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# Sucrose Nephropathy Following IV Immunoglobulin

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**ABSTRACT:** *Treatment with Intravenous Immunoglobulin (IVIg) has been found to be useful in patients with variety of diseases. IVIg infusions can produce allergic reactions. These adverse reactions are thought to be caused by activation of the complement cascade by the aggregation of IgG. To avoid this, a variety of stabilizing agents, including sucrose, are used. Sucrose is metabolized in the intestines by sucrase. If sucrose is given intravenously, this will be reabsorbed in to the proximal convoluted tubule and produce osmotic nephropathy which will present clinically as oliguric acute kidney injury. Patients with preexisting renal insufficiency, diabetes mellitus, elderly (>65 years), volume depletion and sepsis are more prone for these adverse effects and care should be taken not to use the IVIg with sucrose as a stabilizer in this population. If no other options are available, reductions in dose, concentration, and/or rate of administration of IVIg are warranted to reduce the incidence of renal failure. Pharmacist should be aware of the clinical scenario of the patient and choose the IVIg with appropriate stabilizer.*

## KEY WORDS:

Intravenous Immunoglobulin, Sucrose, Acute kidney injury

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## BACKGROUND

Treatment with Intravenous Immunoglobulin (IVIg) has been demonstrated to be useful in patients with variety of diseases and Food Drug and Administration has approved the use of IVIg in primary immune deficiencies, immune thrombocytopenic purpura, kawasaki syndrome, chronic B cell lymphocytic leukemia, CMV infection in transplantation patients and also in pediatric HIV infection. Recently the indications for IVIg have broadened and they are also used in immune mediated disorders like myasthenia gravis, Guillain- Barre syndrome and demyelinating neuropathies. Some IVIg contains sucrose as a stabilizer, which can produce a rare form of nephropathy called Sucrose Nephropathy, which has to be identified and managed quickly. Here we are presenting an interesting case of Sucrose nephropathy.

## CASE PRESENTATION

A 62 year old woman with a history for hypertension, diabetes, and stable congestive Heart Failure was hospitalized with petechiae, diagnosed as Acute Idiopathic Thrombocytopenic Purpura. At the time of admission her labs are noted for thrombocytopenia and her renal functions were stable with Blood Urea Nitrogen (BUN) of 24 and Serum Creatinine of 0.8 mgs%. Her urine output is 1800 ml/24 hrs and she was not on any nephrotoxic medications. She was treated with Steroids (Prednisone 60mg/day); during this period her glycemic status was controlled with Insulin. At the end of one week, her platelet counts remained low. Thus one more week of trial with prednisone was continued as she was stable clinically without any bleeding, except for the petechiae in extremities. Despite two weeks of steroid therapy her platelet count was not improving and hence it was decided to start IV Immunoglobulin. She was commenced with IVIg (Sandoglobulin<sup>R</sup>) in a dosage of

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**Table 1: Renal Parameters for the Patient**

Day	1*	2	3 <sup>l</sup>	4*	5	6	7	8	9
BUN	24	26	27	35	49	63	54	40	37
Sr.Creatinine	0.8	0.9	0.9	1.3	2.8	4.2	3.1	2.4	1.3

\*IVIg Started

†IVIg Stopped

**Table 2: Concentration of Various Stabilizers in available IVIg Preparations**

Name of the Product	Stabilizer Concentration in Grams	% of ARF
Gamimune N <sup>R</sup>	Maltose 1.0	5
Gammagard <sup>R</sup>	Glucose 0.4	4
Gammar P <sup>R</sup>	Sucrose 1.0	22
Iveegam <sup>R</sup>	Glucose 1.0	0
Panglobulin <sup>R</sup>	Sucrose 1.67	69
Polygam S/D <sup>R</sup>	Glucose 0.4	4
Sandaglobulin <sup>R</sup>	Sucrose 1.67	69
Venoglobulin I <sup>R</sup>	Mannitol 0.4	0
Venoglobulin S <sup>R</sup>	Sorbitol 1.0	0

0.4g/kg/day for a total of 5 consecutive days. Her platelet count improved significantly following the initial 3 doses. However, on day 4, her BUN and Creatinine were raised from the base line. Hence IVIg was stopped. She became oliguric in fifth day. Her BUN and Creatinine kept on rising (see table 1) and she was oliguric for next 3 days. Slowly her BUN and Creatinine improved and were back to normal, after 6th day of stopping the IVIg. She did not need any renal replacement therapy during this period. She recovered from the illness without any significant morbidity

## DISCUSSION

Up to 15% of IVIg infusions can produce adverse reactions including fever, myalgia, headache, flushing, shortness of breath and chest pain. The adverse reactions are thought to be caused by activation of the complement cascade by the aggregation of IgG<sup>1</sup>. To prevent the aggregation, a variety of stabilizing agents are used. These include: Disaccharides like sucrose and maltose, Monosaccharides like Glucose, D-sorbitol,

Glycine and Albumin<sup>2</sup>. All of these stabilizing sugars are metabolized in the liver except sucrose, which is enzymatically degraded by sucrase, an enzyme present only in small intestine<sup>3</sup>. Sucrose containing IVIg are the most widely used preparations in USA. Disproportionate shares (88% of US reports) of IVIg induced Acute Kidney Injury (AKI) have been associated with sucrose containing products<sup>4</sup>.

When IVIg is administered intravenously sucrase is unavailable to metabolize the sucrose, thus sucrose is delivered unchanged to the kidneys. In human kidneys, the proximal convoluted tubular (PCT) cells are responsible for reabsorption of filtered carbohydrates including sucrose, via pinocytosis. After absorption, these pinocytotic vesicles coalesce with lysosomes. As the PCT cells cannot hydrolyze sucrose, accumulation of sucrose within the PCT cells results in an increased osmotic gradient, prompting water entry in to the cells via water channels in the apical cell membrane. This in turn causes cellular swelling, vacuolization and tubular luminal occlusion from swollen tubular cells. This is the proposed underlying pathophysiological mechanism for osmotic nephrosis which clinically manifests as acute renal failure<sup>2</sup>. The clinical course of IVIg associated AKI generally follow a similar clinical picture. Acute renal insufficiency developing approximately 3 days after the initiation of IVIg and the average duration of renal insufficiency is about 13 days<sup>2</sup>. Oliguric renal failure is the predominant feature. AKI was reversible in these situations and usually renal function returned to base line after about 5-10 days of discontinuing the IVIg. Rarely these patients may need renal replacement therapy too.

## CONCLUSION

With IVIg infusion, particular caution needs to be exercised in patients with preexisting renal insufficiency, diabetes mellitus, elderly (>65 years), volume depletion, sepsis, paraproteinemia<sup>3</sup>. Concomitant nephrotoxic drugs should be avoided. Reductions in dose, concentration, and/or rate of administration of IVIg in patients at risk for AKI are the reasonable ways to reduce the risk<sup>4</sup>. Periodic monitoring of renal function tests and urine output is particularly important in patients judged to have a potential risk for developing AKI. At the earliest

sign of renal insufficiency, IVIg should be discontinued promptly, as this is potentially reversible. Pharmacists should be aware of this potentially preventable complication and should select the appropriate product of IVIg in patients with risk factors for developing AKI.

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