**Guidelines for use of Sodium Thiosulphate for Adults Patients with Calciphylaxis**

**for Sussex Kidney Unit Use Only**

**Aim and purpose of guideline**

Provide recommendations on the management of patients affected by calciphylaxis treated with Sodium Thiosulfate.

**Introduction**

Calciphylaxis is a rare condition in which calcium accumulates in small blood vessels and results in painful ulceration of the skin which in turn can cause infection and further damage to tissues. The causes remain poorly understood and treatment options aim to control symptoms.

Diagnosis is predominantly clinical and might include a skin biopsy. Skin biopsy can also be associated with the development of new non-healing, painful ulcers therefore it is not always recommended.

Calciphylaxis should be considered in all patients presenting with lesions with the following features:

* Tender indurated plaques or livedo reticularis
* Palpable subcutaneous deposits (calcium)
* Surrounding pallor or ecchymosis and associated hyperesthesia
* Severe pain (often disproportionate to the appearance of the lesion)
* Ulceration is a late presentation.

**Management**

There are no national or international guidelines available for the management of calciphylaxis. Management should be individualised dependent upon the patient’s circumstances. Supportive therapy including pain relief, referral to Tissue Viability teams and avoidance of subcutaneous injections should be offered to all. All the exacerbating factors depending on individual should also be reduced. These include:

* Vitamin K antagonists – consider anticoagulation alternatives if appropriate.
* Infection and inflammatory conditions – treat when appropriate.
* Phosphate, calcium and PTH – optimise management by avoiding the use of calcium-based phosphate binders, vitamin D and calcium supplements and consider starting cinacalcet or etelcalcetide
* Haemodialysis – consider increasing frequency and use of low calcium dialysate.

Administration of sodium thiosulphate forms calcium-thiosulphate complexes which are highly soluble and excreted in the urine or removed by haemodialysis. It also reduces anti-oxidant activity which may reduce the endothelial dysfunction and the pain experienced. Numerous case reports have suggested a beneficial effect. It’s clearance on peritoneal dialysis is unknown. There are no published clinical trials on its use in calciphylaxis. Patients might note symptomatic improvement in pain within a few weeks, but the ulcers may take months to heal.

**Adverse effects**

* Diarrhoea
* Diuresis
* Electrolytes disturbances (hypernatraemia, hypocalcaemia)
* Headache
* Increased appetite and taste disturbances
* Metabolic acidosis
* Nausea and vomiting (most common)
* Oedema
* QT interval prolongation
* rhinorrhoea
* Severe hypotension

**Formulation available**

* Sodium Thiosulfate (20mL) 50% 10g in 20mL injections – UNLICENSED
* Sodium Thiosulfate (50mL) 25% 12.5g in 50mL injection – UNLICENSED

**Dose and administration**

|  |  |
| --- | --- |
| Dose | Start with 12.5g THREE times a week on haemodialysis. Aim to up titrate to 25g THREE times a week on haemodialysis if tolerated. |
| Time | Over the last 30 to 60 minutes of haemodialysis |
| Route | Intravenously via venous port of dialyser |
| Tolerability | On initiation it may not be well tolerated. In such circumstances lower doses should be used and titration dependant on tolerability. |
| Duration of treatment | 6 weeks to 34 months |
| Dilution | 50-100mLs of sodium chloride 0.9% or glucose 5%. Expiry: 24 hours |
| Flush | With sodium chloride 0.9% or glucose 5% |
| Additional information | Extravasation may cause tissue damage due to high osmolality.  Anti-emetics might be used as pre-medication if nausea is experienced. |

\*If the patient is not on haemodialysis a central line should be used and the renal team should be contacted.

**Monitoring**

* Blood pressure during the infusion.
* Progression of the calciphylaxis – monitor skin lesions and ulcers.
* Manage pain relief appropriately and titrate medications as tolerated.

**References**

* [Calciphylaxis - Symptoms and causes - Mayo Clinic](https://www.mayoclinic.org/diseases-conditions/calciphylaxis/symptoms-causes/syc-20370559#:~:text=Calciphylaxis%20(kal%2Dsih%2Dfuh,that%20can%20lead%20to%20death.)
* Nigwekar SU, Thadhani R, Brandenburg VM. Calciphylaxis. N Engl J Med. 2018 May 3;378(18):1704-1714
* McCarthy, JT et al. Survival, Risk Factors, and Effect of Treatment in 101 Patients with Calciphylaxis, Mayo Clinic Proceeding. 2016 91(10):1384- 1394.
* Dutta P et al. Correlation between clinical and pathological features of cutaneous calciphylaxis. PLoS ONE 2019 14(6): e0218155.
* Nigwaekar SU et al. Sodium thiosulphate therapy for calcaemic uremic arteriolopathy. cJASN, 2017 July 8(7):1162-1170.
* 5. Raymond et al. Sodium thiosulfate, bisphosphonates, and cinacalcet for treatment of calciphylaxis. Am. J. Health Syst. Pharm 2008; Aug 1;65(15):1419-29