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Clinical efficacy of clonazepam in the treatment of status epilepticus

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Abstract: To explore the clinical efficacy of clonazepam in the treatment of status epilepticus. Totally 60 patients with status epilepticus were identified as research subjects and assigned (1:1) via the randomized double-blind method to receive either diazepam (Valium) comparison group) or clonazepam (observation group). After treatment and follow-up visits, the treatment efficacy, incidence of adverse reactions, quality of life, and recurrence were evaluated and compared between the two groups. The total effective rate of the observation group was 93.33%, which was higher than that of 66.67% in the comparison group (P<0.05). A longer mean duration of drug effect was observed in the observation group than in the comparison group (P<0.05). The observation group outperformed the comparison group in terms of quality of life (P<0.05). The observation group had a lower incidence of adverse reactions than the comparison group (P<0.05). The overall recurrence rate in the comparison group was 23.33%, which was significantly higher than that of 6.67% in the observation group (P<0.05). Clonazepam yields a promising efficacy in the treatment of patients with status epilepticus.

Keywords: Status epilepticus, clonazepam, curative effect, adverse reactions, reoccurrence.

INTRODUCTION

Status epilepticus is a common clinical critical condition that threatens the life and health of patients and delayed or ineffective treatment may easily lead to serious brain damage, resulting in sequelae or even death (van *et al*., 2020). It has an estimated incidence of up to 61 episodes per 100,000 population per year. Predictably, its substantial morbidity and mortality could incur high health care costs. Therefore, reasonable treatment regimens should be developed for the patient's condition to obtain desired therapeutic efficacy. Currently, there is high level evidence only for the first-line medications of SE including intravenous benzodiapines. But it remains unavailable in some countries or areas, alternative treatment hence is necessary. Some of the conventional agents including phenytoin, phenobarbital, and valproate were available as second-line treatment, toxicity yet limited the applications. Therefore, newer, more effective and less toxic drugs for management of status epilepticus were needed.Clonazepam is a benzodiazepine with excellent sedative, anticonvulsant and anxiolytic effects, showing a definite application value in the treatment of status epilepticus patients (den *et al*., 2020). Herein, the clinical efficacy of clonazepam in the treatment of status epilepticus was observed to provide a clinical reference.

MATERIALS AND METHODS

General information

Total 60 patients with status epilepticus were identified as research subjects, including 33 males and 27 females, aged from 1 to 45 years, with a mean age of (20.95±1.05) years. Their duration of the disease ranged from 3 months to 10 years, with a mean duration of (5.21±0.35) years.

Inclusion and exclusion criteria

Inclusion criteria

Patients with confirmed diagnosis; patients with complete general information; patients or guardians of children who were informed of the process and purpose of the study and signed informed consent forms; patients with good compliance to cooperate with the treatment and follow-up.

Exclusion criteria

Patients with mental illness that prevented normal communication; patients with incomplete clinical data; patients with allergies to the drugs applied in the present study.

The patients were randomly assigned (1:1) to a comparison group or an observation group. All investigators and eligible patients were masked to the grouping. The two groups showed no significant difference in terms of general information (P>0.05), as shown in table 1.

Ethical considerations

The specific process regarding this study protocol and the associated risks and other issues were reviewed and approved by our ethics association. The ethical approval number is 2020-10-05.

Treatment methods

The observation group was treated with clonazepam, and treatment protocols varied in different patients. Children were given an intravenous infusion of clonazepam, 1 ~ 2 mg each time, once a day. If the condition was controlled

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after first dosing, the doses were then increased to 4 ~ 6 mg. Adult patients were administered clonazepam by an intravenous push at a dose of 3-20 mg once daily. All patients were administered maintenance therapy according to the above protocols with a gradual reduction in the dose administered (Munckhof *et al*., 2020).

The comparison group was given diazepam (Valium), and treatment protocols varied in patients. The dose for children was 0.3-0.5mg/kg, administered by intravenous push or rectal administration (0.5mg/kg for rectal administration), while the dose for adults was 10-20 mg/kg, administered by intravenous push. The patient's clinical condition was closely monitored after administration, and repeated administration was required in the case of recurrence within 15-20 min after administration.

Patients in both groups were treated for 7 consecutive days and were closely monitored during treatment to observe their clinical performance, including timely oxygen supply, effective airway management, prompt rehydration, electrolyte balance maintenance, avoidance of infection by antibiotics, and prevention of adverse reactions such as cerebral edema. Patients in both groups were followed up for 6 months after treatment and the recurrence of patients and the number of cases with recurrence occurred were recorded to calculate the total recurrence rate.

Observational indicators

The treatment efficacy, incidence of adverse effects, quality of life and recurrence were assessed and compared between the two groups after treatment and follow-up. (1) Clinical efficacy. The clinical efficacy of the two groups was evaluated by observation of the alleviation of the patients' symptoms before and after treatment and electroencephalogram (EEG) examination results. The treatment was considered markedly effective if the seizures were efficiently controlled or the episodes were reduced by more than 50% and the EEG results showed disappearance or significant reduction of discharges. The treatment was considered effective if the episodes were reduced by 30% to 50% in patients and the EEG results showed a reduction in discharges after treatment. The treatment was considered ineffective if the seizures showed no significant clinical improvement in patients, with less than 30% reduction in episodes and no improvement in discharges as shown by EEG results (H and H, 2020; M *et al*., 2020). (2) Duration of drug effect. The duration of drug effect in both groups was monitored and the mean value was calculated. (3) Quality of life. The quality of life of the patients was assessed before and after treatment, respectively, using the quality of life in epilepsy (QOLIE-31) scale and the higher the score, the better the quality of life (Qixuan and Xiaobing, 2021; Wei *et al*., 2021). (4) Adverse reactions. The occurrence of various adverse reactions in patients was observed and their types and number of cases were recorded. (5) Clinical recurrence. After treatment and a six-month follow-up, the recurrence was observed and the number of cases with recurrence was accurately recorded to calculate the total recurrence rate (CC *et al*., 2021).

STATISTICAL ANALYSIS

The statistical software SPSS 19.0 was used for data processing. The measurement data were expressed as (x±s) and analyzed using the t-test. The count data were expressed as [n(%)] and analyzed using the chi-square test. A difference was considered statistically significant at $P<0.05$.

RESULTS

Comparison of clinical efficacy

The overall effective rate of the observation group was higher than that of the comparison group ($P<0.05$). See table 2.

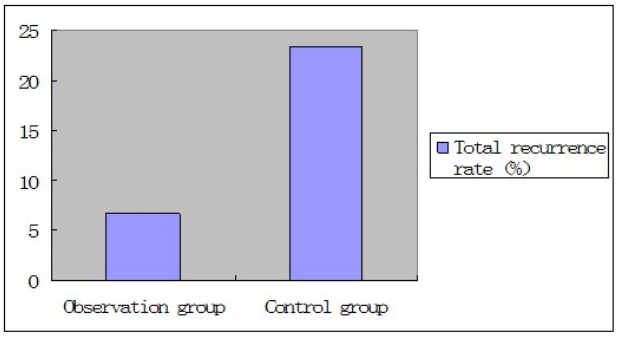

Fig. 1: Comparison of recurrence between the two groups

Comparison of duration of drug effect

The mean duration of drug effect in the observation group was longer than that in the comparison group ($P<0.05$) (table 3).

Comparison of quality of life

After treatment, the observation group had a higher quality of life score than the comparison group ($P<0.05$). As shown in table 4.

Comparison of adverse reactions

A lower incidence of overall adverse reactions was observed in the observation group than in the comparison group ($P<0.05$) (table 5).

Comparison of recurrence

All patients in both groups were successfully followed up. The overall recurrence rate in the comparison group was significantly higher than that in the observation group ($X2 = 10.8845$, $P<0.05$), as shown in fig. 1.

Table 1: Comparison of general information of two groups of patients

Groups	N	Male/female (n)	Mean age (x±s, years)	Mean course of disease (x±s, years)	Mean BMI (x±s, kg/m^2)
Observation group	30	17/13	20.89±1.01	5.23±0.17	23.71±1.17
Comparison group	30	16/14	21.05±1.03	5.19±0.15	23.82±1.20
t/X^2	-	0.0673	0.6075	0.9664	0.3595
P	-	0.7953	0.5459	0.3379	0.7205

Table 2: Comparison of clinical efficacy between the two groups

Groups	N	Markedly effective (n)	Effective (n)	Ineffective (n)	Total effective rate (%)
Observation group	30	18	10	2	93.33
Comparison group	30	10	10	10	66.67
X^2	-	-	-	-	22.211
P	-	-	-	-	0.0000

Note: The total effective rate of each group in the table is the sum of the markedly effective rate and the effective rate.

Table 3: Duration of drug effect in the two groups (X±S, h)

Groups	N	Mean duration of drug effect
Observation group	30	8.35±0.13
Comparison group	30	4.56±0.12
t	-	117.335
P	-	0.0000

Table 4: Comparison of quality of life between the two groups before and after treatment (X±S, points)

Groups	N	Before treatment	After treatment
Observation group	30	42.36±2.03	64.23±1.03
Comparison group	30	43.05±1.98	55.36±1.01
t	-	1.3327	33.6781
P	-	0.1878	0.0000

DISCUSSION

Status epilepticus is defined as a seizure lasting more than 30 min, or the occurrence of multiple consecutive seizures without return of consciousness or neurological function to normal levels during the interictal period (Arzimanoglou *et al*., 2020; Hogan *et al*., 2020). It is extremely hazardous, may elicit severe neurological damage and compromes the patient's quality of life, leading to a significant increase in the risk of focal neurological symptoms, brain atrophy, and chronic encephalopathy (Chamberlain *et al*., 2020; French *et al*., 2014; von *et al*., 2021). Accordingly, patients with diagnosed status epilepticus require effective and timely treatment to control seizures for a satisfactory prognosis (Lyttle *et al*., 2019). Currently, drug therapy is a major treatment modality for status epilepticus (Pera *et al*., 2013; Shangguan *et al*., 2015), with the emphasis of treatment on effective seizure control and active prevention of various complications and recurrence (LH, 2019; Shoucheng *et al*., 2021). Diazepam (Valium) has been extensively used in the clinical management of status epilepticus and has achieved certain effects in controlling patients' seizures (Chang-Liang *et al*., 2019). However, clinical experience has found limited effectiveness of diazepam (Valium) for status epilepticus, with a short duration of drug effect and a propensity for recurrence. Clonazepam is a highly effective tranquilizer anticonvulsant drug that is antiepileptic, with a rapid onset of action and a long duration of action (J *et al*., 2021). In recent years, clonazepam has been increasingly applied in the treatment of status epilepticus. To the best of our knowledge, clinical treatment of status epilepticus requires effective seizure control, improvement of the patient's quality of life and prevention of recurrence.

The results of this study found that the total effective rate in the observation group was 93.33%, which was significantly higher than that of 66.67% in the comparison group. The observation group had a longer mean duration of drug effect and better quality of life compared to the comparison group. It indicates that clonazepam for status epilepticus is effective in mitigating seizures and improving patient’s quality of life. In addition, the overall incidence of adverse reactions was observed to be lower in the observation group than in the comparison group in this study. The total recurrence rate in the comparison group was 23.33%, which was significantly higher than

Table 5: Comparison of the incidence of adverse reactions in the two groups

Groups	N	Respiratory depression (n)	Dizziness (n)	Nystagmus (n)	Reduced sleep (n)	Hepatic impairment (n)	Memory loss (n)	Other (n)	Overall incidence of adverse reactions (%)
Observation group	30	0	1	0	1	0	1	0	10.00
Comparison group	30	1	1	1	1	1	1	1	23.00
X^2	-	-	-	-	-	-	-	-	6.1332
P	-	-	-	-	-	-	-	-	0.0133

that of 6.67% in the observation group. Accordingly, clonazepam was found in the present study to be effective, safe and reliable in the treatment of status epilepticus. In the treatment of patients with status epilepticus, clonazepam provides a rapid onset of action when entering the body, promotes the inward flow of chloride ions in nerve cells, hyperpolarizes the cells and reduces the excitability of the patient's nerve cells to achieve seizure suppression (MG *et al*., 2021). Moreover, it maintains a prolonged therapeutic effect, which contributes to an enhanced prognosis (Yuying, 2021). Similarly, these results are in an agreement with our results.

CONCLUSION

In conclusion, the implementation of clonazepam treatment in patients with status epilepticus can better control clinical seizures, improve the efficacy and quality of life of patients, with long duration of efficacy, few adverse effects, and low recurrence rate, which is a safe and effective treatment regimen that is worthy of clinical application and promotion. The limitations of the current study lie in the small sample size and the absence of long-term efficacy studies, which may lead to bias in the results of this study. Therefore, future studies will be conducted with larger sample sizes and observation and analysis of long-term effects to obtain more comprehensive and accurate findings.

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