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ORIGINAL ARTICLE

Intravenous immunoglobulin accompanied with high-dose methylprednisolone therapy for 17 children with anti-*N*-methyl-D-aspartate receptor encephalitis: Clinic and nursing

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ABSTRACT

Objective: An increasing number of pediatric patients are being diagnosed with anti-*N*-methyl-D-aspartate receptor (NMDAR) encephalitis, whose treatment requires immunotherapy through nursing interventions. This study aimed to analyze the clinical features and long-term prognosis of pediatric anti-NMDAR encephalitis and to gather nursing experiences of immunotherapy.

Methods: Seventeen children diagnosed with anti-NMDAR encephalitis were admitted to the pediatric department. They were subjected to a therapy of intravenous immunoglobulin (IVIG) accompanied with high-dose methylprednisolone (HDMP). Multidisciplinary cooperation and intensive care were used to manage them. The effects of nursing intervention and therapy were repeatedly assessed and analyzed throughout the course of treatment and recovery.

Results: None of the patients manifested adverse drug reaction (ADR) during IVIG administration. At the first administration of HDMP, ADRs were promptly and efficiently treated in four patients (24%; i.e., one case each of hyperglycosemia, hypertension, aggravated symptoms, and gastrointestinal bleed). Two patients underwent rehabilitation, and six patients received hyperbaric oxygenation during hospitalization. Nine patients with indwelling gastric tubes experienced four times of unplanned extubation. Hospital stay ranged from 11 days to 59 days, with the mean duration of 26 days. Discharge evaluation revealed that 16 patients who scored 0–2 on the modified Rankin scale presented obvious remission, and one patient who had a mRS score of 4 exhibited less improvement. The mRS scores of hospitalization, discharge, and six-month follow-up displayed statistically significant differences.

Conclusions: Nursing interventions of immunotherapy ensures the security of IVIG administration. Multidisciplinary cooperation promotes remission. Our findings can serve as reference for healthcare teams.

1. Introduction

Anti-NMDAR encephalitis is a new and treatable autoimmune disease with complex neuropsychiatric symptoms [1,2]. Anti-NMDAR encephalitis associated with ovarian teratomas was first reported in 2005 [3]. In 2007, a study described the anti-NMDAR encephalitis associated with the anti-NMDA receptor antibody, which is predominantly expressed in the cell membrane of the hippocampus [4]. This disease affects patients of all ages, regardless of whether they have tumors or not; nonetheless, the majority of cases had been reported among children and young adults [5,6]. Utilizing a large sample, Titulaer et al. found that ovarian teratomas was the most common type of tumor (94%), and that <6% of the patients below 12 years old had tumors [7]. Thus, females are more

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susceptible, because pediatric patients are less likely to have tumors [5,6,8]. The pathogenesis of anti-NMDAR remains unclear. Given its complex clinical manifestations without specificity, anti-NMDAR encephalitis is often misdiagnosed as viral encephalitis or other diseases. A definitive diagnosis is achieved by detecting the anti-NMDAR antibody in the serum or the cerebrospinal fluid (CSF) [9–12]. The main treatment approaches for anti-NM|DAR encephalitis include first-line immunotherapy (corticosteroids, IVIG, and/or plasmapheresis), second-line immunotherapy (rituximab, cyclophosphamide), teratoma resection, and supportive care during the acute stage [6,10]. The majority of patients are admitted to the intensive care unit during the acute stage [10]. Neurologists, psychiatrists, oncologists, neuro-oncologists, immunologists, and intensivists must become familiar with the clinical presentations and potential complications of anti-NM|DAR encephalitis [8,11]. Multidisciplinary cooperation is needed for the optimal management of the disease.

At present, more than 20,000 encephalitis-related hospitalizations are recorded in the United States every year. Nearly half of encephalitis survivors incur permanent neurologic damage and thus require long-term care. In 2010, the cost of providing care to all hospitalized encephalitis patients in the United States was approximately $2 billion [13–15]. The frequency of anti-NMDAR encephalitis has surpassed all viral encephalitides in patients having encephalitis of unknown etiology [16]. Neurological manifestations of seizures, status epilepticus, dystonia, verbal reduction, or mutism are common among children with anti-NMDAR encephalitis [17,18]. Careful observation and intensive care are important intervention procedures in ensuring patient safety and facilitating immunotherapy. Nurse practitioners (NPs) play a key role in providing effective administration. However, no detailed and unified nursing standard has been established for anti-NMDAR encephalitis, and this topic has been rarely investigated in the literature. This lack of standard is causing challenges in providing care. In this study, we collected nursing experiences about immunotherapy and highlighted the nursing of anti-NMDAR encephalitis.

2. Patients and methods

2.1. Patients and treatment

A total of 17 children (6 males (35%) and 7 females (65%); mean age: 7 years; age range: 2–13years) who were diagnosed with acute-stage anti-NMDAR encephalitis from September 2014 to November 2015 were included in our study. Imaging analysis indicated that all patients had no tumors. The patients underwent first-line immunotherapy, which consisted of intravenous immunoglobulin (IVIG, 1 g/kg/day for 2 days) accompanied with high-dose methylprednisolone (HDMP) pulse therapy (15–30 mg/kg/day for 3 days), followed by oral prednisolone (2 mg/kg/day), the dose of which was subsequently tapered off. The patients concurrently received adjunctive therapy (e.g., antipsychotic medication, fluid therapy, and gastroprotective therapy). Rehabilitation and hyperbaric oxygenation were employed to promote recovery. The patients' information and treatment are listed in Table 1, and their clinical symptoms at hospitalization are shown in Fig. 1A.

Table 1
Patients' information and treatment.

Item	Male	Female	Total
Number of patients	6 (35%)	11 (65%)	17
Mean age (range), y	8 (2–13)	6 (3–12)	7 (2–13)
Associated tumor	0	0	0
Positive anti- NMDAR antibodies (CSF)	6 (35%)	10 (59%)	16 (94%)
Positive anti-NMDAR antibodies (serum)	6 (35%)	8 (47%)	14 (82%)
Abnormal EEG	6 (35%)	11 (65%)	17 (100%)
Abnormal MRI	3 (18%)	2 (12%)	5 (29%)
Initial symptom			
Seizures	0	4 (24%)	4 (24%)
Behavior problems	6 (35%)	5 (29%)	11 (65%)
Others	0	2 (12%)	2 (12%)
Treatment			
IVIG:1 cycle	4 (24%)	8 (47%)	12 (70%)
IVIG:2 cycles	2 (12%)	3 (18%)	5 (30%)
HDMP:1 cycle	3 (18%)	8 (47%)	11 (65%)
HDMP:2 cycles	1 (6%)	2 (12%)	3 (18%)
HDMP:3 cycles	2 (12%)	1 (6%)	3 (18%)
Prednisolone/per os	6 (35%)	11 (65%)	17 (100%)
Rehabilitation	1 (6%)	1 (6%)	2 (12%)
Hyperbaric oxygen treatment	2 (12%)	4 (24%)	6 (36%)
Indwelling gastric tube	4 (24%)	5 (29%)	9 (53%)

Data were n (%).The distribution of all cases with ratio according to different gender could be listed as items. Female with 65% was obviously more than male. None had an underlying tumor. 94% cases had positive anti- NMDAR antibodies in CSF. EEG of all cases presented abnormal. The initial symptom predominantly presented with psychiatric symptoms. More than half of patients relied on nasal feeding.
Anti-NMDAR, anti-*N*-methyl-D-aspartate receptor; CSF, cerebrospinal fluid; EEG, electroencephalography; MRI, magnetic resonance imaging; IVIG, intravenous immunoglobulin; HDMP, high-dose methylprednisolone.

2.2. Nursing interventions

2.2.1. Pre-administration evaluation and preparation

Medication history, transfusion, and adverse drug reaction (ADR) were first thoroughly examined. Then, the vessels were assessed (i.e., joint sites should be avoided; straight and erromenus vessels should be selected), and the peripheral venous catheters (PVCs) were inserted. Indexes, such as micro blood sugar (MBS) and vital signs, were monitored.

2.2.2. Nursing intervention of administration

IVIG was infused with speed of 15 mL/h at the first 15min and was regulated according to medical order. In the duration of HDMP infusion, continuous electrocardiogram monitoring must last 6 h, at this time, measuring BP must be Q2h for 3 times and later Q4h for 2 times. When HDMP delivery was finished, measuring MBS was carried out immediately and again at 3 h later. Test urine routine was done at 12 h later. Administration was paused when the patient's temperature reached 38.5 °C or higher. The patients were carefully observed to determine whether their symptoms aggravated or new symptoms appeared.

At the end of the first HDMP administration in our study, one patient presented an increased blood pressure (BP), reaching up to 140/100 mm Hg (1 mm Hg = 0.133 kPa). Hypotensor was given orally, and the frequency of BP monitoring was increased. After an hour, the patient's BP slowly descended to normal, and the speed of infusion was reduced. The BP was monitored once per hour for 6 h in the subsequent HDMP pulse therapy. The BP was maintained in the normal range.

The highest recorded MBS was 15 mmol/L, which was detected in one patient at the end of the administration of the first HDMP pulse therapy. The vital signs were normal. The MBS returned to its normal levels within 6 h, with only enhanced management implemented as intervention. The speed of the subsequent administrations were slowed down to control the MBS.

Approximately 20 mL of a coffee-like substance was found through suction by connecting a nasogastric (NG) tube in one patient 3 h after the end of the first HDMP administration. The results of the gastric occult blood test was positive. Thus, normal saline irrigation of stomach was performed, followed by the injection of thrombin into the stomach and the administration of vitamin k1. The patient with parenteral nutrition fasted for 6 h. Suction via NG tube was conducted every 2 h. Venoclysis of cimetidine was