MEMBRANA PERITONEAL

| FARMACOS
VIA D’ADMINISTRACIÓ DE MEDICACIÓ

INTERACCIONS AMB MEDICACIÓ

En negatiu

En positiu
HEPARINA
Effect of self-administered intraperitoneal bemiparin on peritoneal transport and ultrafiltration capacity in peritoneal dialysis patients with membrane dysfunction. A randomized, multi-centre open clinical trial.

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Abstract

BACKGROUND: Progressive peritoneal membrane injury and dysfunction are feared repercussions of peritoneal dialysis (PD), and may compromise the long-term feasibility of this therapy. Different strategies have been attempted to prevent or reverse this complication with limited success.

METHODS: We performed a randomized, open multi-centre trial, aimed at scrutinizing the efficacy of self-administered intraperitoneal (i.p.) bemiparin (BM) to modulate peritoneal membrane dysfunction. The main outcome variables were peritoneal creatinine transport and the ultrafiltration (UF) capacity, estimated during consecutive peritoneal equilibration tests. The trial included a control group who did not undergo intervention. The treatment phase lasted 16 weeks with a post-study follow-up of 8 weeks.

RESULTS: Intraperitoneal BM did not significantly improve creatinine transport or the UF capacity, when the whole group was considered. However, we observed a time-limited improvement in the UF capacity for the subgroup of patients with overt UF failure, which was not observed in the control group. Intraperitoneal injection of BM did not carry an increased risk of peritoneal infection or major haemorrhagic complications.

CONCLUSIONS: Our data do not support the systematic use of BM for management of peritoneal membrane dysfunction in PD patients. Further studies on the usefulness of this approach in patients with overt UF failure are warranted. Intraperitoneal administration of BM is safe in PD patients, provided regulated procedures are respected.

PMID: 21993377 [PubMed - as supplied by publisher]
BETA BLOQUEJANTES
An instructive example of a long-latency adverse drug reaction--sclerosing peritonitis due to practolol.

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Abstract

OBJECTIVE: By examination of the original Yellow Card data to determine the duration of the latent period of the sclerosing peritonitis which formed part of the oculomucocutaneous syndrome that was associated with practolol, the beta-adrenergic receptor blocking agent that was withdrawn from clinical usage in the UK in December 1975 in response to reports of the syndrome.

METHOD: Relevant drug analysis prints (DAPs) for practolol were obtained from the Medicines and Healthcare Products Regulatory Agency (MHRA) and, by application to the Interim Committee on Yellow Card data, copies were obtained of the anonymised Yellow Card reports for all the 201 cases of sclerosing peritonitis that were reported in patients treated with practolol. These data were used to determine the latent period of this iatrogenic adverse drug reaction.

RESULTS: It was shown that no other cause than practolol operated in all or a majority of the cases of sclerosing peritonitis and the suspected adverse reaction could properly be attributed to the drug. The latent period (the time period between the drug start date and the reaction start date) of the sclerosing peritonitis associated with practolol averaged 201 weeks (range 26-606 weeks; standard deviation 130 weeks).

CONCLUSION: The latent period of the sclerosing peritonitis that formed part of the practolol oculomucocutaneous syndrome averaged about 4 years and had a range of from 0.5 to over 11.5 years. The Yellow Card Scheme could detect this ultra long-latency adverse reaction.

PMID: 17853493 [PubMed - indexed for MEDLINE]
Testing Times: The Emergence of the Practolol Disaster and its...

20 Feb 2006 ... Summary. This article analyses how practolol, the first British drug disaster of the modern, post-thalidomide regulatory period, related to the ...

shm.oxfordjournals.org/content/19/1/127.abstract - Semblants
Sclerosing encapsulating peritonitis associated with propranolol usage: a case report and review of the literature.
Kaira S, Atia A, McKinney J, Borthwick TR, Smalligan RD.
Department of Internal Medicine, James H. Quillen VA Medical Center, Johnson City, Mountain Home, Tennessee 37684, USA.
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PMID: 19906115 [PubMed - indexed for MEDLINE]

Sclerosing peritonitis associated with metoprolol.
Clark CV, Terris R.
PMID: 6132256 [PubMed - indexed for MEDLINE]

Sclerosing peritonitis and timolol.
Nancarrow JF.
PMID: 79892 [PubMed - indexed for MEDLINE]
CALCI ANTAGONISTES
Calcium channel blocker-induced chylosus ascites in peritoneal dialysis.

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Comment in
Kidney Int. 2010 Jan;77(2):165; author reply 165.

PMID: 19337227 [PubMed - indexed for MEDLINE]
Incidence and clinical course of lercanidipine-associated cloudy effluent in continuous ambulatory peritoneal dialysis.

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Abstract

BACKGROUND: Lercanidipine, a novel dihydropyridine calcium channel antagonist, has been reported to cause sterile cloudy effluent in patients on continuous ambulatory peritoneal dialysis (CAPD). The purpose of the study was to evaluate the incidence and clinical course of cloudy effluent associated with lercanidipine in uremic patients on CAPD.

METHODS: We designed a consecutive observation study in 40 non-diabetic uremic patients on CAPD treated with lercanidipine 5 mg daily. Lercanidipine-induced cloudy effluent was defined as acellular and culture-negative effluent associated with the use of this drug and exclusion of other causative factors. Time to develop cloudy effluent, dwell effluent amount and the associated symptoms were recorded. Baseline peritoneal membrane characteristics, net ultrafiltration per session and routine biochemistry in serum and dialysate were compared between patients with and without the development of cloudy effluent.

RESULTS: 9 patients (22.5%) developed cloudy effluent within 2 days of lercanidipine initiation. The triglyceride concentration in cloudy effluent was greater than 10 mg/dl (19.3 ± 6.3 mg/dl). There was a significant increase in dwell effluent amount (93.3 ± 64 ml/exchange, p < 0.05). Clinical symptoms as abdominal cramping or fullness were observed in 3 patients. All cloudy effluent disappeared after ceasing lercanidipine but recurred after resumption of lercanidipine. Baseline dialysate to plasma (D/P) creatinine ratio (0.7 ± 0.1 vs. 0.51 ± 0.1; p = 0.07) tended to be higher and dialysate total protein (93.4 ± 33 vs. 61.5 ± 24 mg/dl; p < 0.05) were significantly higher in patients with than without the development of cloudy effluent.

CONCLUSION: The incidence of lercanidipine-associated cloudy effluent is relatively higher with transient benign clinical symptoms. Patients with lercanidipine associated cloudy effluent tend to have a higher membrane transport with an increased effluent amount.
Comparative effects of carvedilol and lercanidipine on ultrafiltration and solute transport in CAPD patients.

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Abstract

BACKGROUND: Peritonitis, the type of buffer used in the dialysate, continue ambulatory peritoneal dialysis (CAPD) of greater than two years duration, increased exposure to dialysate glucose, diabetes mellitus, and the use of beta blockers may contribute to impaired ultrafiltration.

OBJECTIVES: The aim of the present study is to compare the effects of a calcium-channel blocker and a beta-blocker on the peritoneal transport and clearance.

METHODS: We studied 48 patients with ESRD on chronic peritoneal dialysis, included 27 females and 19 males with mean age 42.6 +/- 16.4 years. Two patients were excluded from the study due to peritonitis. Patients were treated either with carvedilol or lercanidipine. In all patients, peritoneal equilibration test (PET), ultrafiltration (UF), \( \text{Kt/V} \) ratio, creatinine clearance (CrCl), systolic blood pressure, diastolic blood pressure, serum BUN, creatinine, glucose, sodium, potassium, albumin, cholesterol, and triglyceride values were obtained before and after 8 weeks from the start of the drug treatment.

RESULTS: Lercanidipine and carvedilol showed a good antihypertensive effect in CAPD patients. Both drugs had a good tolerability profile and showed no effect on plasma lipids. There were no differences in terms of PET, ultrafiltration, \( \text{Kt/V} \) ratio, CrCl, systolic blood pressure, diastolic blood pressure, serum BUN, creatinine, glucose, sodium, and potassium values between both patient groups. After antihypertensive treatment, neither group showed a difference in the above-mentioned parameters \( (p > 0.05) \) except potassium, which was significantly higher in the carvedilol group \( (p < 0.05) \).

CONCLUSIONS: In CAPD patients, short-term usage of carvedilol has no effect on ultrafiltration and solute transport like lercanidipine. Both drugs showed a good antihypertensive effect.
Effect of oral administration of losartan, prazosin, and verapamil on peritoneal solute transport in continuous ambulatory peritoneal dialysis patients.

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Abstract

BACKGROUND: Several intraperitoneally administered drugs have been shown to modify transport of peritoneal solute and fluid. Fewer studies, however, have evaluated the effect of orally administered drugs. The present study was performed to evaluate the effects of oral losartan, prazosin, and verapamil on peritoneal membrane transport during a peritoneal equilibration test (PET), as well as the effects on creatinine clearance (CrCl), Kt/V urea, 24-hour protein in drained dialysate, and drained volume.

METHODS: This was an open, controlled, crossover clinical trial performed in 20 patients on continuous ambulatory peritoneal dialysis. All subjects used four 2-L 1.5% glucose dialysis exchanges per day. After a 7-day washout period (without antihypertensives), they had a baseline standard PET and dialysis adequacy assessment performed. Subsequently, they were randomly allocated to receive the first of three study drugs (losartan, prazosin, and verapamil), which were administered orally for a 7-day period. Immediately after each drug period, patients had a new 3-day washout and subsequently started the next drug, until they had received each of the three drugs. On the last day of administration of each drug, patients were subjected to a new PET and adequacy of dialysis evaluation.

RESULTS: None of the studied drugs significantly modified the peritoneal transport of creatinine, glucose, urea, sodium, potassium, or total protein as evaluated by PET. Verapamil significantly increased peritoneal CrCl [51.3 (44.3 - 53.3) vs baseline 45.8 (41.4 - 50.5) L/week/1.73 m2, p < 0.05], weekly Kt/V urea [1.75 (1.60 - 1.78) vs baseline 1.59 (1.54 - 1.73), p < 0.05], and drained dialysate volume [8.80 (8.30 - 8.96) vs baseline 8.44 (8.20 - 8.50) L/day, p < 0.05].

CONCLUSIONS: Oral administration of losartan, prazosin, and verapamil did not modify the peritoneal transport of solutes during a 4-hour PET. Oral verapamil significantly increased CrCl, Kt/V urea, and 24-hour drained dialysate volume. It is most likely that verapamil increases peritoneal (hydraulic) conductivity, and then net ultrafiltration volume and convective transport of urea, creatinine, and protein. Verapamil could be considered as an alternative in patients requiring increased dialysis dose and/or ultrafiltration.
SISTEMA RENINA ANGIOTENSINA
PROTECCIO DEL GLOMERUL

PREVENCIÓ DE NEFROPATIA DIABETICA
Expression patterns of connective tissue growth factor and of TGF-beta isoforms during glomerular injury recapitulate glomerulogenesis.

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Abstract
Transforming growth factor (TGF)-beta(1), -beta(2), and -beta(3) are involved in control of wound repair and development of fibrosis. Connective tissue growth factor (CTGF) expression is stimulated by all TGF-beta isoforms and is abundant in glomerulosclerosis and other fibrotic disorders. CTGF is hypothesized to mediate profibrotic effects of TGF-beta(1) or to facilitate interaction of TGF-beta(1) with its receptor, but its interactions with TGF-beta isoforms in nonpathological conditions are unexplored so far. Tissue repair and remodeling may recapitulate gene transcription at play in organogenesis. To further delineate the relationship between CTGF and TGF-beta, we compared expression patterns of CTGF and TGF-beta isoforms in rat and human glomerulonephritis and in various human glomerulopathies. CTGF mRNA was present in the immediate precursors of glomerular visceral and parietal epithelial cells in thecomma- and S-shaped stages, but not in earlier stages of nephron development. During the capillary loop and maturing glomerular stages and simultaneous with the presence of TGF-beta(1), -beta(2), and -beta(3) protein, CTGF mRNA expression was maximal and present only in differentiating glomerular epithelial cells. CTGF protein was also present on precursors of mesangium and glomerular endothelium, suggesting possible paracrine interaction. Concomitant with the presence of TGF-beta(2) and -beta(3) protein, and in the absence of TGF-beta(1), CTGF mRNA and protein expression was restricted to podocytes in normal adult glomeruli. However, TGF-beta(1) and CTGF were again coexpressed, often with TGF-beta(2) and -beta(3), in particular in podocytes in proliferative glomerulonephritis and also in mesangial cells in diabetic nephropathy and IgA nephropathy (IgA NP). Coordinated expression of TGF-beta isoforms and of CTGF may be involved in normal glomerulogenesis and possibly in maintenance of glomerular structure and function at adult age. Prolonged overexpression of TGF-beta(1) and CTGF is associated with development of severe glomerulonephritis and glomerulosclerosis.
Transforming growth factor beta1 and additional renoprotective effect of combination ACE inhibitor and angiotensin II receptor blocker in hypertensive subjects with minor renal abnormalities: a 24-week randomized controlled trial.


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End of treatment, significant (P < 0.05) reductions in systolic, diastolic and mean blood pressure, UAE and TGF beta1 levels were observed in all the groups. No change in renal function measurements were observed. The absolute and percentage reduction in UAE and TGF beta1 were significantly higher in the combined group than in the losartan or ramipril groups.
Hemodynamics and TGF-β₁ Plasma Levels in a Crossover Trial in Renal Transplant Recipients

PABLO IÑIGO, *† JOSEP M. CAMPISTOL, *† SERGIO LARIO, †† CARLOS PIERA, ‡‖ BEGOÑA CAMPOS, ‡‖ MÓNICA BESCÓS, †† FEDERICO OPPENHEIMER, *‖ and FRANCISCA RIVERA †‖

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...tion fraction significantly. Losartan and amlodipine had opposite effects on TGF-β₁. Amlodipine did not affect TGF-β₁ concentrations. In contrast, losartan reduced the plasma levels of TGF-β₁ by approximately by 50% (from baseline, 5.2 to 2.6 ng/ml: P = 0.01):
ESCLEROSI PERITONEAL

CANVIS A NIVELL DE MEMBRANA

Fibrosi o esclerosi simple

Peritonitis esclerosant

CANVIS A NIVELL DE VASOS

Hialinització: Relacionada amb la fibrosi, molt similar a la diabètica amb reduplicació de la membrana subendotelial.

Neoangiogènesi. També similar a la diabetis. Es relacionaria amb la forma esclerosant i hi haurien mediadors de la inflamació implicats com el TGF beta.
Role of the renin-angiotensin system in the pathogenesis of peritoneal fibrosis.

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Abstract
BACKGROUND: Although the effects of angiotensin type 1 receptor blocker (ARB) have been studied, little is known about ARBs in hypertensive patients undergoing dialysis. In the present study, we evaluated the effect of an ARB, olmesartan medoxomil (CS866), on the progression of peritoneal fibrosis in peritoneal dialysis by examining its effect in a model of peritoneal fibrosis in hypertensive rats.

MATERIALS AND METHODS: We allocated 40 male Wistar rats with 2-kidney, 1-clip renovascular hypertension (2K1C-RVH) to 4 groups (each n = 10) that were dialyzed using various solutions for 42 days as follows: Group I-10 mL pH 3.5 dialysis solution containing 1.35% glucose Group II-10 mL pH 3.5 dialysis solution, plus oral administration of CS866 5 mg/kg daily Group III-10 mL pH 3.5 dialysis solution, plus oral administration of the calcium channel blocker (CCB) amlodipine 3 mg/kg daily Group IV-10 mL pH 7.0 dialysis solution Dialysis solution was injected every day for 42 days.

RESULTS: Treatment with CS866 and amlodipine induced a significant reduction of blood pressure in 2K1C-RVH rats. In rats treated with pH 3.5 dialysis solution, necropsy findings revealed features identical to those of encapsulating peritoneal sclerosis (EPS). The typical appearance was multiple surfaces covered with granulation tissue or fibrosic tissue or both. Multiple adhesions were present. Microscopic findings revealed that acidic dialysis solution induced peritoneal fibrosis and loss of mesothelium. Treatment with CS866 prevented the progression of peritoneal fibrosis and adhesions. However amlodipine did not improve the progression of peritoneal fibrosis and peritoneal adhesions. In CS866-treated rats, no signs of EPS were present.

CONCLUSIONS: Long-term intraperitoneal exposure to acidic dialysis solution produced features typical of EPS. Acidic dialysis solution induces activation of the peritoneal renin-angiotensin system and progression of peritoneal fibrosis. For the peritoneum undergoing peritoneal dialysis, ARB protects against progression of peritoneal fibrosis and peritoneal adhesions.
Isoangustone A suppresses mesangial fibrosis and inflammation in human renal mesangial cells.

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Abstract
Development of diabetic nephropathy with fibrosis is associated with hyperglycemia-linked inflammation. Increased levels of proinflammatory factors have been found in diabetic patients with nephropathy. The present study was to test the hypothesis that isoangustone A, a novel compound present in licorice, can inhibit renal fibrosis and inflammation induced by high glucose (HG) in human mesangial cells through disturbing transforming growth factor β (TGF-β) and nuclear factor κB (NF-κB) pathways. Serum-starved mesangial cells were cultured in 33 mmol/L glucose media. Cells were treated with 1-20 μmol/L isoangustone A isolated from Glycyrrhiza uralensis licorice for three days. Exposure of cells to HG elevated connective tissue growth factor and collagen production, which was dose-dependently reversed by isoangustone A. Isoangustone A boosted HG-plummetered membrane type matrix metalloproteinase (MMP)-1 expression and diminished HG-elevated tissue inhibitor of MMP-2 expression. HG activated mesangial TGF-β1-SMAD-responsive signaling, which was repealed by ≥10 μmol/L isoangustone A. Furthermore, HG upregulated intracellular cell adhesion molecule-1 (ICAM-1) level and monocyte chemoattractant protein-1 (MCP-1) mRNA expression, and such increases were dose-dependently suppressed by isoangustone A most likely through hampering TGF-β signaling pathways. Blockade of NF-κB signaling appeared to be responsible for attenuating HG-triggered induction of ICAM-1 and MCP-1. Our findings provide the first evidence that isoangustone A dampens mesangial sclerosis associated with inflammation in response to HG through hindering TGF-β and NF-κB signaling.