

Calciophylaxis – A multi-interventional treatment regimen including Vitamin K supplementation might reduce mortality in chronic kidney disease patients



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Background: Calciophylaxis is a rare disease predominantly affecting patients with chronic kidney disease (CKD) with a high mortality mainly due to wound infection and sepsis. Recently, multimodal therapy schemes including sodium thiosulfate (STS) have been established for the treatment of this challenging disease. The role of a standardized Vitamin K supplementation remains unclear



Results: Twenty patients with newly diagnosed Calciophylaxis at different CKD stages (CKD 5, n= 15; CKD 4, n= 3; CKD 3, n= 1; no CKD, n= 1;) were included. The mortality was 25% versus 52% compared to recent literature. Gender distribution and amount of biopsy proven cases were comparable to other retrospective studies. 12 patients (60%) had a preceding event such as micro-trauma possibly having triggered development of calciophylaxis. The period between the events and the diagnosis was 103 ± 94 days. 19 patients (95%) received STS. In contrast to other multimodal therapeutic concepts 95% (19) of our patients additionally received high dose vitamin K supplementation.

SOP: Calciophylaxis Clinical Department of Nephrology, Medical University Graz	
1) Stabilisation of Ca x P	
Ionized Ca ⁺⁺ at subnormal levels and PO ₄ ⁻ low-normal levels	
Stop Vitamin D administration	
Stop Ca-containing phosphatebinders, start Sevelamer or Lanthanum carbonate	
Low- calcium and -phosphorus diet	
Avoid phosphate containing laxatives	
Use cinacalcet to control sec. hyperparathyroidism	
Parathyroidectomy if primary hyperparathyroidism is present	
2) Modify anticoagulation	
Stop coumarins	
Vitamin K 10mg/1ml 3x/week p.o. or i.v.	
LMW Heparine s.c. alternative anticoagulation	
3) Avoid triggers	
Reduce punctions or other tissue trauma to a minimum	
S.c. injections use proximal extremities rather than abdomen	
4) Woundmanagement	
Gentle necrectomy preceding local anesthetic ointment, avoid freshening of the wound margin	
Change dressings gently	
Consider maggottherapy (biosurgery)	
Consider plastic coverage	
5) Antiinfective therapy	
Longterm antibiotic treatment for extensive laesions	
Use probiotics	
6) Analgesia	
Metamizole, opiates, accompanying laxatives	
massive pain use Ketamine 1-8mg/h i.v., 10mg 3-4x/d p.o.	
7) Antioxidative therapy	
Sodiumthiosulfate 25g 3x/week i.v. during the last hour of dialysis	
Sodiumthiosulfate 10g 3x/week i.v. over 1h for non CKD 5D per Port-a-Cath	
For nausea and vomiting use metoclopramide	
8) Modify dialysis	
Change from peritonealdialysis to haemodialysis	
Intensify dialysis up to 5x/week	
Reduce dialysate sodium, increase dialysate bicarbonate, dialysate calcium at 1,0	
9) Other measures	
Stop ironsupplementation	
Intensify nursing measures	

Methods: In a retrospective study we evaluated the impact of a standardized, multimodal treatment regimen on the mortality of calciophylaxis patients treated at the Clinical Department of Nephrology, Medical University of Graz, Austria between January 2009 and February 2014. All patients were treated with STS, dermatological wound management and high dose oral or intravenous supplementation of vitamin K (Phytomenadion 30mg/week). The primary endpoint was mortality compared with the present literature. Secondary endpoints included gender distribution, percentage of biopsy proven cases, analysis of triggering events or time between these events and diagnosis of calciophylaxis. Data were collected from medical records.

	total (n=20)	survivors (n=15)	Non survivors (n=5)
Female n, (%)	14, (70)	10, (66,7)	4, (80)
Male n, (%)	6, (30)	5, (33,3)	1, (20)
Age of onset (in years)	69,6 ± 10,2	68,5 ± 10,1	72,6 ± 9,7
Bodymassindex (kg/m ²)	30 ± 5	30 ± 5	29 ± 7
On dialysis n, (%)	14, (70)	9, (60)	5, (100)
HD n, (%)	11, (55)	7, (46,7)	4, (80)
PD n, (%)	3, (15)	2, (13,3)	1, (20)
Nicotine abuse n, (%)	4, (20)	3, (20)	1, (20)
Comorbidities:			
CHD n, (%)	12, (60)	8, (53,3)	2, (40)
MI (STEMI oder NSTEMI) n, (%)	5, (25)	3, (20)	2, (40)
PAOD n, (%)	12, (60)	9, (60)	3, (60)
Art. hypertension n, (%)	20, (100)	15, (100)	5, (100)
Diabetes mellitus n, (%)	13, (65)	9, (60)	4, (80)
Sec. hyperparathyroidism n, (%)	17, (85)	12, (80)	5, (100)
Medication:			
Phosphatebinders n, (%)	13, (65)	9, (60)	4, (80)
Ca-containing phosphatbinders n, (%)	6, (30)	3, (20)	3, (60)
Coumarintherapy before and @ BL n, (%)	13, (65)	10, (66,7)	3, (60)
Coumarintherapy duration before manifestation (in months)	111 ± 130	111 ± 130	18 ± 16
Heparine n, (%)	6, (30)	3, (20)	3, (60)
Vitamine D3 n, (%)	6, (30)	3, (20)	3, (60)
Vitamine D i.v. n, (%)	10, (50)	6, (40)	4, (80)
Iron supplementation n, (%)	6, (30)	4, (26,7)	2, (40)
Cinacalcet n, (%)	7, (35)	7, (46,7)	0, (0)

Conclusion: In our cohort calciophylaxis was associated with a markedly reduced mortality as compared to published outcome data. We hypothesize that suprphysiological supplementation of vitamin K in addition to sodium thiosulfate therapy seems to play a critical role in the treatment of calciophylaxis.

