



NEPHROLOGY AND UROLOGY LITERATURE

Curr Opin Nephrol Hypertens. 2008 Nov;17(6):629-34.

Calcific uraemic arteriopathy: an update.

Rogers NM, Coates PT.

PURPOSE OF REVIEW: Calcific uraemic arteriopathy (CUA) or calciphylaxis is a rare but important cause of morbidity and mortality in patients with chronic kidney disease. The prevalence of CUA is increasing in patients with renal failure, and the condition is also being recognized in nonuraemic patients.

RECENT FINDINGS: There has been increasing understanding of the molecular basis of vascular calcification, in particular on the important role of the uraemic microenvironment in the factors implicated in the differentiation of vascular smooth muscle cells into osteoblasts. New options for treatment of hyperphosphataemia and secondary hyperparathyroidism in patients with chronic kidney disease have become available in the last few years and these have begun to be used in patients with CUA. These include bisphosphonates, newer noncalcium/nonaluminium-containing phosphate binders and case reports of use of cinacalcet. Other treatments for CUA that are not targeted directly at calcium/phosphate homeostasis include hyperbaric oxygen and the antioxidant cation chelator sodium thiosulphate.

SUMMARY: Clinicians managing patients with CUA should consider a combination approach of treating deranged calcium/phosphate with newer therapeutic agents and promoting wound healing with other older modalities such as hyperbaric oxygen and sodium thiosulphate infusions. Randomized controlled trials for treatments in CUA are still lacking.

Clin Nephrol. 2008 Sep;70(3):261-4.

Management of calcific uremic arteriopathy (calciphylaxis) with a combination of treatments, including hyperbaric oxygen therapy.

Arenas MD, Gil MT, Gutiérrez MD, Malek T, Moledous A, Salinas A, Alvarez-Ude F.

Calcific uremic arteriopathy (CUA) is a rare but serious complication of end-stage renal disease presenting as painful cutaneous lesions and progressing to non-healing ulcers and gangrene. This syndrome is associated with calcium and phosphorus deposits within small arteries of the skin. The pathognomonic lesion is vascular calcification with intimal arterial hypertrophy and superimposed small-vessel thrombosis. The condition is being increasingly recognized and reported as a contributing factor to death in dialysis patients, with secondary infection and sepsis as the major cause of mortality. No standard treatment has been established for this syndrome. We present the therapeutic approach employed in two patients, which successfully resulted in healing of the lesions, using a combination of measures to control the factors potentially related to development of CUA and hyperbaric oxygen therapy.

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Aktuelle Urol. 2008 Jul;39(4):289-97

The complexity of chronic pelvic pain exemplified by the condition currently called interstitial cystitis.

Binder I, Rossbach G, Ophoven A.

The so-called interstitial cystitis is a chronic pain syndrome rather than a purely end organ disease of the urinary bladder. New suggestions for definitions and nomenclature take this into consideration. Since aetiology and pathogenesis are still unknown a treatment of the cause is still not possible. There are neither evidence-based treatment algorithms nor a so-called standard therapy. Numerous therapeutic approaches have been tried up to now. These attempts can be divided into oral, intravesical, surgical and physical procedures. There are also meaningful supplementary therapy procedures beyond the boundaries of classical school medicine. The WHO staging scheme provides the basis for every pain therapy. For the oral therapeutic procedures in current use the following medications with differing levels of evidence have been recommended: amitriptylin, hydroxyzin, pentosan polysulfate. Many other orally administered drugs have also been used although in many cases evidence of efficacy is lacking, these included anticonvulsants, L-arginine and various immunomodulators and immunosuppressants. Among the intravesical therapeutic procedures botulinum toxin A, dimethyl sulfoxide, heparin and glycosaminoglycan substitutes have been used. For the physical procedures, besides bladder distension, hyperbaric oxygen therapy shows efficacy. When the conventional therapeutic methods fail, surgical (partial) removal of the urinary bladder or urinary diversion procedures represent the therapeutic ultimo ratio. There are hardly any controlled studies on alternative curative procedures although rather good results have been obtained in chronic pelvic pain syndrome with acupuncture as an additional therapeutic modality.

Int J Urol. 2008 Jul;15(7):639-41.

Hyperbaric oxygen therapy for radiation-induced hemorrhagic cystitis.

Yoshida T, Kawashima A, Ujike T, Uemura M, Nishimura K, Miyoshi S.

Hyperbaric oxygen (HBO) therapy has recently emerged as a potential primary option for the management of hemorrhagic cystitis. We review our experience treating hemorrhagic cystitis with HBO. Between January 2001 and May 2007, eight patients with radiation-induced hemorrhagic cystitis underwent HBO therapy. There were five men and three women with a mean age of 64.3 years (47-73). Radiation was given for local disease, and the mean dosage delivered was 56.6 Gy (42-70). The mean duration between the onset of hematuria and the beginning of HBO therapy was 8.9 months (3-34). Mean follow-up period was 15.5 months (2-31). Hematuria resolved completely in six of the eight patients, one of whom suffered recurrence of hematuria and was treated with HBO until the hematuria resolved again. The response rate was 75%, compatible with the previous reports, and no side-effects of HBO were noted. HBO treatment should be attempted for radiation-induced hemorrhagic cystitis.

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Advances in Urology

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Preclinical Evidence for the Benefits of Penile Rehabilitation Therapy following Nerve-Sparing Radical Prostatectomy

M. Albersen, S. Joniau, H. Claes, and H. Van Poppel

Erectile dysfunction following radical prostatectomy remains a frequent problem despite the development of nerve-sparing techniques. This erectile dysfunction is believed to be neurogenic, enhanced by hypoxia-induced structural changes which result in additional veno-occlusive dysfunction. Recently, daily use of intracavernous vasoactive substances and oral use of PDE5-inhibitors have been clinically studied for treatment of postprostatectomy erectile dysfunction. Since these studies showed benefits of “penile rehabilitation therapy,” these effects have been studied in a preclinical setting. We reviewed experimental literature on erectile tissue preserving and neuroregenerative treatment strategies, and found that preservation of the erectile tissue by the use of intracavernous nitric oxide donors or vasoactive substances, oral PDE5-inhibitors, and hyperbaric oxygen therapy improved erectile function by antifibrotic effects and preservation of smooth muscle. Furthermore, neuroregenerative strategies using neuroimmunophilin ligands, neurotrophins, growth factors, and stem cell therapy show improved erectile function by preservation of NOS-containing nerve fibers.

Urology. 2007 May;69(5):983.e3-5.

Successful penile replantation with adjuvant hyperbaric oxygen treatment.

Zhong Z, Dong Z, Lu Q, Li Y, Lv C, Zhu X, Zhao X, Zhang X, Morales F, Ichim TE.

Penile amputation and successful replantation is very uncommon, and routine standardized procedures for dealing with this medical condition do not exist. A case of a penile amputation and successful replantation is presented. This report presents the microsurgical procedure and postoperative care that led to successful engraftment and function. Of particular interest was the use of hyperbaric oxygen to accelerate the healing process. A review of the published data and future methods of increasing success of such surgical procedures is provided.



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Semin Dial. 2007 Mar-Apr;20(2):150-7.

Calcific uremic arteriolopathy: advances in pathogenesis and treatment.

Rogers NM, Teubner DJ, Coates PT.

Calcific uremic arteriolopathy (CUA) is a rare but serious life-threatening complication of CRF that manifests as painful nonhealing eschars in association with panniculitis and dermal necrosis. This condition is being increasingly recognized and reported as a contributing factor to death in dialysis patients. The pathognomic lesion is vascular calcification with intimal arterial hypertrophy and superimposed small vessel thrombosis. Hyperparathyroidism and elevated concentrations of serum phosphate remain consistent clinical features of most cases reported. Controversy still exists regarding the role of parathyroidectomy in this condition with some studies suggesting improved outcome with surgical intervention. A number of potential new etiological factors have been identified including reduced serum levels of a calcification inhibitory protein alpha₂-Heremans-Schmid glycoprotein (Fetuin-A) and abnormalities in smooth muscle cell biology in uremia. Promising new treatment options including hyperbaric oxygen therapy and sodium thiosulfate infusion have been reported in case series. Benefits from biphosphonates and tissue plasminogen activator have also been reported. Overall these new treatment approaches and understanding of potential mechanisms underlying this important severe clinical condition offer new hope in the diagnosis and management of this severely morbid and often fatal condition.

Eur Urol. 2004 Jul;46(1):108-13.

Hyperbaric oxygen for the treatment of interstitial cystitis: long-term results of a prospective pilot study.

van Ophoven A, Rossbach G, Oberpenning F, Hertle L.

OBJECTIVE: We conducted a prospective pilot study to assess the safety and efficacy of hyperbaric oxygen (HBO) for the treatment of interstitial cystitis (IC). **METHODS:** Six patients underwent 30 sessions of 100% oxygen inhalation in a hyperbaric chamber and were followed up over 15 months. The measures of efficacy were changes in pain and urgency (visual analog scales), alteration in the patient's assessment of overall change in his well-being (Patient Global Assessment Form), and changes in frequency and functional bladder capacity (48-hours voiding log). Evaluation of symptom severity regarding pain and voiding problems was done using the O'Leary-Sant index. **RESULTS:** Four patients rated the therapeutic result as either excellent or good and assessed their well-being after HBO treatment as improved. Two patients showed only short-term amelioration of some of their symptoms. At 12 months follow-up the baseline functional bladder capacity increased from 37-161 ml (range) to 160-200 ml in the responder group. The 24-hour voiding frequency decreased from 15-27 to 6-11 voids per day, a pain scale improvement from 20-97 mm at baseline to 3-30 mm at 12 months follow-up and an urgency scale improvement from 53-92 mm to 3-40 mm, respectively was observed at 12 month follow-up. The symptom and pain index score decreased from 23-35 at baseline to 3-17 at 12 months follow-up. **CONCLUSION:** HBO appears to be effective to treat IC patients. Treatment was well tolerated and resulted in a sustained decrease of pelvic pain and urgency, improvement of voiding patterns and increase of functional bladder capacity for at least 12 months.



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J Nephrol. 2002 Nov-Dec;15(6):676-80.

Hyperbaric oxygen therapy for calcific uremic arteriopathy: a case series.

Basile C, Montanaro A, Masi M, Pati G, De Maio P, Gismondi A.

Calcific uremic arteriopathy (CUA), also referred to as calciphylaxis, is a syndrome of small vessel calcification of unknown etiology causing painful violaceous skin lesions that progress to non-healing ulcers and gangrene. It is observed mainly in patients with end-stage renal disease, is associated with high morbidity and mortality and has no standard treatment at the present time. Although parathyroidectomy (PTX) has been advocated in some cases, other studies have not found this effective. Hyperbaric oxygen therapy (HOT) consists of breathing 100% O₂ at higher than ambient pressure, with the patient inside a sealed chamber. HOT has been used with some success in the treatment of selected problem wounds (those that fail to respond to established medical and surgical management). They are often severely hypoxic; restoration of tissue PO₂ to normal or above-normal enhances fibroblast proliferation and collagen production as well as angiogenesis. The present is the largest retrospective case series of CUA treated by means of HOT reported so far and comprises 11 chronic uremic patients on dialysis (9 hemo- and 2 peritoneal dialysis, 6 females and 5 males, mean age 56 +/- 7 SD years, time on dialysis 163 +/- 84 SD months). Four patients had biopsy-proven CUA; 3 had diabetic nephropathy as a cause of uremia; 2 were obese and 3 had a consistent increase of serum calcium x phosphorus product; 3 patients had severe secondary hyperparathyroidism (II(nd) HPTH) and two had been submitted to subtotal PTX some years before CUA; two others had already had the limb amputated. Lesions were in the legs, except for one in a hand, and were prevalently ulcers and necrosis. The number of sessions in each HOT cycle ranged from a minimum of 20 to a maximum of 108 (mean 40.6 +/- 29.0). The results of two therapies cannot be evaluated (one was interrupted by the patient after 10 sessions, and one ended with the death of the patient due to ventricular arrhythmia after eight sessions). Eight of the nine remaining had excellent results with healing of the skin ulcers, but the ninth got worse, making it advisable to amputate the foot. In conclusion, CUA appears to result from a multitude of predisposing and/or sensitizing events that are commonly present in the uremic milieu. The specific factors that induce this disorder in an individual patient are not known. The present retrospective study supports a role of HOT in many cases of CUA, especially considering that, in the absence of severe II(nd) HPTH, there are very few therapeutic options.

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Nephrol Dial Transplant. 2001 Nov;16(11):2176-80.

Hyperbaric oxygen in the treatment of calciphylaxis: a case series.

Podymow T, Wherrett C, Burns KD.

BACKGROUND: Calciphylaxis, also referred to as calcific uraemic arteriopathy, is a syndrome associated with end-stage renal disease (ESRD), and causes necrotic skin ulcers, often leading to a fatal outcome. Hyperbaric oxygen (HBO(2)) therapy has been used to enhance wound healing, but its role in the treatment of calciphylaxis is unclear. **METHODS:** We undertook a retrospective study of patients on renal replacement therapy with biopsy-proven calciphylaxis who were treated with HBO(2) between March 1997 and February 2000. **RESULTS:** Five patients were treated with HBO(2): three patients were on continuous ambulatory peritoneal dialysis (CAPD) and two were on chronic haemodialysis therapy. None of the patients had uncontrolled hyperparathyroidism and none underwent parathyroidectomy. The patients each received 25-35 treatments of HBO(2) at 2.5 atmospheres for 90 min per treatment. Two of these patients had complete resolution of extensive necrotic skin ulcers, with no adverse effects of HBO(2) therapy. Both had improvement in wound area transcutaneous oxygen pressure (P(tc)O(2)) with administration of 100% oxygen when measurements were taken at normobaric and hyperbaric pressures. In the other three patients receiving HBO(2), the skin lesions did not resolve. P(tc)O(2) was measured in two of these patients, neither of whom showed improvement with 100% oxygen administered at normobaric pressure. **CONCLUSIONS:** The data support a role for HBO(2) in the treatment of some patients with calciphylaxis, particularly as in the absence of uncontrolled secondary hyperparathyroidism there are few therapeutic options.

Am J Kidney Dis. 1998 Sep;32(3):384-91.

Cutaneous necrosis from calcific uremic arteriopathy.

Coates T, Kirkland GS, Dymock RB, Murphy BF, Brealey JK, Mathew TH, Disney AP.

Calcific uremic arteriopathy (calciphylaxis) is an uncommon complication of chronic renal failure that is associated with high morbidity and mortality. We report 16 patients (13 female) who presented between 1985 and 1996. All patients developed painful livido reticularis that progressed to cutaneous necrosis and ulceration (11 cases on the proximal extremities and five cases on the distal extremities). Two patients with predominately distal leg disease survived; the cause of death in the other 14 patients was sepsis (six patients), withdrawal from dialysis (three), cardiac arrest (three), and gastrointestinal hemorrhage (two). Mesenteric ischemia from intestinal vascular calcification occurred in two cases. Clinical factors identified included the use of warfarin therapy in seven cases and significant weight loss (>10% body weight) in seven cases in the 6 months preceding the development of calcific uremic arteriopathy. Skin pathology was studied in 12 cases, with all showing calcific panniculitis and small vessel calcification. Electron microscopic spectral analysis of the mineral content of the calcific lesions in the subcutaneous tissue showed only calcium and phosphorous. In two cases, substitution of low molecular weight heparin for warfarin therapy resulted in clinical improvement. Current theories of pathogenesis and treatment are reviewed. This study confirms the high morbidity and mortality of calcific uremic arteriopathy producing ischemic tissue necrosis while drawing attention to significant weight loss and warfarin therapy as risk factors for the development of ischemic tissue necrosis. Hyperbaric oxygen therapy warrants further study.



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J Urol. 1998 Aug;160(2):601-4.

Effect of hyperbaric oxygen therapy on testicular ischemia-reperfusion injury.

Kolski JM, Mazolewski PJ, Stephenson LL, Texter J, Grigoriev VE, Zamboni WA.

PURPOSE: Testicular torsion is a urologic emergency representing a form of ischemia-reperfusion (IR) injury that requires prompt care to achieve tissue salvage and a reduction in post-torsion morbidity. Hyperbaric oxygen (HBO) has shown benefits in previous musculoskeletal models of IR. We evaluated the efficacy of HBO treatment in a rat testicular torsion model. **MATERIALS AND METHODS:** Four groups of male Wistar rats were included in this study: 1) Sham (n=16), spermatic cords exposed but not occluded; 2) Control (n=16), 4 hours of bilateral spermatic cord occlusion; 3) HBO during ischemia (n=18), 4 hours of occlusion and administration of HBO during the last 90 minutes of ischemia; and 4) HBO on reperfusion (n=8), HBO administered immediately upon reperfusion of the testes. The animals were sacrificed at two weeks and architecture and germinal epithelial cell thickness were determined by histological examination on each testicle. Average thickness (in cell layers) of each group was compared with control using Student's t test. **RESULTS:** Control testicles showed a significant reduction in germinal cell thickness compared with sham (1.7 versus 6.3, $p < 0.05$). The animals treated with HBO during ischemia showed a significant increase in epithelial cell thickness compared with control (2.8 versus 1.7, $p < 0.05$). Hyperbaric oxygen treatment during reperfusion had the greatest beneficial effect compared with control (5.1 versus 1.7, $p < 0.05$). **CONCLUSIONS:** Adjunctive HBO therapy administered during ischemia or reperfusion significantly reduced injury to the testicle in this animal model. These results suggest a potential benefit of HBO treatment in clinical situations of testicular torsion.