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Case Report

Beneficial Effect of Prolonged and Repeated Administration of Sodium Thiosulphate in a Patient Undergoing Dialysis Presenting Recurrent Ulcers in the Lower Extremities

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1. Abstract

We present a case of a female patient receiving dialysis with severe vascular calcification suffering from recurrent ulcers and treated with infusions of sodium thiosulphate three times per week over 9 months. Our results suggest the safety of the prolonged and repeated administration of STS, even in non-calciphylaxis related injuries.

2. Keywords

Sodium thiosulfate, Ulcers, Lower extremities, End-stage renal disease

3. Introduction

Hemodialysis is a method of replacement of the renal function in patients with end-stage renal disease. It is well established thatpatients undergoing dialysis may suffer from skin disorders that may vary from pruritus to severe ulcers not always related to diabetes. [1-4]. This situation may negatively influence their quality of life.

Calciphylaxis is a rare pathological disorder related to skin lesions that usually occurs in patients undergoing hemodialysis. Its main feature is calcification of the vascular wall of the skin vessels resulting in necrosis and ulceration. [5-7]. Sodium thiosulphate is an inorganic compound used to treat cyanide poisoning. Its off-label use in the treatment of calciphylaxis in patients undergoing dialysis is proven by a series of case reports and systematic reviews thus optimal dose is not established nor the period of safe administration of the drug [9-10].

In this paper we report a case of prolonged and repeated administration of STS to a female patient on dialysis for 24 years suffering from skin lesions similar to those found in patients suffering from calciphylaxis but with gradual evolution and frequent relapses.

4. Patient & Method

An 82-year-old female patient undergoing hemodialysis for 24 years, diagnosed with severe vascular calcification suffered from recurrent abrasions of the skin of the lower limbs which resulted in sustained superficial ulcers.

Due to significant thinning of the skin, severe lack of regenerative capacity and patient's reluctance, a skin biopsy for definitive diagnosis could not be performed. Based on literature concerning the use of STS in calciphylaxis [5,9,10] - even though calciphylaxis was not histologically proven - we administered 250ml of STS 25% to our patient, half an hour before the end of hemodialysis during a period of 9 months. No wound care dressings were used throughout the treatment. Calcification of the small vessels of the lower limbs was assessed radiologically before and after the treatment (Picture 1).

BEFORE AFTER

Picture 1

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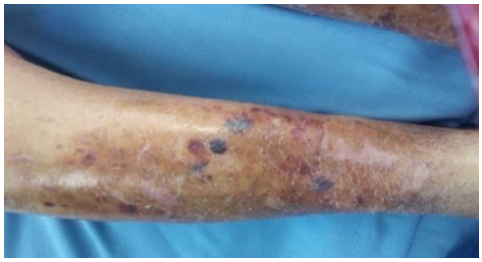
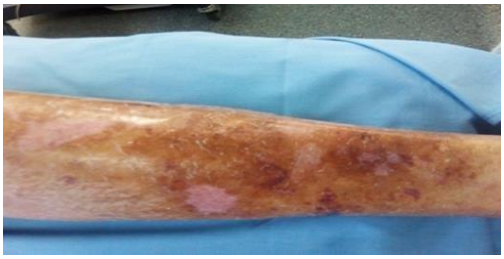
Picture 2: Initial wound

Picture 3: 2nd month of treatment

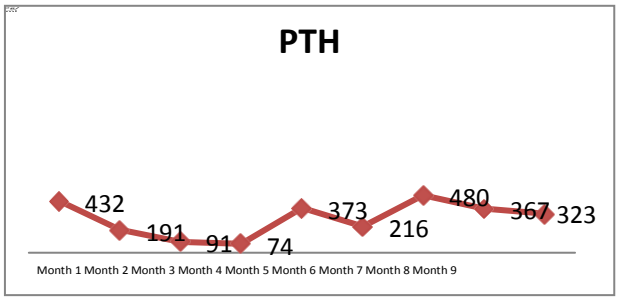


Picture 4: 4th month of treatment

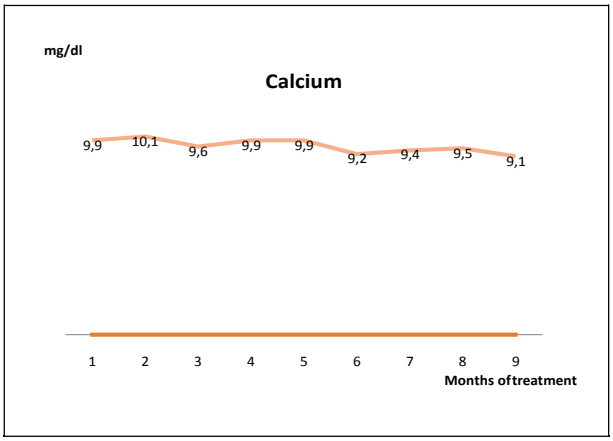


Picture 5: 9th month of treatment

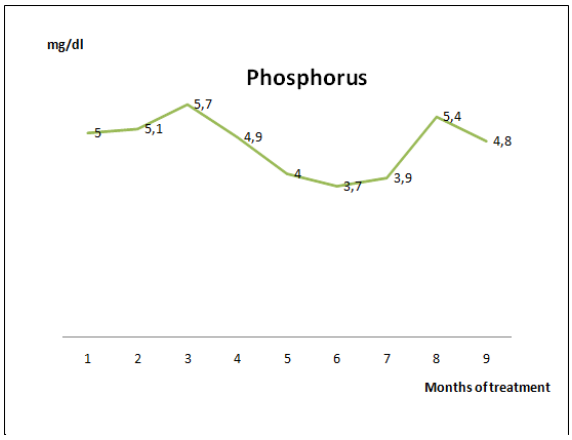
Picture 2-5: Pictures of the affected limb were taken periodically in order to record the progress of the healing.



Graphic 1



Graphic 2



Graphic 3

We also measured the values of Calcium (Ca), Phosphorus (P) and Parathyroid hormone (PTH) once a month during the period of administration of the STS. The patient was under intravenous treatment for secondary hyperparathyroidism (etelcalcetide, 3/week), and p.os treatment for hyperphosphatemia (sevelamer). (Graphic 1-3)

The patient did not present extremely high rates of PTH, neither an abnormal calcium/phosphorus ration.

No complications were observed, the drug was well tolerated and the ulcers on the lower limbs healed completely within the first four months. Even though the primary ulcers healed the treatment continued for another five months due torecurrent micro-traumatism secondary to unsteadygait.

Due to a fall 14 months after completing the treatment the patient presented lacerations of the skin, anew. We administered STS for another six (6) months with beneficial results, without any side effects proving the safety after repeatability of STS treatment.

5. Results

The therapeutic results began to be evident one month after the initial administration of STS with complete healing of thesuperficial ulcers within the fourth month of administration. The prolonged treatment due to recurrent micro-traumatisms was completely un-

complicated.

One year after completing the treatment regimen, the patient did not present any new ulceration of the lower limbs while any new skin abrasions healed rapidly without progression. As far as the radiological image of the lower extremities is concerned, there was no significant change after the end of the treatment cycle.

After a fall that the patient sustained a 14 months after treatment resultinginanumber ofecchymosisandabrasions, administration of STSacceleratedthehealingprocess withoutpresenting anyside effects. The possibility of prolonged and repeated use of STS not onlyin cases ofproven calciphylaxis but also in severelyatherosclerоticpatientsundergoingdialysiswhosufferfromrecurrentulcers and abrasions possibly accelerates healing time and thus prevents local and systemicinfections.

6. Discussion

Patients undergoing dialysis are more prone to skin lesions, based on several studies [3,4,8,11-13]. Ecchymosis, secondary to platelet dysfunction and high levels of guanidinosuccinic acid, is quite frequent in end-stage renal disease, especially in patients undergoing dialysis [14,15]. Dialysis itself seems to be an independent risk factor for ulcerations of the lower limbs in non-diabetic patients as well [2,9]. Studies in mice suggest that the reduced healing time in people with end-stage chronic kidney disease is associated with an underlying chronic inflammatory condition and a low rate of vascularization and cell proliferation, caused by delayed rate of wound granulation tissue formation [16].

Sodium thiosulphate is an inorganic salt which can inhibit the formation and favor the solubility and the mobilization of calcified plaques. Its off-label use started in the‘80s in the set ofprophylaxis, used with intraperitoneal administration of cisplatin, in order to reduce the nephrotoxicity associated with chemotherapy [17]. Since then it has been widely used in the treatment of documented calciphylaxis [9,10] but not in the treatment of recurrent superficial skin lesions in the dialyzed patient. Since the use of STS in the treatment of dermatological manifestation in end-stage renal disease is still off-label, there is no specific dose or duration of treatment especially in patients without hyperphosphatemia or calcium/phosphorus abnormal ratio.

The use of prolonged and repeated use of STS was both uncomplicated and highly effective showing that it may be used not only as an acute phase treatment but also in the set of maintenance for patients presenting recurrent ulcers mostly of traumatic nature.

7. Conclusions

Administration of sodium thiosulfate accelerated the healing process resulting in complete healing of the ulcers in our patient. While in this case both prolongation and repeatability of the regime proved to be safe and efficient, more studies need to be undertaken in order to confirm these results.

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