Proteinuria in an African HIV-infected patient: effects of telmisartan

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INTRODUCTION

ntensive use of combined antiretroviral therapy (cART) has considerably altered the prognosis of HIV infection resulting in a decline of mortality and in a diversity of HIV-related causes of death [1]. As patients survive longer, renal disease has become an important contributing factor to morbidity and mortality [2]. Kidney disease in HIV may be primarily caused by traditional risk factors, such as hypertension, and by metabolic complications of HIV infection and its treatment, such as diabetes [2, 3]. Cross-sectional studies have described a 4-17% prevalence of reduced kidney function in diverse HIV-infected populations, as well as an increased prevalence of microalbuminuria and proteinuria [4-7]. Among patients with established chronic kidney disease (CKD), HIV infection has been associated with an increased rate of kidney function decline and progression to end-stage renal disease [2]. HIV-associated renal disease with overt proteinuria has been associated with poorer outcomes and increased mortality [6]. Moreover, an increased urinary albumin excretion rate, even in the microalbuminuric range, is an indicator of glomerular damage and has been found to be associated with increased risk of cardiovascular disease (CVD) and mortality in the general population [8]. The pathophysiological mechanism underlying urinary albumin excretion and the increased risk of CVD are not fully understood. Both HIV and non-HIV-related factors may play a role. Recently, systemic endothelial dysfunction and inflammation has been suggested as a link between HIV infection, renal damage and CVD [6]. Microalbuminuria predicts the development of proteinuria among HIV-infected persons [9]. Because proteinuria is a major risk factor for the progression of renal disease and it has been linked to poorer outcomes, strategies to affect microalbuminuria should be tested. The renin-angiotensin-aldosterone system (RAAS) is a major regulator of blood pressure and vascular response to injury. RAAS inhibition exerts an antiproteinuric effect independent of blood pressure reduction [10]. Angiotensin II receptor blockers (ARBs) provide renoprotective effects in non-infected patients with mild-to-moderate CKD [9]. Telmisartan, an ARB partial agonist of the PPAR-γ approved for the treatment of hypertension, seems to exert a nephro-protective effect independent from blood pressure reduction in the general population, but no data are known about telmisartan effects in HIV positive patients with proteinuria [11]. A case is described of an African HIV-infected, cART-treated patient with hypertension and severe proteinuria treated with telmisartan.

CASE REPORT

A 52-year-old African male HIV-infected (CDC A1) patient came to our examination because of discovered HIV antibody positivity. He had familiarity for hypertension and his personal history included promiscuous sexual relations, and previous hospitalization in Italy because of high blood pressure (BP) and chronic kidney disease (CKD) consequent to nephrosclerosis. For these reasons he took 30 mg nifedipine twice a day, 100 mg atenolol daily, 4 mg doxazosin twice a day, 250 mg/day furosemide, and 150 mg allopurinolo daily. On admission he had 738 CD4/ mmc; CD4/CD8 ratio 0.99; HIV-
RNA 1790 copies/ml; anti HBs and anti HBc antibodies positive; transaminases, glucidic and lipidic parameters within normal limits; BP 130/80 mmHg; glomerular filtration rate (GFR) assessed by the simplified MDRD logarithmic model (MDRD-GFR) 33 ml/min x 1.73m², serum creatinine 2.65 mg/dl, proteinuria 150 mg/dl, microalbuminuria 60.30 mg/dl, and cystatin C 2.28 mg/L. A renal biopsy was proposed but the patient refused it. After two months, since alterations of BP values and parameters of kidney function persisted, 40 mg telmisartan once daily was started without changes in remaining therapy. After nine months of therapy with telmisartan, proteinuria (30 mg/dl), microalbuminuria (6.75 mg/dl), and cystatin C (2.08 mg/L) decreased while mean BP values, MDRD-GFR remained stable. Even though the patient was not treated with cART, viro-immunological parameters were stable.

**DISCUSSION**

CKD in HIV-infected patients can manifest as diminution in the GFR, abnormal urinary protein excretion, or abnormal urinary findings [2]. The most common cause of CKD in patients HIV positive is the HIV-associated nephropathy (HIVAN), a form of focal segmental glomerulosclerosis usually associated with features of collapsing glomerulopathy [2]. However, proteinuria in the presence or absence of changes in GFR might be caused by multiple different conditions in HIV-infected patients [12]. Epidemiologically, black race is the most important determinant of kidney disease prevalence in HIV-infected persons. In a cohort study of HIV-infected subjects, blacks were at an increased risk of CKD and progressed to end stage renal disease (ESRD) at a markedly faster rate compared with whites [13]. The recent identification of polymorphisms in the genetic locus MYH9 are thought to influence susceptibility of blacks to HIVAN and to renal disease in general [2]. In our case the patient was of black race and had a CKD, although the histological diagnosis was not defined. Limited experimental data show that ARBs could be beneficial in the treatment of HIV-associated kidney diseases, inhibiting the development and progression of HIVAN in a mouse model [14]. Clinical data on ARBs employment in HIV-infected patients are anecdotal and there is only one designed study on this subject to date [15-17]. Telmisartan is an ARB with high lipophilicity, a high level of angiotensin II type-1 (AT1) receptor binding and a long half-life. On the basis of these properties it has been hypothesized to be an ideal drug to achieve a greater anti-proteinuric effect. Really, there is sufficient clinical evidence to support that telmisartan has renoprotective effects in patients with hypertension, diabetes and CKD in the general population [11]. But data in HIV-infected proteinuric patients are lacking. In our case telmisartan was well tolerated and effective in decreasing proteinuria, microalbuminuria, and cystatin C. Serum cystatin C is an alternative marker of kidney function and its serum levels have been correlated with renal function and cardiovascular risk in HIV-infected patients [18]. So, decreased proteinuria, microalbuminuria and cystatin C observed in this case could be indicative of nephro-protective effects of telmisartan also in a HIV-infected black race patient. This case shows that therapy with telmisartan has renoprotective effects in an African HIV-infected patient and allowed proteinuria to be improved. Additional investigations and controlled trials are needed to confirm the efficacy and safety of telmisartan in HIV-infected patients.

**Key words:** microalbuminuria, sartan, hypertension, kidney failure.
La malattia renale resta una delle maggiori comorbidità dell’infezione da HIV, in particolare nei soggetti di etnia africana. La nefropatia HIV-correlata, con franca proteinuria, è associata ad una prognosi peggiore e a un’aumentata mortalità. Il telmisartan è un farmaco che blocca il recettore dell’angiotensina II e che espleta anche azione di parziale agonista del recettore PPAR-\(\alpha\). Approvato per il trattamento ell’ipertensione, il telmisartan ha dimostrato di possedere anche un effetto nefroprotettivo indipendente dalla riduzione pressoria nella popolazione generale. Tuttavia, attualmente non vi sono dati su telmisartan nei pazienti HIV positivi con proteinuria. Viene qui descritto il caso di un paziente africano con infezione da HIV e marcata proteinuria che è stato trattato con il telmisartan. Il farmaco è stato ben tollerato e ha consentito la riduzione della proteinuria. Pertanto questo caso dimostra, per la prima volta, che il trattamento con telmisartan può espletare effetti renoprotettivi anche in un paziente di etnia africana con infezione da HIV.

**RIASSUNTO**

La malattia renale resta una delle maggiori comorbidità dell’infezione da HIV, in particolare nei soggetti di etnia africana. La nefropatia HIV-correlata, con franca proteinuria, è associata ad una prognosi peggiore e a un’aumentata mortalità. Il telmisartan è un farmaco che blocca il recettore dell’angiotensina II e che espleta anche azione di parziale agonista del recettore PPAR-\(\alpha\). Approvato per il trattamento dell’ipertensione, il telmisartan ha dimostrato di possedere anche un effetto nefroprotettivo indipendente dalla riduzione pressoria nella popolazione generale. Tuttavia, attualmente non vi sono dati su telmisartan nei pazienti HIV positivi con proteinuria. Viene qui descritto il caso di un paziente africano con infezione da HIV e marcata proteinuria che è stato trattato con il telmisartan. Il farmaco è stato ben tollerato e ha consentito la riduzione della proteinuria. Pertanto questo caso dimostra, per la prima volta, che il trattamento con telmisartan può espletare effetti renoprotettivi anche in un paziente di etnia africana con infezione da HIV.

**REFERENCES**


