Dialysis Disequilibrium Syndrome after Discontinuation of Hemodialysis for a Week

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We report on a 10-year dialysis patient who discontinued hemodialysis for a week. He came to the hospital and results of examination revealed hyperkalemia and high blood urea nitrogen level. He suffered a generalized convulsion after urgent hemodialysis. Several studies were performed urgently and they showed none of the obvious variety of acute onset diseases that cause sudden consciousness impairment except dialysis disequilibrium syndrome (DDS). The day after admission, his consciousness recovered with mannitol treatment. We experienced this rare case that presented with DDS immediately after emergency hemodialysis using glycerol; moreover, this patient had inducted maintenance dialysis 10 years earlier.

Key Words: dialysis disequilibrium syndrome (DDS), reverse urea effect, urea transporter (UT), dosage calculation of glycerol, discontinuation of hemodialysis

INTRODUCTION

In 1962 Kennedy et al first reported that neurological complications in end-stage renal disease may result from dialysis procedures to remove urea nitrogen as Dialysis Disequilibrium Syndrome (DDS). DDS is known as a clinical condition at the introduction period of hemodialysis (HD) due to an acute removal of blood urea nitrogen (BUN). We experienced a rare case with a 10-year HD patient who presented DDS immediately after emergency HD despite using glycerol.

CASE

A 45-year-old male who had undertaken HD for 10...
years presented at our hospital due to extreme fatigue, because of discontinuation of HD for a week on his own judgment. His Japan Coma Scale (JCS) was 0. His body weight at admission was 66 kg (dry weight 54.7 kg), blood pressure was 180/90 mmHg, pulse rate was 68 bpm, body temperature was 35.3℃, and SpO2 was 100 percent (ambient air).

The laboratory findings on admission are shown in Table 1. An electrocardiogram at admission showed a wide QRS change and a peaked T wave. (Figure 1)

We conducted urgent HD for hyperkalemia (blood flow rate: 200 ml/min; dialysate flow rate: 500 ml/min; dialysate solution: Kindaly AF-3®; dialysis membrane: FB150U®; and, 4-hour treatment) with glycerol (50 ml/h) to prevent DDS.

Immediately after HD, his consciousness became impaired (JCS Ⅲ-200) and he suffered a generalized convulsion. We administered diazepam 5 mg via intravenous injection. The generalized convulsion was suppressed, but the impairment of his consciousness was prolonged.

In order to evaluate the cause of his consciousness impairment and the generalized convulsion, an urgent computerized tomography scan of the brain, an electrocardiogram, and a laboratory examination were conducted. These showed no signs of obvious cerebral bleeding, arrhythmia, hypoxia, hypoglycemia, hyponatremia or infectious disease. The patient did not receive any drugs, such as insulin or opioid, that could have caused impaired consciousness. The result of his BUN was 53.1 mg/dL. We strongly suspected DDS and administered a total of 300 ml of mannitol immediately.

The patient recovered consciousness with mannitol treatment the next morning. We conducted further study to identify the cause of the impairment of consciousness. The laboratory exams showed normal thyroid function and Vitamin B1 value. The brain magnetic resonance imaging showed no evidence of Wernicke’s encephalopathy. We finally diagnosed DDS. On the 6th day after admission, he was discharged without any complications.

**DISCUSSION**

The mechanism of DDS is brain edema due to an osmolar gap between brain cells and plasma. Two major mechanisms, reverse urea effect and organic osmolytes, are known to cause the osmolar gap. When the brain cells are exposed to high BUN over a period of time, the number of urea transporters (UTs) is decreased. The reduction in the number of UTs was thought to be related to the pathogenesis of DDS in the introduction period of HD. In animal experiments, mRNA expression of UT−B1 in the brain decreased to approximately 30 percent of normal at five weeks post nephrectomy. If the role of UT−B1 in the normal brain is indeed to facilitate urea transport between astrocytes and the surrounding interstitium as is reported, considerable reduction in its expression in chronic renal failure can be the cause of DDS due to brain edema. The same mechanism can apply in humans as well.

The pathogenesis of DDS in our case was very rare because he was a long-term HD patient and we used glycerol during HD. This fact suggests that discontin-
RATIONALE: The administration of HD for a week might reduce the number of UTIs, which may depend on individual differences.

We should have administered more glycerol to prevent DDS. However, as for prophylaxis of DDS, it has not yet been clarified how much or how fast glycerol should be administered. Therefore, we hypothesized a way to calculate an appropriate dosage of glycerol to prevent DDS. We can prevent DDS if we estimate the osmotic pressure of BUN that will be removed by HD, then compensate with an equal osmotic pressure of glycerol. We showed this hypothesis in the appendix. According to the calculation in the appendix, the ideal dosage of glycerol is 590 ml, but in our case we only used 200 ml glycerol.

The above calculation has several limitations. First, glycerol consists of 10% glycerin, 5% fructose and 0.9% sodium chrolide. We use all of these components in our osmotic pressure calculation. Fructose and sodium chrolide do not have the same osmotic effect as glycerin. Second, we do not consider the rate of metabolism of fructose. Third, we hypothesize that the rate of urea reduction is constant throughout hemodialysis treatment. Adjustment of the infusion rate of glycerol is needed to refine the protocol since the theory of diffusion predicts that more urea is removed in the first half of dialysis treatment. Finally, the hypothesis we applied to the calculation in our study, that theoretical Kt/V was equivalent to the Daugirdas formula, has not been validated by previous studies.

To prevent DDS, we must carefully conduct hemodialysis by low blood flow for patients who discontinue hemodialysis even for a relatively short period of time, or we should conduct continuous hemodiafiltration. As in our present case, when urgent hemodialysis for hyperkalemia, a potentially fatal condition, is being performed, we are in a fight against time. In order to reduce potassium quickly, a sufficient blood flow is needed, so this situation of treating hyperkalemia makes a reverse urea effect likely.

**Figure 1.** An electrocardiogram at admission showed a wide QRS change and a peaked T wave.
In conclusion, we experienced a case of DDS after the patient discontinued hemodialysis for a week. An acute reduction of BUN caused a reverse urea effect even in a long-term HD patient with the use of glycerol. We hypothesized a new way of calculating ideal glycerol dosage for the prophylactic care of DDS patients, but it is hypothetical theory based on only one case, so further study is indicated.

Appendix

Hypothesis to calculate an ideal dosage of glycerol to prevent DDS:

**Step 1: Estimate the Post BUN Concentration Utilizing Daugirdas Formula**

We conducted urgent HD (body weight: 66 kg; blood flow rate: 200 ml/min; dialysate flow rate: 500 ml/min; and, 4-hour treatment)

Theoretical Kt/V

\[
= (0.2 l/min \times 240 min) / (66 kg \times 0.6) = 1.21
\]

We knew the figure for the BUN before HD was 140.2 mg/dL. We can therefore calculate the figure for BUN after HD utilizing theoretical Kt/V and the Daugirdas formula. Daugirdas et al showed that theoretical Kt/V correlated with postdialysis to predialysis BUN ratio.

Daugirdas Formula: Kt/V

\[
= -1.18 \ln \left( \frac{\text{BUN Post}}{\text{BUN Pre}} \right)
\]

\[
1.21 = -1.18 \ln \left( \frac{\text{BUN Post}}{140.2} \right)
\]

We can get the BUN Post, 50.2 mg/dL, by solving the above equation.

**Step 2: Presume the Osmotic Pressure of BUN Which is Removed by HD**

The theoretical removal of BUN concentration by HD is 90 mg/dL (140.2 mg/dL – 50.2 mg/dL). Our total body water (TBW) is estimated by body weight × 0.6, so this patient’s TBW is 39.6 l (66 l × 0.6 = 39.6 l).

Utilizing TBW, we know the total amount of removed BUN by HD.

The total amount of removed BUN by HD is 35640 mg (90 mg/dL × 39.6 l × 10). We can translate 35640 mg into osmotic pressure of BUN utilizing the molecular weight of urea nitrogen, which is 28.

The osmotic pressure of BUN, which is removed by HD is 1273 mOsm (35640 mg/28 = 1273 mOsm).

**Step 3: Calculate the Appropriate Dosage of Glycerol**

The calculated osmotic pressure of glycerol is about 2156 mOsm/L. In order to compensate for the 1273 mOsm, which is removed by HD, 0.59l of glycerol is needed (1273 mOsm/2156 mOsm/l = 0.59l); therefore, 0.59l of glycerol is the appropriate dosage of glycerol to prevent DDS during HD.

**General Formula for Ideal Glycerol Speed:**

\[
\text{Ideal glycerol speed (ml/h)} = 0.1 \times \frac{1}{\text{time (h)}} \times \text{BW (kg)} \times \text{BUN Pre (mg/dL)} \times \left[ 1 - \frac{1}{e^{\text{Qb (ml/min)} \times \text{time (h)} / 11.8 / \text{BW (kg)}}} \right]
\]

Time (h): HD period
BW (kg): Body weight, before HD
BUN Pre (mg/dL): BUN concentration level, before HD

**References**


