitis in preterm neonates with posthemorrhagic hydrocephaly can be difficult because CSF findings in these patients are often abnormal even in the absence of infection¹⁸. Many of the patients have high protein levels in CSF and pleocytosis in absence of CSF culture growth. CSF pleocytosis, decreased glucose and increased protein levels may result from intraventricular hemorrhage (IVH) and can also be found in

patients with shunt dysfunction but without infection¹⁹. In this study group most of the patients developed ventriculitis after posthemorrhagic hydrocephaly so effect of treatment was difficult to interpret because of pleocytosis and high protein levels without culture positivity. The most commonly encountered bacteria are staphylococci and enterobacteraceae with a high percentage of coagulase-negative staphylococci in ventriculostomy associated ventriculitis. But also gram negative bacilli are commonly isolated in CSF shunt infections³. In our study group *Klebsiella* and *Pseudomonas* were most common isolated microorganisms in CSF cultures.

The goal of treatment in neonatal ventriculitis should be directed to achieve a high concentration of antimicrobial concentration of antimicrobial agent in the mentioned tissue. There are many reports suggesting intraventricular route for applying antimicrobial therapy^{6,9,13,20,21}. Despite, in some other reports, the use of intraventricular antibiotics in addition to intravenous antibiotics resulted in increased mortality compared to standard treatment with intravenous antibiotics alone⁷. On the other hand intraventricular installation of antibiotic appears to be beneficial in selected cases¹. Intraventricular vancomycin with amikacin are accompanied with appropriate intravenous antibiotics. Intraventricular application of vancomycin is an effective treatment especially in drainage associated staphylococcal ventriculitis²². Despite relatively high levels of vancomycin in the cerebrospinal fluid, no evidence of toxicity was seen⁶. In this study, during hospitalization toxic signs of vancomycin were not detected however blood vancomycin levels could not be checked. Within the confines of this study, it has been impossible to check ototoxicity of vancomycin and amikacin in each patient because of the parents insisting on discharging and noncontinuing to polyclinic controls. Also aminoglycosides; gentamicin, tobramycin and amikacin are appropriate alternatives for

intraventricular therapy^{2,13,15,21}. On the other hand ventricular pleocytosis was directly correlated and glucose levels were inversely correlated with penetration of ampicillin (23). Despite parenteral and intralumbar antibiotic therapy, clinical and autopsy data indicate that ventriculitis persists¹⁷.

In summary, improved survival of low birth weight, premature babies have increased the incidence of posthemorrhagic hydrocephaly in premature infants. Ventriculitis is a serious complication of ventricular or lumbar taps. Aim has to prevent IVH in premature babies. Effect of intraventricular antibiotic treatment could not be demonstrated in this study.

REFERENCES

- Volpe JJ. Bacterial and Fungal Intracranial Infections. In: Neurology of Newborn 4th eds. Saunders, Philadelphia. 2001; 774-810.
- Kaiser AB, McGee ZA. Aminoglycoside therapy of gram-negative bacillary meningitis. *N Engl J Med*. 1975; 11;293:1215-20.
- De Bels D, Korinek AM, Bismuth R, Trystram D, Coriat P, Puybasset L. Empirical treatment of adult postsurgical nosocomial meningitis. *Acta Neurochir*. 2002 ;144: 989-95.
- Pfausler B, Spiss H, Beer R, Kampl A, Engelhardt K, Schober M, Schmutzhard E. Treatment of staphylococcal ventriculitis associated with external cerebrospinal fluid drains: a prospective randomized trial of intravenous compared with intraventricular vancomycin therapy. *J Neurosurg*. 2003 ;98:1040-4.
- Schultz M, Moore K, Foote AW. Bacterial ventriculitis and duration of ventriculostomy catheter insertion. *J Neurosci Nurs*. 1993; 25:158-64.
- Bayston R, Hart CA, Barnicoat M. Intraventricular vancomycin in the treatment of ventriculitis associated with cerebrospinal fluid shunting and drainage. *J Neurol Neurosurg Psychiatry*. 1987; 50:1419-23.
- Shah S, Ohlsson A, Shah V. Intraventricular antibiotics for bacterial meningitis in neonates. *Cochrane Database Syst Rev*. 2004; 18; CD004496.
- Nieto Del Rincon N, de Alba Romero C, Egea Nadal P, Mateos Beato F, Peralta Ibanez ML, Ramos Amador JT, Miralles Molina M, Gomez del Castillo E. Experience with ventriculitis at a neonatology department. *An Esp Pediatr*. 2000 ;52:245-50.
- Schretlen E, Muytjens H, Slooff J. Neonatal meningitis, ventriculitis, intraventricular therapy or not? *Tijdschr Kindergeneesk*. 1985 ;53:136-41.
- Hammersen G, Wille L. Technique for intraventricular application of antibiotics in bacterial meningitis of the newborn (author's transl). *Monatsschr Kinderheilkd* 1981 ;129:525-8.
- Baumeister FA, Hofer M, Kuster H, Belohradsky BH. CSF interleukin-6 in neonatal *Citrobacter* ventriculitis after meningitis. *Infection*. 2000 ;28:243-5.
- Barnes BJ, Wiederhold NP, Micek ST, Polish LB, Ritchie DJ. *Enterobacter cloacae* ventriculitis successfully treated with cefepime and gentamicin: case report and review of the literature. *Pharmacotherapy*. 2003 ;23:537-42.
- Wen DY, Bottini AG, Hall WA, Haines SJ. Infections in neurologic surgery. The intraventricular use of antibiotics. *Neurosurg Clin N Am*. 1992 ;3:343-54.
- Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm *J Pediatr*. 1978 ;92:529-34.
- Raine PA, Young DG, McAllister TA, Tait SC. Tobramycin in pediatric use. *J Infect Dis*. 1976;134:165-9.
- Winking M, Schroth I, Joedicke A, Boeker DK. Technical note: external cerebrospinal fluid (CSF) drainage by percutaneous needle puncture in newborn children. *Acta Neurochir*. 1999;141:1093-4.
- Calderon E, Hernandez M, Gonzalez N, Cob C, Martinez E. Neonatal meningoventriculitis. *Bol Med Hosp Infant Mex*. 1977; 34:117-28.
- Baumeister FA, Pohl-Koppe A, Hofer M, Kim JO, Weiss M. IL-6 in CSF during ventriculitis in preterm infants with posthemorrhagic hydrocephalus. *Infection*. 2000;28: 234-6.

19. Feigin RD, Matson DO: the compromised host. In: Feigin RD, Cherry JD(eds): Textbook of pediatric infectious diseases. Saunders, Philadelphia. 1992; 960-89.
20. Yeung CY. Intrathecal antibiotic therapy for neonatal meningitis. Arch Dis Child. 1976 ;51:686-90.
21. Bruckner O, Alexander M, Collmann H. Tobramycin levels in cerebrospinal fluid of patients with slightly and severely impaired blood-cerebrospinal barrier. Chemotherapy. 1981; 27:303-8.
22. Nagl M, Neher C, Hager J, Pfausler B, Schmutzhard E, Allerberger F. Bactericidal activity of vancomycin in cerebrospinal fluid. Antimicrob Agents Chemother. 1999; 43:1932-4.
23. Yogev R, Kolling WM. Intraventricular levels of amikacin after intravenous administration. Antimicrob Agents Chemother. 1981; 20:583-6.

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