RESEARCH ARTICLE / *Araştırma Makalesi*

Guillain-Barre Syndrome Followed in the Pediatric Intensive Care Unit; 3-year Experience

Çocuk Yoğun Bakım Ünitesinde Takip Edilen Guillain Barre Sendromu Olguları; 3 Yıllık Deneyim

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Geliş Tarihi / Received : **06.01.2021** Kabul Tarihi / Accepted : **31.03.2021**

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(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(2):231-237) DOI: 10.31832/smj.855110**

Abstract

Objective	After the poliomyelitis eradicated, Guillain-Barre Syndrome (GBS) is the most common cause of acute flaccid paralysis in healthy child. It is one of the neuromuscular disorders required treatment to pediatric intensive care unit. Aim of this study is to present the three-year's experience of caring for patients with GBS admitted the PICU in the university hospital.
Materials and Methods	Patients who were admitted to the PICU with diagnosed GBS between March 2016 and March 2019 were evaluated retrospectively.
Results	Twenty-two patients were diagnosed with GBS during study period. Seven of them needed PICU in 8 admissions, and they formed the study group. Four of them were female and 3 of them were male. They were 3 to12 years old. All of them were admitted in the PICU because of respiratory distress symptoms. The paralysis followed a nonspecific respiratory or gastrointestinal infection by 3 to 7 days, and ascending progress was present. Intravenous immunoglobulin infusion was administered in all patients. Five of them need to plasmapheresis and mechanical ventilator support. Stay to PICU length was 2 to 87 days and hospitalization length was14 to 98 days. All of them were discharged, and became able to walk unaided.
Conclusion	Our results show that PICU follow-up is very important in children with GBS. Although duration of mechanical ventilation, and hospitalization length is long, prognosis is good with effective management strategies.
Keywords	Guillain-Barre syndrome; plasmapheresis; intravenous immunoglobulin; pediatric intensive care unit

Öz

Amaç	*Poliomiyelit eradike edildikten sonra akut flask paralizinin sğlıklı çocuklardaki en sık nedeni Guillain-Barre Sendromu (GBS) olmuştur. GBS, çocuk yoğun bakım (ÇYB) ünitesinde tedavi olmayı gerektiren nöromusküler hastalıklardan birisidir. Bu çalışmanın amacı, GBS tanısı ile ÇYB ünitesinde yatırılarak tedavi edilen hastalarla ilgili bir üniversite hastanesinin üç yıllık deneyimini sunmaktır.*
Gereç ve Yöntemler	*Mart 2016 ve Mart 2019 tarihleri arasında GBS tanısı ile ÇYB ünitesinde takip edilen hastalar retrospektif olarak değerlendirildi.*
Bulgular	*Çalışma süresi boyunca 22 hasta GBS tanısı aldı. Bu hastalardan 7 tanesinin ÇYB ünitesinde takip edilmesi gerekti. Bu 7 hastanın 8 yatışı çalışma grubunu oluşturdu. Dört tanesi kız, 3 tanesi erkek idi. Yaşları 3 ile 12 yıl arasındaydı. Hastaların tümü solunum sıkıntısı semptomları ile ÇYB ünitesine yatırıldı. Hastalarda asendan paralizinin başlangıcından 3 ile 7 gün önce nonspesifik bir solunum yolu enfeksiyonu veya gastrointestinal enfeksiyon vardı. Tüm hastalara intravenöz immunoglobulin infüzyonu verildi. Beş hasta yatışında plazmaferez tedavisine ve mekanik ventilasyon desteğine ihtiyaç duyuldu. ÇYB ünitesinde yatış süresi 2 ile 87 gün ve hastanede yatış süresi 14 ile 98 gün idi. Hastaların hepsi taburcu edildi ve yardımsız yürüyebildi.*
Sonuç	*Sonuçlarımız, GBS tanılı hastalarda ÇYB takibinin çok önemli olduğunu gösterdi. Mekanik ventilatörde kalma süresi ve hastanede yatış süresi çok uzun olmasına rağmen, etkili bir ÇYB desteği ile bu hastalarda prognoz iyidir.*
Anahtar Kelimeler	*Guillain-Barre sendromu; plazmaferez; intravenöz immunoglobulin; çocuk yoğun bakım ünitesi*

INTRODUCTION

After the poliomyelitis eradicated, Guillain-Barre syndrome (GBS) is the most common cause of acute flaccid paralysis in healthy children.[1,2] One of the proposed mechanisms for GBS is that an antecedent infection such as nonspecific respiratory or gastrointestinal infection evokes an immune response. The result is an acute polyneuropathy. The classic presentation of GBS begins with paresthesia in the toes and fingertips followed by lower extremity symmetric or rarer asymmetric weakness. This may ascend over hours to days to involve the arms. The muscles of respiration are affected in severe cases.[3,4] Autonomic dysfunction occurs in approximately one-half of children with GBS.[5,6] The initial diagnosis of GBS is based upon the clinical presentation. Cerebrospinal fluid (CSF) assessment, electrodiagnostic studies and magnetic resonance imaging (MRI) are the supportive diagnostic approaches. GBS treatment includes administration of IVIG and plasmapheresis (PF) in addition to supportive therapy. In some patients, GBS is one of the neuromuscular disorders required treatment to pediatric intensive care unit (PICU).[7] Aim of this study is present the three-year's experience of caring for patients with GBS admitted the PICU in the university hospital.

MATERIALS and METHODS

This study is designed as a single-center retrospective and descriptive study (Ataturk University Faculty of Medicine, Division of PICU). Seven patients (with 8 admissions) who were admitted to the PICU with the complaints of GBS between March 2016 and March 2019 were included in this study. Medical records of these patients were evaluated and the clinical features of the ones who were followed in the PICU are presented. Age, gender, symptoms and signs on admission, indications for PICU admission, applied treatments, length of stay in the PICU, total length of hospital stay and the outcomes were noted from the medical records.

Mean ± SD was given for numerical data, and number and percent were given for nominal data.

Approval for the study was obtained from the Faculty of Medicine of Ataturk University ethics committee (Ethics Committee Year/Number: 26.09.2019/20). The study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

Twenty-two patients were diagnosed with GBS during study period. Seven of them needed PICU in 8 admissions, and they formed the study group. Four of them were female and 3 of them were male. They were 3 to12 years old. All of them were admitted in the PICU because of respiratory distress symptoms. The paralysis followed a nonspecific respiratory or gastrointestinal infection by 3 to 7 days, and ascending progress was present.

After appearance of lower extremity weakness, respiratory distress symptoms were progressed rapidly in some patients (pt1, pt3, pt4, pt5, pt7) while the others (pt2, pt6) had a slow progression. Patient 6 stayed only for two days in the PICU due to respiratory distress. After an uneventful two weeks, he developed respiratory insufficiency again and readmitted to PICU.

Intravenous immunoglobulin infusion was administered in all patients (1 g/kg/d for 12h IV infusion, 2 times). When mechanical ventilation support was required or previously present need was still going on (pt3, pt4, pt5, pt6b, pt7), PF was performed (daily 1.5 volumes PF for 5 times), after 72h of IVIG administration.

All patients, who needed mechanical ventilation support developed pneumonia and all had facilitating factors of pneumonia (hypersalivation, aspiration). In addition, some other complications like sepsis, acute respiratory distress syndrome (ARDS), acute renal failure (ARF), and Steven Johnson Syndrome (SJS) were also developed in some patients. Three of them (pt4, pt5, pt7) were needed

tracheostomy. All patients were discharged, and became able to walk unaided. Individual demographic and clinical features of the patients shown in Table 1.

Table 1. Demographic and clinical features of the patients

Patient Number			**1**	**2**	**3**	**4**	**5**	**6a**	**6b**	**7**
Age(year)/Gender			8/M	10/F	12/F	4/F	6/M	12/M		3/F
Indication for PICU			RM	RM	RF	RF	RF	RD	RF	RF
PRISM 3 score			0	0	11	0	9	6	6	12
Neurologic Symptoms	**Bulbar weakness**		Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
	Upper extremity weakness		No	Yes(4/5)	Yes(2/5)	Yes(3/5)	Yes(1/5)	Yes(4/5)	Yes(2/5)	Yes(0/5)
	Lower extremity weakness		Yes(3/5)	Yes(4/5)	Yes(1/5)	Yes(1/5)	Yes(1/5)	Yes(3/5)	Yes(1/5)	Yes(0/5)
	Facial weakness		Yes	Yes	No	Yes	No	No	No	No
	Extraocular muscle weakness		Yes	No	No	Yes	No	No	No	No
	Neck weakness		No	No	Yes	Yes	Yes	No	No	No
	6th cranial nerve involvement		Yes	No	No	No	No	No	No	No
	7th cranial nerve involvement		Yes	No	No	Yes	No	No	No	No
	Areflexia		No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Autonomic	**Dysfunction**	**Bradycardia**	Yes	No	No	No	No	No	No	No
		Tachycardia	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
		Hypotension	No	No	No	No	No	No	No	Yes
		Hypertension	Yes	Yes	Yes	Yes	Yes	No	No	Yes
		Paralytic ileus	Yes	No	No	No	No	No	No	Yes
LP time after PICU admitted (d)/ACD			1/None			10/Yes	1/None			2/None
EMG time after PICU admitted (d)/EMG Result			1/N and 7/AMAN	3/ AMSAN	6/N and 22/ AMSAN	22/ AMAN	13/ AMSAN	4/ AMSAN	10/ AMSAN	5/AMAN And 18/ AMAN
MRI time after PICU admitted (d)/MRI Result			10/N	6/N			1/Pointed GBS*		7/N	30/Pointed GBS*
Mechanic ventilation (d)			0	0	11	45	41	0	15	25
Treatment			IVIG	IVIG	IVIG+PF	IVIG+PF	IVIG+PF	IVIG	IVIG+PF	IVIG+PF
PICU/Hospital stay (d)			8/14	5/14	25/33	59/98	87/95	2/14	22/43	63/90
Complications			None	None	P,S,ARF	P,S,ARDS	P,S	None	P,S	P,S,SJS
Tracheostomy placement/decanulation time after diagnosed (d)						44/No	25/120			21/No
Symptom onset time before PICU admit (d)			2	6	2	1	2	10	46	2
Aided walking/ Walking time after diagnosed (d)			14/60	90/180	30/60	130/180	87/210	No	55/120	180/270

ACD: albuminocytologic dissociation, AMAN: acute motor axonal neuropathy, AMSAN: acute motor sensory axonal neuropathy, ARDS: acute respiratory distress syndrome, ARF: acute renal failure, CT: computed tomography, EMG: electromyography, F: Female, GBS: Guillain-Barré syndrome, IVIG: intravenous immunoglobulin, LP: lumbar puncture, M: male, MRI: magnetic resonance imaging, N: normal, P: pneumonia, PF: plasmapheresis, PICU: pediatric intensive care unit, PRISM: pediatric risk of mortality, RD: respiratory distress, RF: respiratory failure, RM: respiratory monitoring, S: sepsis, SJS: Steven Johnson syndrome, *: extensive contrast enhancement of nerve roots

DISCUSSION

Respiratory failure is one of the most serious complications of GBS. These patients should be followed in intensive care unit for close monitorization and mechanical ventilation support. In adult population, about a third of patients of GBS require mechanical ventilation.[8] In a study[9] whom all GBS patients had been evaluated during one-year period, 17.3% of the patients needed mechanical ventilation. In another study, in which nine-years period had been evaluated, the same ratio was 9.5%.[10] It has been reported that 75% of GBS patients who had been admitted to PICU, needed mechanical ventilation.[11] In our study, 21.7% of all admissions with the diagnosis of GBS needed mechanical ventilation. This ratio was apparently higher (62.5%) among admissions to PICU.

Our patients who were admitted at PICU showed three clinical conditions. In two admissions (pt1 and pt2), patients had bulbar weakness, hypersalivation and moderate tachypnea, and only respiratory monitorization was done. In one admission (pt6), the patient had respiratory distress without bulbar weakness. He needed noninvasive respiratory support. In five admissions (pt3, pt4, pt5, pt6b, pt7), the patients had bulbar weakness and respiratory failure, so they needed invasive mechanical ventilation support.

The frequency of acute or acute-on-chronic neuromuscular disorders among PICU admissions are reported to be very low.[7] During the study period, approximately 900 admissions occurred in our PICU, and the frequency of admissions for GBS was extremely low among total PICU admissions (less than 1%). Although the frequency was very low, it was an important group of patients due to the prolonged hospitalization in PICU.

Diagnosis of GBS depends on the clinical findings. All of our patients had typical findings with ascending progression of flaccid paralysis with preceding respiratory or gastrointestinal infection. One of the patients (pt1), although onset was classical, had silent ascending progression, positive tendon reflexes and symptoms of pronounced autonomic dysfunction. Although positive tendon reflex is an atypical finding for GBS, it has been reported in about 10% of the patients.[12]

The supportive diagnostic approaches for GBS include CSF assessment, electromyography (EMG) and MRI. Analysis of CSF may show albuminocytologic dissociation. Electromyography may demonstrate acute motor axonal neuropathy (AMAN) or acute motor sensory axonal neuropathy (AMSAN). MRI may demonstrate extensive contrast enhancement of nerve roots. But all of these supportive diagnostic approaches may be normal.[13,14] CSF analysis was performed in 4 of 8 admissions at our patients. In patients in whom CSF analysis was performed in early phase (pt1, pt5, pt7), albuminocytologic dissociation was not determined. On the other hand, it was determined in pt4. Her CSF was analyzed on the 10th day. EMG was performed in all patients. While the first EMGs were normal in pt1 and pt3 (in first and 6th day, respectively) subsequent ones demonstrated AMAN (pt1, 7th day) and AMSAN (pt3, 22nd day). In remaining patients, the first EMGs (performed 3rd to 22nd days) demonstrated AMAN or AMSAN. MRI was performed in 5 of 8 admissions. While two patients (pt5, 1st day and pt8, 30th day) had extensive contrast enhancement of nerve roots, in three (pt1, 10th day; pt2 6th day and pt6b, 7th day) MRI was normal. Not all patients had the expected results for GBS in supportive diagnostic approaches. This finding emphasizes again the importance of the clinical approach.

Autonomic dysfunction is reported in approximately one half of the children with GBS.[5,6] Our patients had tachycardia in all admissions and hypertension in 6 admissions. It is not clear whether these symptoms are the result of autonomic dysfunction or not. Because some other environmental factors can result in tachycardia and hypertension. The symptoms of autonomic dysfunction were very evident in only pt1.

Early relapses occur in about 4% of cases of childhood GBS.[5] Early relapse was observed in only one of the seven patients. Pt6 was monitored in PICU in his first admission due to respiratory distress. Following a prominent regression, he was discharged from PICU, and readmitted two weeks later with more severe symptoms (Table 1).

In treatment, data for children is limited. Despite that guidelines from the American Academy of Neurology (AAN), treatment with IVIG or PF for children with severe GBS are suggested.[15,16] In many centers, IVIG is preferred to PF for children because of the relative safety and simplicity of administration. Every other day or daily performed PF are being suggested by American Society for Apheresis (ASFA) as the primary treatment of GBS.[17] Kesici et al. suggested a novel treatment strategy for severe GBS, called "Zipper Method".[18] According to this method, each plasma exchange session was followed by IVIG administration. Preference of IVIG or PF in treatment varies between clinics. There is no difference between treatments success.[19,20] IVIG was our first preference at the practical applications. We administered IVIG in dose of 1 g/kg/day for 2 consecutive days. After 72h of IVIG treatment, PF was performed at ineffective responses. Intravenous immunoglobulin infusion was administered in all patients. In five admissions (pt3, pt4, pt5, pt6b, pt7) enough response could not be obtained, they needed mechanical ventilation support, and plasmapheresis was performed to these patients.

All patients developed pneumonia and sepsis. All of them had facilitating factors for pneumonia (i.e. hypersalivation, aspiration) and they had ral and rhonchi at the admission to PICU, present lung infection could not be considered as ventilation associated. In some patients (pt3, pt4 and pt7), sepsis led to some other complications like ARF, ARDS and SJS.

If within one to three weeks of intubation and mechanical ventilation support still required in the patients, tracheostomy is often considered. There is no consensus for optimal time to performed it among the physicians.[21] In our practice, decision of tracheostomy is individualized according to the patient's clinical circumstances and the parent's approved. Therefore, tracheostomy performed in some patients (pt4, 44th day; pt5, 25th and pt7, 21st day). Delay in timing of pt4 was due to her parent's indecision. All discharged with tracheostomy, and only one (pt5) could be decanulated after 120 days.

The mortality rate is reported between 8% and 16% in children with GBS.[9,11,22] The mortality risk was calculated depending on the Pediatric Risk of Mortality Score (PRISM 3)23 score of first 24 hours of PICU admission. It was between 0.8% and 8.9%. Of course the complications that developed during PICU follow-up increased this risk. We think that effective management strategies and the ability to cope with complications eliminated mortality. At this point, supportive treatment which provides by PICU becomes more important. All patients were discharged, and become able to walk unaided.

CONCLUSION

Our results show that PICU follow-up is very important in children with GBS. Although duration of mechanical ventilation, and hospitalization length is long, prognosis is good with effective management strategies.

Financial Support

This research received no specific grant from any funding agency, commercial, or not for profit sectors.

Conflict of interest

The authors declare that there is no conflict of interest.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Ethical approval

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation in Turkey and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval was given for this study from the Faculty of Medicine of Ataturk University (Ethics Committee Year/Number: 26.09.2019/20).

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