

# Dysautonomia complicated by DDAVP use for diabetes insipidus

## Abstract

This is the case of a normal, healthy 42-year-old woman who sustained injuries in a spinning motor vehicle accident, leaving her with a series of diagnoses including Dysautonomia, that stumped all doctors. Because she was a Stanford-trained anesthesiologist and intensivist, she was able to self-diagnose several major illnesses, including traumatic brain injury (TBI), diabetes insipidus (DI), vertebral artery dissection (VAD) with aneurysm, oculo-vestibular dysfunction, and hypothyroidism. The DI required prescription DDAVP therapy to prevent dehydration and death. Here, we focus on the entities of the “see-saw” effect that DDAVP has on Total Body Water (TBW), hyponatremia, hypernatremia, and the complications arising from the chronic, underlying hypovolemic state of dysautonomia. Dysautonomia, an “Invisible Illness” causing dysfunction of the autonomic nervous system, is a frequently undiagnosed, hypovolemic state that can lead to syncope. The best-case scenario is to titrate the DDAVP clinically with a tendency to under rather than to over-dose, preventing hypervolemia and hyponatremia. One can also provide ambient temperature and avoid overheating, consider insensible water loss, allow the pituitary gland healing, prevent further falls or head injuries, and recognize when it is time to go off the DDAVP. There are a paucity of scientific data on DI, and its incidence is rare with coincidental dysautonomia. These entities need to be appreciated and diagnosed, especially when they occur simultaneously. The patient is in a precarious position of dying from either too much TBW (i.e., hyponatremia, brain swelling, orbital swelling) or from too little TBW (i.e., decreased glomerular filtration rate, need for dialysis, death, and the need for fluid resuscitation that can also lead to death). Let us learn in a step-by-step fashion.

## “Brittle” Dysautonomia complicated by DDAVP after Post-Traumatic Diabetes Insipidus

**Keywords:** dysautonomia, traumatic brain injury, diabetes insipidus, post-traumatic diabetes insipidus, total body water, ddavp, hypovolemia, hyponatremia, hypernatremia

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**Abbreviations:** TBI, traumatic brain injury; DI, diabetes insipidus; TBW, total body water; DDAVP, deamino-8-d-arginine vasopressin desmopressin; VAD, vertebral artery dissection; PICC, percutaneous intravenous cutaneous central; PTSD, post-traumatic diabetes insipidus; SUV, sports utility vehicle; MRI, magnetic resonance imaging; CT, computed tomography; Im, intramuscular; BUN, blood Urea nitrogen; Cr, creatinine; Cl, clearance; GFR, glomerular filtration rate; IV, Intravenous; ER, emergency room

## Introduction

Traumatic brain injury has been associated with pituitary gland dysfunction and a ‘knock-out’ of the normal reflex arc from the hypothalamus (i.e., ‘higher’ center) to the posterior pituitary gland, such that it no longer “listens” to stimuli telling it to “stop urinating.” Hence, the net effect is that the patient presents with polyuria (i.e., production of too much urine) and polydipsia (i.e., extreme thirst and constant drinking of fluids) that can never “catch up” to the Total Body Water (TBW) losses. Electrolyte disturbances, mental fog, dehydration, renal failure, seizures, coma and death will ensue without intervention. Traditionally, this occurs in teenagers who do not recognize the symptoms as being a problem. They are simply found dead in their beds.

The state-of-the-art treatment is DDAVP prescription drug, taken both day and night, to prevent polyuria. This is one Case Report that illuminates the need for patient diagnosis, consideration of confounding variables, and forethought to treat “overtreatment,” should it occur. In probably the most common situation, the patient is given too much DDAVP, holds on to too much TBW, develops “water-balloon brain” and “water-balloon eyeballs,” may be hyponatremic down to 127mcg/ml. On the opposite spectrum, a patient given too little DDAVP will continue to have polyuria, developing hypernatremia perhaps to the tune of 155mcg/ml.

Either way, the brain undergoes massive microscopic and macroscopic intra- and extra-cellular water changes that greatly influence the quality of life of the patient. When all this occurs in a patient with Dysautonomia who is also taking prescribed Midodrine hydrochloride as a vasopressor to increase blood pressure, so (s) he can stand without syncope, confounding variables exist: the medication used to increase the blood pressure, salt intake, the use of Jobs® stockings, and an abdominal binder. Herein lies a comprehensive Case Report that builds layers upon layers of information, in the hopes that should the clinician encounter a patient with Dysautonomia, the treatments for traumatic brain injury (TBI) with diabetes insipidus (DI) are not worse than the syndrome, Post-Traumatic Diabetes Insipidus (PTDI) itself.

## Case presentation

In retrospect, it was determined that the patient's SUV was T-boned and as she underwent a spinning torque injury of the brain and neck; her daughter in the back seat remained well. Initially, the patient presented with sun poisoning from waiting for all ambulances and fire trucks to clear the scene in Malibu, California. Then she began sleeping all day, for day after day. She saw her Primary Care Physician on Day #1 after injury, with normal head and neck x-rays. She was sent home.

She continued to sleep profusely, and then lost her concentration. For example, she went north on the 405 freeway to pick up someone at the airport, when she knew she had to go south. She stopped her husband and made him sit down to listen to her worries. He agreed to accompany her to all future doctor visits. In the interim, she became severely ataxic, was tripping on the dogs, tripping over home flooring leftovers, and almost lunged into the 11-foot emptied pool that was being remade. This is when she sought help from a neurologist.

After about two months, a head and neck MRI with contrast was negative. She continued to present to the Emergency Room for headaches, vomiting, ataxia, and confusion. During one admission, the ER doctor ordered a spiral CT scan that showed a vertebral artery dissection (VAD). She was taken by ambulance to a major medical center, where an angiogram confirmed a VAD from C3-5, Extracranial, with a 2cm aneurysm at the base. Treatment can include stent placement<sup>1</sup> and the cause of death for most patients is cerebral clotted stroke, so she was placed on a platelet-inhibitor (e.g., Plavix®) and an anti-lipid drug (i.e., Lipitor®). She underwent a month of neurorehabilitation at a large institute, where she slowly learned how to walk and talk again. At the time of discharge, she still required follow-up speech, occupational, and physical therapy sessions as well as nurse visits for her 3year long stint with a life-saving PICC line. She remained wheel-chair bound for threeyears, and has been nearly non-ambulatory for almost 10years.

Eventually, she graduated to a walker and then to a cane. When she almost tripped on the cane, she threw it away. She was recuperating over time until approximately March of 2014, when a neurologist thought that she was "malingering" and let her fall to the hard wood floor unobstructed, during Clinical Examination, while her eyes were closed. She has no proprioception, so she fell, once again suffering the 2<sup>nd</sup> PTDI. After using a walker for two moreyears, she began to develop more stamina, becoming a Patient Advocate and author.

Both bouts of DI presented with dry mouth, polyuria, and polydipsia despite attempts to keep fluid intake up. When it was clear to the physician: patient that "something was wrong," she presented to her Cardiologist and both times, was admitted to the hospital.

On the first PTDI diagnosis, she was not dehydrated, so she was given the Water Deprivation Test for over 4hours, during which time she had almost 5liters urine output. Urine output slowed to a screeching halt with a dose of IM DDAVP. So she went home with SQ DDAVP, and took it twice/day. The patient diagnosed DI resolution when she had 500 cc dark yellow urine output in the morning, with decreased frequency of urination around-the-clock. Her doctors confirmed this.

On the second bout of PTDI after the fall, the onset was insidious, perhaps 2weeks after the event. It was a hot summer, and she had much insensible water loss. She first used the nasal spray DDAVP at night and a po dosage by day. As time progressed, she weaned herself

to small inhaled doses, the last one at bedtime. Eventually, she used inhaled DDAVP by night and po DDAVP by day. She weaned off of DDAVP by following weight gain + 2 lbs/day, volume of 'light colored' vs. 'dark colored' urine, and clinical onset of thirst. Both times, she was able to wean off DDAVP in 6months time.

## Discussion

### Dysautonomia

This is a hypovolemic illness whose cause is generally unknown or hereditary, and whose symptoms range from gradual to severe onset. Other names for Dysautonomia include Familial Dysautonomia, Autonomic Dysfunction, Orthostatic Intolerance, and Riley-Day Syndrome. There is no cure for Dysautonomia, but supportive measures (i.e., medications, fluids, salt, abdominal binder, Jobst® stocking thigh-highs, Spanx®) can temper clinical symptoms for improved quality of life. Prognosis is variable, dependent on etiology, with underlying nervous system degeneration often leading to a poor prognosis. In this case, death is often due to acute respiratory failure, aspiration pneumonia, or cardiopulmonary arrest. Helpful resource organizations include the NIH Recruitment for Dysautonomia Clinical Trials, Supportive Organizations, and free publications.<sup>2</sup>

**Lifestyle:** Typically, the lifestyle scenario for a patient with Dysautonomia involves:

- Aggressive fluid intake: this patient required a PICC line for over threeyears to sustain life;
- Dietary changes: increased salt, "immunosuppression" meals and fish oil;<sup>3</sup>
- Compression wear: Jobst® stockings, thigh high; abdominal binder or Spanx® wear;
- Pharmacologic treatment with vasopressors and/or steroids, and/or salt supplementation; includes flucortisone, midodrine, salt tablets, Medrol dose pack, DDAVP, and oral desmopressin;
- Lifestyle modifications and decreased insensible TBW loss: divert the patient away from an overheated, sunny climate that would lead to either sun-poisoning (i.e., sun allergy including anaphylaxis, tongue and throat swelling) heatstroke (i.e., fever, unconsciousness, failure of central, brain-mediated temperature control so that overheating occurs), or over breathing hot air (the lungs have a surface area the size of half of a tennis court, between 80 -100m<sup>2</sup>).

**Patient complaints:** The average patient with dysautonomia suffers the following:

- Dehydration: frequent trips to the ER requiring fluid boluses of 0.5% Normal Saline over 1-2;
- Physician incompetence: as put by many patients, "Don't tell me how to live my life when you can't even spell the name of my illness."
- Self-education: just as with the Stanford-X Medicine (Stanford Medicine-X, 2016) program, patients learn from other patients, who then become 'teachers' of newly diagnosed patients; and proudly brand themselves as a "health care rebel;"
- Accusations of Malingering: Just because the doctor never heard of it, the patient is treated as if (s) he is faking an illness for drug-

seeking behavior, illicit pursuits or malingering because she is a “drug addict;” this can have devastating psychological sequelae on the patient, and is a frequent patient experience; hence Dr. Aranda drew up a Change.org Petition for more physician education for all “Invisible Illnesses”.<sup>4</sup>

- v. Anxiety, Depression, Suicide: Some patients reach “the end of the rope” when no validation of their disease can be found. Usually, the patient’s family is making fun of the patient, who seeks doctor after doctor consult, only to be told, “It’s all in your head.” This is the crux of the failure of the medical systems worldwide, and it can be remedied with increased medical school and physician knowledge that includes other “Invisible Illnesses” as well.
- vi. Bed-ridden status: Since ‘gravity is the enemy,’ most patients feel comfortable and safe simply living from bed or a chair, without driving or walking into stores or family gatherings. The fear or the realistic occurrence of nausea and then vomiting is an ever-present threat, leading to social isolation, loneliness, anxiety, depression, social cruelty and more.

### Traumatic brain injury

The patient’s TBI was first diagnosed after memory loss, headaches, and fatigue that left her sleeping for a good portion of the day. On a finer level, she was found to have difficulty expressing specific nouns, often-times replacing them with another noun (i.e., expressive aphasia) and losing her train of thought when not allowed to complete a sentence (i.e., derailing). She also had cognitive difficulties. These are common indicators of a head injury.<sup>5</sup>

**Incidence and prevalence:** TBI is primarily due to car accidents (50%), violent head trauma (20%), and 10% are due to sports injuries. Head violence is highest in people ages 15-24. In the very young, TBI can be due to Shaken Baby Syndrome, child abuse, or it is unintentional (75%). Alcohol is reported to be involved in 50% of all TBI.

- a) Men are 2X more likely to get a TBI than females.
- b) The incidence is 10-100/100,000 people.
- c) The death rate per year is 52,000, and TBI is the leading cause of disability in children and young adults.
- d) Prevalence at any given moment is about 2.5 to 6.5million patients, not considering those with undiagnosed, mild brain injuries due to sports. Since there appears to be no end in sight for car accidents, head violence, or sports injuries, the “prevention” of TBI seems moot, and the NIH Consensus Statement of 1998 focused on the rehabilitation and interventions aimed at improving quality of life and improved brain function after TBI occurred<sup>6</sup> so as not to further disrupt or strain the medical health system. Their conclusion was that TBI is a major disorder with significant public health consequences, as those who survive appear to be “taxing” on “the system.”
- e) TBI research needs to be improved on larger populations of patients, to have an impact.
- f) Family members report depression, anger outbursts, and social isolation, with marital separation and divorce taking its toll on both the children and the legal system.

**Costs:** It is most likely that the economic costs of TBI will never be able to be measured, given the undiagnosed TBIs, lost wages, lost

pension plan contributions and Social Security adjustments, and the value of the family or paid Caregivers for the patient with TBI. The 2008 annual estimate of both acute and chronic rehabilitation in the USA was \$9-10billion. The average lifetime costs per patient may be from \$600,000 - \$1,875,000.<sup>6</sup>

### Diabetes insipidus (DI) and post-traumatic DI (PTDI)

DI is caused when a TBI causes impact to the brainstem, decreasing antidiuretic hormone (ADH), or vasopressin secretion from the supraoptic nuclei of the hypothalamus. When caused by Post-Traumatic Brain Injury, the DI is currently reclassified as “Post-Traumatic DI,” or PTDI. While TBI alone is associated with a high mortality, the addition of PTDI adds additional mortality, especially when occurring very soon after the TBI.

The decreased ADH production can be either from decreased secretion (i.e., central, or neurogenic, or psychogenic DI) or decreased action (i.e., nephrogenic DI). Causes of DI that affect the hypothalamus and the posterior pituitary axis include: brain surgery, TBI, brain tumors, pituitary gland tumors, infections such as meningitis, aneurysms, and more.<sup>7</sup> As with this patient, the most common presentation is a poor general status, severe dehydration (BUN/Cr=108/54), hypotonic polyuria, and hypernatremia (Na=155mEq/ml).

In surviving patients, the PTDI is only there for days or weeks. Only in a small number of cases is it permanent. If not treated with fluid resuscitation, then dehydration and renal failure are imminent. This can be seen by dilute polyuria, hypernatremia, hypovolemia, hypotension, low cerebral perfusion pressure, low platelet quantity (n=30,000) and quality (patient is on Plavix®), with a glomerular filtration rate (GFR) of 30% and a platelet count of 30,000.

Severe water and electrolyte imbalances occur if a timely diagnosis is not made.<sup>8</sup> If (acute) hypervolemic hyponatremia occurs over 24-48 hrs, this is more dangerous than (chronic) hyponatremia that develops over days or weeks. This is an emergency medical situation that needs to be swiftly treated. If the patient’s PTDI is severe, one may simply suspend all IV drips, allowing the PTDI to “declare itself” gradually, over time, with increased urine output and increased TBW loss. Although painful to the patient, seemingly with prolonged agony, this author does not believe that 5% NS is a viable solution for the patient, who is in a hypervolemic state. The patient has the clear sensation that one’s brain and eyes are about to burst, and adding more fluid to “fix” a (Na) “number” is not clinically sound in this scenario. The risk of uncal herniation and death are too great.

**Hypernatremia:** confusion, loss of orientation, hyperreflexia, lethargy, seizures, and then coma, and death.<sup>9</sup>

**Hyponatremia:** confusion, restlessness, muscle cramps or weakness, fatigue, irritability, headache, bloated eyes, loss of appetite, nausea, vomiting, and then convulsions, hallucinations, decreased consciousness, coma, brain herniation, and death.<sup>10</sup> Hyponatremia can be one of 4 types: dilutional hyponatremia, euvolemic hyponatremia, hypervolemic hypernatremia or hypovolemic hyponatremia.

**Brittle dysautonomia:** All of this hyper/hyponatremia and hypo/hypervolemia is exacerbated in the patient who also has an underlying diagnosis of hypovolemic dysautonomia, with small changes in water intake/output resulting in large changes in the “brittle” nature of the dysautonomia. The patient may have more syncope, palpable tachycardia, a sensation of cardiothoracic autonomic stimuli, increased shortness of breath even at rest, and a general feeling that

the dysautonomia is now “Brittle,” with more severe or frequent symptoms. Small changes in DDAVP dosage result in both large clinical symptoms that are uncomfortable, painful, or put the patient in great fear of death, and result in electrolyte variability that is not conducive to a steady and slow progress in the right direction.<sup>11</sup>

“Which drug to take next?” becomes the endless question of each of the multiple days, weeks, and months ahead?

### Pharmacology, physiology and real life

First, we will lay out all the drugs/pills before you, and then we will decide which one(s) to take at different times of the day, depending on present urine output, body weight+2 lbs, the sensation of thirst, the last dosages of drug(s) taken, amount and color of urine, and the way that the patient’s ring on her right ring finger fits her right hand.<sup>12</sup>

**Fludrocortisone (Florinef®):** is on the list of the World Health Organization’s List of Essential Medicines<sup>13</sup> have a molecular mass of 380.45g/mol and a formula of C<sub>21</sub>H<sub>29</sub>FO<sub>5</sub>. The plasma t<sub>1/2</sub> is 3.5hr, and the biological t<sub>1/2</sub> is 18-36hr. It is absorbed from the GI tract with a Tmax of 1.7hr; metabolism is in the liver.<sup>14</sup>

The first line of therapy for dysautonomia is usually fludrocortisone acetate, tablets 0.1 mg po/day. Interestingly, many patients with dysautonomia are prescribed this drug on a long-term basis for orthostatic hypotension; hence, one side effect is hypertension. Other side effects include bruising, sweating, hives, and rash.

Many patients are placed on steroids not only for dysautonomia, but also for brain swelling after TBI, and for PTDI itself.

**Midodrine hydrochloride (Orvaten® and ProAmatine®):** Midodrine has a chemical formula of C<sub>12</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub> and a molecular mass of 254.282g/mol. It is a prodrug, whose active metabolite is desglymidodrine, the α<sub>1</sub>-agonist that activates α-adrenergic receptors on both arteries and veins, causing constriction and higher blood pressure. The cardiac β-adrenergic receptors do not participate in this response and diffusion across the blood: brain barrier is poor. Midodrine lasts about 4hr; adults may take it up to 3times/day. The prodrug peaks at about 30minutes; the metabolite reaches peak concentration at 1-2hr with a half-life of about 3-4hours. The metabolite is 93% bioavailable, and neither form binds to proteins.<sup>15</sup>

Midodrine tablets come in scored pills, in these doses: 2.5mg, 5.0mg, and 10.0mg.

With renal insufficiency, decrease dose to 2.5mg if CrCl is <80ml/min; adjust from there. With liver dysfunction (causes deglycation of midodrine to desglymidodrine, and partially metabolizes both compounds): “use with caution.” Which may really say, “Don’t use.”

Common side effects: Initially, scalp burning to the point where some patients pick at scabs on their head (may last for months or 1-2years); urinary retention or frequency, so beware if you already are incontinent; dry mouth which can contribute to stroke and cardiac disease leading to death (so watch dental hygiene); anxiety; confusion; syncope; dizziness; bradycardia (Drugs, 2016). Because desglymidodrine does not cross the blood: brain barrier, there are no central nervous system effects.

Since midodrine results in supine hypertension, it is recommended that the last dose not be taken after 1800, nor if the patient is going to take a nap. To increase patient safety, it is wise to ask this question

before taking Midodrine Rx: “Is this patient going to get up and walk?” If the answer is “Yes,” then proceed. If one asks the question, “Is this patient going to take a nap?” and the answer is “Yes,” then do not give that dose of Midodrine, or you risk giving the patient a hypertensive stroke during sleep. The patient was already taking life-long midodrine vasopressor for syncope caused by Dysautonomia.

This patient was taking 15.0mg q AM. She always took a 3-4hr nap in the early afternoon, then awakening at 1600 and taking the second dose of 10mg in the afternoon. She then stayed awake until 2300 or 0300.

**Desmopressin acetate (DDAVP® Injection):** This is a man-made formulation of a pituitary hormone that comes in an injectable liquid at 4mcg/ml, synthetic 8-arginine desmopressin. Desmopressin oral pills can come in 0.1 mg or 0.2mg doses. Its molecular weight is 1183.34 with an empirical formula of C<sub>46</sub>H<sub>64</sub>N<sub>14</sub>O<sub>12</sub>S<sub>2</sub>.C<sub>2</sub>H<sub>4</sub>O<sub>2</sub>.3H<sub>2</sub>O and 1mg contains 4.0mcg desmopressin acetate, 9.0mg sodium chloride, and hydrochloric acid to adjust the pH to 4.0 for injection. Chlorobutanol preservative 5.0mg/ml is used per 10ml vial. IV DDAVP has 10X the antidiuretic effect of an equal dose administered by nose. DDAVP undergoes renal excretion, and comes in IV, SQ, oral po, and oral lyophilisate forms (which melt in the mouth).<sup>16</sup>

Nasal DDAVP is subject to a variety of absorption factors that make the net dosage delivered of some question. The absorption is poor, nasal congestion can block absorption, nasal mucosa can atrophy, and severe atrophic rhinitis may result. For patients on concomitant blood thinners, epistaxis can also result from nasal DDAVP.<sup>17</sup>

DDAVP injection is used for patients with mild-to-moderate von Willibrand’s disease (Type I), with Factor VIII levels >5%. It can be administered 30minutes prior to a surgical procedure, and postoperatively. DDAVP is not indicated for classic von Willibrand’s disease (Type I) when there is an abnormal molecular form of Factor VIII antigen. DDAVP is also used for central, AKA psychogenic diabetes insipidus (i.e., PTDI) after head trauma or surgery near the pituitary gland. It is *not* used for nephrogenic diabetes insipidus.

DDAVP is contraindicated with a CrCl<50ml/min, and in patients with hyponatremia or a history of hyponatremia, as rare cases of potentially-fatal water intoxication have been reported. DDAVP may lead to a transient fall in blood pressure and a compensatory increase in heart rate, aggravating heart disease. Use with caution in any patient with electrolyte disorders (i.e., cystic fibrosis, renal disorders, cardiac failure), as these patients have a propensity toward hyponatremia.<sup>18</sup>

**Andidiuretic hormone (ADH), vasopressin, arginine vasopressin, AVP for CPR:** Produced in the posterior pituitary gland, the molecular formula for vasopressin is C<sub>46</sub>H<sub>65</sub>N<sub>15</sub>O<sub>12</sub>S<sub>2</sub>; its molecular weight is 1084.2316 Dalton. All these peptides consist of a sequence of nine amino acids: Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly-NH<sub>2</sub>. The cysteine residues form a disulfide bond. It is structurally similar to oxytocin, which differs by two amino acids. The two genes are on the same chromosome, and the similarity of the two peptides can cause cross-reactions. This is why pregnant women who are pre-term can be given fluids for dehydration for false labor from oxytocin secretion. The body “sees” ADH as oxytocin, beginning uterine contractions.

Not to be confused with desmopressin, (i.e.,) vasopressin has been studied in the following scenarios (not meant as an all-inclusive list (Table 1).

**Table 1** History of Vasopressin in Cardiopulmonary Resuscitation. Not to be confused with desmopressin or DDAVP, vasopressin has been used in the ACLS protocol for resuscitating patients in cardiac arrest. Looks like Vasopressin is here to stay

Diagnosis	Authors	Year	Outcome
Septic Shock, 2nd line therapy to massive fluid resuscitation, in hospital	Stiell, et al. <sup>19</sup>	2001	Not effective.
Decreased vasopressin effectiveness of repeated doses during CPR(Out-of Hospital)	Mukoyama, et al. <sup>20</sup>	2009	Vasopressin vs. vasopressin+epi= comparable.
Cardiopulmonary Resuscitation, Effective in ACLS Protocol	Neumar, et al. <sup>21</sup>	2010	Accepted use.
Acidotic Cardiopulmonary Arrest: Return of Spontaneous Circulation (In-Hospital)	Turner, et al. <sup>22</sup>	2014	No change in hospital discharge.
Combination Vasopressin-Epinephrine	Ghafourian, et al. <sup>23</sup>	2015	May be useful.

for Patients with Cardiac Arrest(Out –of Hospital)

ADH, anti-diuretic hormone; CPR, cardiopulmonary resuscitation

**Patient outcome:** The patient had been on fludrocortisone long-term before, but did not like the skin thinning/bruising. Due to her dire circumstances, though, she was discharged on fludrocortisone tablets from both admissions for PTDI. She stopped taking fludrocortisone after one month.

The patient was given SQ DDAVP Rx during and after her first hospitalization for PTDI. Upon discharge, she was instructed to dose herself in the abdomen. After months went by, her entire abdomen was bruised and purple, and each SQ injection left a welt, like a bee sting. It took about five years for these welts to disappear, and the patient opted for nasal or po vasopressin therapy thereafter, to treat the second episode of PTDI. She was taken off the SQ DDAVP only after presenting after the PTDI had resolved, unbeknownst to her.

On the second case of PTDI, the patient was given intranasal DDAVP for the evenings, so as not to awaken during the night to urinate. During the day, she was given po desmopressin. She suffered multiple bouts of either hypovolemic hypernatremia and near-renal failure, or hypervolemic hyponatremia and the feeling of impending uncal herniation. The “Brittle Dysautonomia” had been severely affected by the PTDI, and fluid management was the priority of the day. The following clinical signs far outweighed the need to go in for serum Na checks over days, weeks, and the impending months:

- Daily body weights in the morning;
- How the same ring fit on the same finger each day;
- color (i.e., “Lasix® pee” that was clear, vs. dark yellow urine);
- Urine volume;
- Increased salt and electrolyte intake, especially Ca, K, and Mg;

The patient was successfully able to wean herself off the nasal spray first by developing a tolerance to it and substituting it for a po pill dose instead. She watched and investigated her clinical symptoms, allowing the PTDI to declare it daily, before taking the remedy. This is of utmost importance, and one can liken it to the sedation and paralyzation of a NeuroICU patient who needs a daily neurological exam. This neurologic patient needs to be<sup>1</sup> easily arouse able and not under deep sedation and<sup>2</sup> not overdosed on paralytic drugs, so that a physical exam can be elicited almost immediately.

In this manner, the management of these patients is to first avoid hypervolemic hyponatremia. If it is caused iatrogenically by overdosing with DDAVP, and the patient has severe clinical complaints, then do not ignore them. These are the shifting water molecules going into the extracellular fluid to cause edema of the brain and eyes, and it is very, very painful. This author does not believe that any in-house patient would have this occur as a “long-term” or “chronic” event. It would only be iatrogenic and “quick”, for example, by both dosing the patient with DDAVP and leaving her IV going at 1ml/kg/hr.

This author’s opinion is to treat in-house hyponatremia as an “acute” event, avoid seizures, uncal herniation and death by avoiding one drop of even 5% saline, and just being patient (it is supposed to be a ‘slow’ correction, anyway) by withdrawing all IVs and PTDI medications, so that the DI can “declare itself” again, self-correcting the hyponatremia in its own time. Be prepared to immediately avoid reinstitution of hypervolemia again, because the patient’s brain is also damaged by the TBI and the less harm, the fewer changes, the more you assess the patient, the better.

ICU admission is a reason for observation and knowing when to check electrolytes and respond to cardiopulmonary arrest or other iatrogenic sequelae. Few endocrinologists have seen PTDI occur in a patient who also has dysautonomia. It is also a situation where the ER doctors need to test the patient’s serum Na upon arrival, then give fluid resuscitation if the patient has heat stroke, migraine, or dehydration, *and then* check the serum Na again, post-fluid resuscitation.

So few doctors know what either dysautonomia or PTDI is, that the patient in pain and agony, with brain fog and expressive dysphagia can hardly be relied upon to be her best advocate. To boot, some doctors view this as all being so foreign that they “chalk the patient up” as being a mental health patient instead of a physical health patient, thus putting the patient through more anguish, duress, and contributing to additional PTSD from not being “believed.” Let us avoid that at all costs. Give the patient and the physician: patient to be her/his own “rebel,” as *this* is the only way that this patient has survived.<sup>23</sup>

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## Conflict of interest

Author declares that there is no conflict of interest.

## References

- Chung J, Kim BS, Lee D, et al. Vertebral artery occlusion with vertebral artery-to-posterior inferior cerebellar artery stenting for preservation of the PICA in treating ruptured vertebral artery dissection. *Acta Neurochir.* 2010;152(9):1489–1492.
- Office of Communications and Public Liaison. *National Institute of Neurologic Disorders and Stroke: NIH Dysautonomia Information Page.* National Institutes for Health, Bethesda, MD, USA; 2015.
- Aranda Margaret. Immunonutrition and Fish Oil. In: Aranda Margaret, editor. *Archives of the Vagina: A Journey through Time.* Mustang, Oklahoma: Tate Publishing; 2014. p. 285–290.
- Petition: Increase Higher Education and Diagnosis of Invisible Illnesses before More Suicides. 2015
- Johnson, Glen. Common Indicators of a Head Injury. In: Johnson, Glen, editor. *Traumatic Brain Injury Survival Guide.* Traverse City, MI, USA; 2010.
- WHO. *Rehabilitation for Persons with Traumatic Brain Injury.* Geneva, Switzerland: World Health Organization; 1998. p. 1–41.
- Capatina C, Alessandro P, Mitchell R, et al. Diabetes Insipidus after Traumatic Brain Injury. *J Clin Med.* 2015;4(7):1448–1462.
- Haddad SH, Arabi YM. Critical care management of severe traumatic brain injury in adults. *Scand J Trauma Resusc Emerg Med.* 2012;20:12.
- Stern RH. Disorders of plasma sodium. *N Engl J Med.* 2015;372:55–65.
- US National Library of Medicine. Low sodium level. Medline Plus, US Department of Health and Human Services, Bethesda, Maryland, USA; 2015.
- Aranda Margaret. *Self-reporting while on Plavix® blood thinner for vertebral artery dissection.* 2016.
- Aranda Margaret. *Self-reporting of finger bloating and inability to take off medical school class ring while hypervolemic; then when hypovolemic, ring slides on same finger, around in a circle.* 2016.
- World Health Organization. *WHO Model List of Essential Medicines.* 18th ed. Geneva, Switzerland: World Health Organization; 2013.
- Anderson LA, Stewart J, Thornton, et al. Fludrocortisone acetate information from Drugs.com. (c2000 - 2016).
- The Internet Drug Index: ProAmatine (Midodrine hydrochloride). Rx List Inc., WebMD Network, New York, USA; 2016.
- Anderson LA, Stewart J, Thornton, et al. DDAVP information from Drugs.com (c2000 - 2016).
- Aranda Margaret Self-reporting of unilateral epistaxis after use of DDAVP nasal spray and subsequent nare inflammation, while on clopidogrel therapy.
- Stiell IG, Hébert PC, Wells GA, et al. Vasopressin versus epinephrine for in-hospital cardiac arrest: a randomized controlled trial. *Lancet.* 2001;358(9276):105–109.
- Mukoyama T, Kinoshita K, Nagao K, et al. Reduced effectiveness of vasopressin in repeated doses for patients undergoing prolonged cardiopulmonary resuscitation. *Resuscitation.* 2009;80(7):755–761.
- Robert W, Charles W Otto, Chair, et al. 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science. *Circulation.* 2010;122:729–767.
- Turner, DW, Attridge RL, DW Hughes. Vasopressin Associated with an Increase in Spontaneous Circulation in Acidotic Cardiopulmonary Arrest Patients. *Ann Pharmacother.* 2014;48(8):986–991.
- Ghafourian N, Manie NH, Taherikalani M, et al. Combination of Vasopressin-Epinephrine as a Novel Candidate in Patients with Cardiac Arrest. *Recent Pat Cardiovasc Drug Discov.* 2015;10(1):65–69.
- Larry Chu. *The intersection of Medicine and Emerging Technologies.* Stanford Medicine-X; 2016.