Case Study: Hyponatremia Post IVIg Infusion

Case study

Mr. L, a 61-year-old male, is a retired air-craft mechanic. He has history of pulmonary sarcoidosis, coronary artery disease with quadruple bypass in 2012, hypertension, hyperlipidemia, and sleep apnea which requires continuous positive airway pressure (CPAP) mask at night.

From April 23, Mr. L developed “flu” like symptoms, and severe diarrhea for 5 days, from which he lost 12 pounds. On May 7, when he woke up, he experienced weakness on his upper limbs and unsteady gait. His upper and lower limbs weakness progressed rapidly and he was unable to ambulate without assistance on May 10.

Mr. L was admitted to a neurology unit, on examination, he had more severe motor weakness in distal (0-1/5) compared to proximal (3/5) on his hands and feet. He needed assistant for stand and unable to walk. He had no facial or bulbar weakness, no diplopia, dysarthria, or dysphagia, and all sensation was intact. CT scan of head did not show any anomalies, and cerebrospinal fluid from lumbar puncture result was protein 0.33g/L (normal 0.15-0.45g/L), white blood cell 1X10^9/L (0-5 X 10^9/L), red blood cell 0 (0 X 10^9/L), and glucose 4.6mmol/L (2.2-3.9mmol/L). His stool culture result was positive for campylobacter jejuni. According to laboratory results and presentation, he was diagnosed with acute motor axonal polyneuropathy (AMAN), a subtype of Guillain-Barré syndrome (GBS).

After the diagnosis was made, a course of IVIG (0.4mg/kg/day for 5 days) was ordered. Other management included force vital capacity (FVC) every 8 hours, low molecular weight heparin for deep venous thrombosis prophylaxis, erythromycin for campylobacter jejuni infection, gabapentin (neurontin) and morphine for pain control. Patient’s vital signs, neurological assessment, and FVC were stable.

On May 14, Mr. L’s serum laboratory results were Na+ 131mmol/L, K+ 4.1mmol/L, Cl− 97mmol/L, and stool sample for campylobacter jejuni remained positive. On May 16, after 5 doses of IVIG, his serum results were Na+ 113mmol/L, K+ 4.6mmol/L, glucose 8.2mmol/L, urea 4.8mmol/L 116mmol/L, and serum osmolality 244 Osmol/kg with an osmolar gap 5. Osmolar gap is the difference between the calculated serum osmolality and measured serum osmolality. Mr. L had developed severe hyponatremia.

Normally, when serum osmolal gap > 10 pseudohyponatremia is considered. Mr. L was still diagnosed with post IVIG pseudohyponatremia even his osmolar gap is only 5. It is because he was also diagnosed with hypovolemia. Clinical examination of Mr. L showed decreased jugular venous pressure (JVP) and his fractional excretion of sodium (FeNa) was only 0.12% (< 1% is considered pre-renal issue, decreased perfusion to the kidneys, or hypovolemia). That means, even with the significant smaller water phase of plasma (see below pseudohyponatremia explanation), the calculated serum sodium is still below normal. If the plasma water phase is re-expended, the serum sodium concentration will be further decreased. To correct Mr. L’s hypovolemic state, continue infusion with saline water 0.9% (normal saline) 250mL/h was commenced.

Mr. L’s serum sodium gradually increased to 130mmol/L over several days. On May 26, his intravenous fluid was reduced to 150mL/h. His motor powers remain very weak and unable to ambulate without assistance. The normalization of his serum sodium concentration may be related to metabolism of the intravenous immunoglobulin G (IVIg) (half-life 18 – 32 days) (Dalakas, 1998), re-expenditure of the water phase of plasma, and infusion of sodium chloride.

Definition of Pseudohyponatremia

Pseudohyponatremia is defined as decreased calculated osmolality or elevated osmolar gap resulted from hyperproteinemia (Tarcan, Gökmen, Dikmenoğlu, & Gürakan, 2005).

Epidemiology

Fourteen percent of patients developed hyponatremia post IVIg infusion (Colls, 2003).

Pathophysiology

Intravenous infusion of immunoglobulin may result in pseudohyponatremia or true hyponatremia.

Normally, 93% of the plasma volume is water (aqueous phase) and the remaining 7% is protein and lipids. Sodium (Na+) ions are only present in plasma water (Nguyen, Rastogi, & Kurtz, 2006). Commercially prepared IVIg is obtained from a pool of 3000 to 10000 donors. The extracted immunoglobulin is stabilized with glucose, maltose, glycine, sucrose, mannitol, or albumin (Dalakas, 1998). After IVIg infusion, the extra protein content in the IVIg decreases the relative percentage of aqueous phase of plasma. Normal laboratory test for serum Na+ measures the Na+ in the aqueous phase of serum. The decreased percentage of water in
serum gave a “false” value of serum Na⁺, which presented as pseudohypo-natremia (Nguyen, Rastogi, & Kurtz, 2006).

### Normal percentage of protein and water in plasma

Normally, in one liter of plasma, 93% volume (930mL) is water and 7% volume (70mL) is protein and lipids. If the Na⁺ concentration in the water portion of plasma is 148mmol/L, the Na⁺ concentration of plasma (total volume of water and protein) will be 137.64mmol/L.

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(148\text{mmol/L} \times 930\text{ml}) \div 1000\text{mL} = 137.64\text{mmol/L}
\]

### Percentage of protein, IVIg, and water volume in plasma post IVIg infusion

For the same patient, after IVIg infusion, the IVIg occupied part of the volume of the aqueous phase of plasma. Even the Na⁺ concentration in the aqueous phase of plasma remain the same (148mmol/L), the Na⁺ concentration of the total volume of plasma [plasma water (870mL) + IVIg (60mL) + protein (70mL)] will be decreased to 128.76mmol/L.

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(148\text{mmol/L} \times 870\text{ml}) \div 1000\text{mL} = 128.76\text{mmol/L}
\]

True hyponatremia may also be resulted from administration of IVIg. The extra components (glucose, maltose, glycine, sucrose, mannitol, or albumin) in the commercial prepared IVIg are hypertonic, after infusion, it increases serum osmolality and promotes the translocation of water from intracellular space into extracellular space (including intravascular space). In addition, the commercial prepared IVIg contains a large volume of water. These two factors cause the hemo-dilution effects and result in true hyponatremia (Nguyen, Rastogi, & Kurtz, 2006).

Pseudohyponatremia is suspected when there is an elevated osmolar gap (>10mOsmol/L), that is the difference between measured (measured with osmometer) serum osmolality and calculated (2 Na + 2 K + Glucose + Urea) serum osmolality (Steinberger, Ford, & Coleman, 2003; Tarcan, Gökmen, Dikmenoğlu, & Gürakan, 2005).

### Treatment

It is essential to differentiate pseudohypo-natremia from true hyponatremia when determining treatment options. In true hyponatremia, restriction of fluid intake is indicated, whereas in pseudohyponatremia, fluid restriction may lead to volume depletion and may further increase serum viscosity and predispose to thromboembolic events (Tarcan, Gökmen, Dikmenoğlu, & Gürakan, 2005).

### Nursing Implications

Significant hyponatremia is a common complication post IVIG infusion. It is one of the indicators for poor prognosis in patients with Guillain-Barré syndrome (Colls, 2003; Steinberger, Ford, & Coleman, 2003). Close monitoring is required for complications from hyponatremia such as fatigue, muscle weakness, confusion, headache, tremors, hyperreflexia, convulsions, nausea & vomiting, abdominal cramps, and diarrhea. Also monitor for signs of deep venous thrombosis such as pain, redness, and edema on the lower extremities, and low grade fever.

### Highlight of the case study

Acute motor axonal polyneuropathy is not common in North America. It only affects the motor function while the sensory function is intact. Patients diagnosed with AMAN usually have good recovery. On June 2, Mr. L starts to have some control and movement of his fingers.

Infusion of Ig is a common treatment for patients with GBS. Mild hyponatremia is common post IVIG infusion. Severe hyponatremia presented in this case study is uncommon. It was related to the hypovolemic state of the patient. Careful fluid and electrolyte replacement and close monitoring with patient’s fluid intake and output balance, and serum electrolyte concentration can prevent complications from the pseudohyponatremia.
Reference

More information on “Guillain-Barré syndrome” can be accessed from: [www.neuro4nurses.com](http://www.neuro4nurses.com).

Post Reading Quiz
1) Guillain-Barré syndrome affects which part of the nervous system?
   a) Cranial nervous
   b) Peripheral nervous system
   c) Central nervous system
   d) Autonomic nervous system

2) Neuropathic pain is better controlled by which group of medications?
   a) Opioid
   b) Non steroid anti-inflammatory agent
   c) Anti-epileptic agent
   d) Gamma aminobutyric acid (GABA)

3) What is the change in plasma composition after IVIG?
   a) Decreases plasma volume
   b) Increases plasma water phase
   c) Decreases plasma cell volume
   d) Increases plasma protein content

4) What is the reason for increased risk of deep venous thrombosis post-IVIG pseudohyponatremia?
   a) Increases blood viscosity
   b) Increases clotting factors
   c) Decreases blood flow rate
   d) Decreases plasma volume

5) What are the signs and symptoms of hyponatremia?
   a) Hyporeflexia, nausea, headache
   b) Diplopia, vomiting, hyperreflexia
   c) Abdominal cramp, agitation, fatigue
   d) Muscle weakness, seizure, tremor

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