related to elevated calcium levels with resultant nephrolithiasis and nephrocalcinosis. Other manifestations, including granulomatous interstitial nephritis, several forms of glomerulonephritis and even immunotactoid glomerulonephritis, may occur. Motile proximal tubular cell cilia have even been reported in a patient with renal sarcoidosis and hypercalcaemia [14]. The idea that sarcoidosis is an inappropriate reaction to an ubiquitous microorganism, *P. acnes*, has interesting therapeutic considerations. Sarcoidosis continues to be a disease that confuses, confounds and surprises the non-aware clinicians.

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Contrast-enhanced sonography as early diagnostic tool of chronic allograft nephropathy

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Keywords: chronic allograft nephropathy; colour Doppler ultrasonography; contrast-enhanced sonography; kidney transplantation; renal allograft

A resistance index (RI) obtained by colour Doppler ultrasonography is a standard procedure in the routine diagnosis of renal allografts, and has recently been shown to be associated not only with allograft, but also with patient survival [1]. Although the value of colour Doppler ultrasonography of the renal allograft—especially in the early post-operative period—is undisputed, uncertainties persist as to its diagnostic and prognostic value and its clinical application. It is worth noting that RI not only reflects renovascular resistance, but also indirectly reflects haemodynamic parameters such as elasticity of the large upstream capacity vessels [2,3]. In the interpretation of RI values, surrogate markers for reduced vascular compliance such as intima media thickness, pulse pressure

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or—preferably if possible—pulse wave velocity should thus be ascertained [3]. In addition, it has been demonstrated that a threshold value of the RI of 0.8 is very limited and results in lower sensitivity and specificity in the diagnosis of, for example, chronic allograft nephropathy (CAN) [4]. CAN is difficult to diagnose by non-invasive methods and an estimation of the RI value is not a reliable tool for its diagnosis [5,6]. For this reason, the degree of CAN is frequently underestimated when using conventional colour Doppler ultrasonography, especially when post-transplantation serum creatinine is close to the normal range [4]. However, early diagnosis of CAN may play a major role in a long-term allograft survival and requires additional therapeutic interventions. Any technique which can evaluate the microvascular integrity of the renal allograft and which can image and quantify the perfusion of the allograft, is thus important [7,8].

A new option in the ultrasonographic diagnosis of biopsy-proven CAN is the real-time contrast-enhanced sonography technique (CES) [4]. Various animal and clinical trials have verified the practicability and safety of CES [9]. CES is a technique which is easy to perform, non-invasive, reproducible and provides the assessment of parenchymal blood perfusion. CES is based on the use of an ultrasonographic contrast medium containing gas-filled microbubbles, which is administered intravenously as a bolus injection for 10–20 s. Before application of the contrast medium, the imaging mode is performed with a low mechanical index in accordance with international guidelines for the use of contrast media in ultrasonography [10]. The initial visibility of the contrast medium occurs after a time of 15–30 s. When optimal renal visibility has been achieved after 35–50 s, a short-lasting pulse with a high mechanical index is transmitted to destroy the microbubbles. After the emission of the high-mechanical index, the ultrasound machine automatically reverts back to the low-mechanical index and the replenishment kinetics are recorded over a period of 10–20 s.

A region of interest (ROI) is subsequently placed in the renal cortex for quantitative analysis of the allograft tissue perfusion. Interlobar and arcuate arteries must be carefully excluded from the ROI. The images are analysed quantitatively offline. The maximum visibility of the contrast medium and its increase over time are obtained and calculated by means of an exponential function as described elsewhere [4].

It has been shown that, in cases of biopsy-proven CAN, CES is superior in terms of sensitivity and specificity than the simple estimation of colour Doppler RI in the diagnosis of CAN [4]. CES can evaluate microvascular integrity in renal allografts and is able to diagnose CAN early, i.e. before the increase of serum creatinine or before the onset of irreversible damage. By means of CES, CAN can be diagnosed more accurately and earlier than by conventional colour Doppler ultrasonography techniques. Further studies are, of course, necessary to confirm these investigations; in particular, the evaluation of the significance of CES in other diseases such as vascular rejection or calcineurin inhibitor toxicity. Although CES is a very promising procedure which enables early diagnosis of CAN, modern techniques such as CES are limited in clinical routine due to the lack of investigators' experience with the new method and the lack of histological data necessary for the interpretation of new methods. Further studies are necessary because up to now, the number of renal allograft patients investigated by CES has been relatively small. In addition, in the case of bolus injection of the ultrasonographic contrast medium, the performance of the microbubble-containing contrast medium is probably not consistent and confounders may influence the calculation of the perfusion estimated in a ROI. The use of continuous infusion might provide more accurate results, however, bolus injection is an exact alternative and still feasible, as shown in earlier studies, and still presents a more practical approach in clinical settings [11,12]. It has not yet been determined what threshold value indicates a good cut-off point and, therefore, further studies are necessary.

In conclusion, the estimation of the colour Doppler ultrasonography RI alone in any diagnostic and prognostic interpretation, is as yet subject to many uncertainties. Modern techniques, such as CES, are very promising procedures which enable at least an early diagnosis of CAN. CES is not only associated with an improved diagnostic value compared with colour Doppler ultrasonography for the detection of CAN, but is also able to provide quantitative information on microvascular integrity and perfusion in an area of interest in kidney allografts. In addition, CES is a relatively cheap, non-invasive and reproducible technique.

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Are peroxisome proliferator-activated receptors new therapeutic targets in diabetic and non-diabetic nephropathies?

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Keywords: diabetic and non-diabetic nephropathies; peroxisome proliferator-activated receptors (PPAR) α, γ and β/δ agonists; renal protection

suggest a potential benefit of PPAR agonists on diabetic and non-diabetic nephropathies. Herein, we describe the currently known effects of PPARα, -γ and -β/δ agonists on diabetic and non-diabetic nephropathies, and more precisely, focus on their potential positive impact on kidneys.

Introduction

Peroxisome proliferator-activated receptors (PPAR), members of the nuclear hormone-receptor superfamily of ligand-binding-transcription factors, are involved in the pathophysiology of the metabolic syndrome. Agonist activation of PPAR provides a new pharmacological pathway to the treatment of the metabolic syndrome and its complications. Since one of the major complications of this syndrome is nephropathy, the potential benefit of PPARα, -γ and $-\beta/\delta$ agonists on kidney merits examination. Moreover, numerous studies have demonstrated that, in addition to their hypolipidaemic and anti-diabetic effects, these drugs possess anti-inflammatory, anti-fibrotic and anti-proliferative properties. These data strongly

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Renal effects of PPARα agonists

PPARα agonists are involved in lipid-metabolism regulation primarily by increasing fatty acid β oxidation. PPARα are predominantly expressed in tissues with high peroxisomal β oxidation and mitochondrial activities (liver, heart, skeletal muscle, intestine and kidney) and, to a lesser extent, in other tissues. Pharmacological PPARα agonists, such as fibrates, are also involved in almost all steps of lipoprotein metabolism. They lower hepatic triglyceride production by increasing fatty acid β oxidation, increase the high-density lipoprotein (HDL)-cholesterol level by raising expression of apolipoproteins AI and AII, favour reverse cholesterol transfer by increasing hepatic scavenger-receptor class B type 1 (SR-B1), necessary for the uptake of HDL-cholesterol and promote HDL-mediated cholesterol efflux from macrophages located in the vascular wall by inducing ATP-binding