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Pulse oximetry is useful for screening sleep apnoea syndrome in dialysis patients

Sir,

Sleep apnoea syndrome (SAS) is characterized by repetitive nocturnal hypoxia, while it is also known to be a risk factor for cardiovascular disease [1]. The prevalence of SAS in dialysis patients has been shown to range from 20 to 50% in comparison to a range of 2–4% in the general population [2,3]. Although the main type of SAS in the general population is obstructive type, SAS in dialysis patients includes features of both central and obstructive types [3]. Moreover, uraemia and metabolic acidosis are good predictors of SAS in dialysis patients [3].

The gold standard diagnostic test for SAS is overnight polysomnography (PSG). However, PSG is costly in terms of both time and money. Pulse oximetry and Epworth Sleepiness Scale (ESS), a questionnaire about daytime sleepiness have been widely used to screen for obstructive SAS because these are simple and easy methods to perform [4,5]. However, no screening method for SAS in dialysis patients has yet been clearly evaluated. The purpose of this study is to evaluate the usefulness of pulse oximetry and ESS for screening SAS in dialysis patients.

We studied 54 maintenance haemodialysis (HD) patients [male: 50%, age: 66.0 $\pm$ 24.2 years, diabetes mellitus: 39.9%, duration of HD: 5.7 $\pm$ 5.1 years and BMI: 22.7 $\pm$ 9.1] in Koga Red Cross Hospital during the period from April 2004 to March 2005. Patients with active malignancy and pulmonary disease were excluded. The validity of the pulse oximetry was confirmed by the synchronous recording of both PSG (Morpheus, Teijin Pharma Ltd, Japan) and pulse oximetry (PULSOX-Me300, Teijin Pharma Ltd, Japan) on dialysis day. We used the 3% oxygen desaturation index (ODI) and 4% ODI by pulse oximetry as a screening marker. In addition to pulse oximetry, ESS was used to investigate daytime sleepiness. We compared the apnoea–hypopnoea index (AHI) by PSG to 3% ODI, 4% ODI and ESS scores, respectively.

Using a cutoff of AHI$\geq$15 and 3% ODI (4% ODI) $\geq$15, the sensitivity and specificity were 100% (76.0%) and 55.2% (93.1%) respectively (Table 1). On the other hand, the sensitivity and specificity using a cutoff of AHI$\geq$15 and ESS scores$\geq$11 were 20.0% and 82.8% respectively (Table 1).

Both 3% ODI and 4% ODI were significantly correlated with AHI (3% ODI: $r = 0.657$, $P < 0.0001$; 4% ODI: $r = 0.618$, $P < 0.0001$) (Figure 1). However, no significant correlation was seen between ESS scores and AHI ($r = 0.149$, $P = 0.283$) (Figure 1).

In dialysis patients, pulse oximetry is superior to ESS for detecting SAS. The less efficacy of ESS may be due to the unique characteristics of SAS in dialysis patients [2,3]. We therefore suggest that pulse oximetry is useful for screening SAS in dialysis patients.

Conflict of interest statement. None declared.

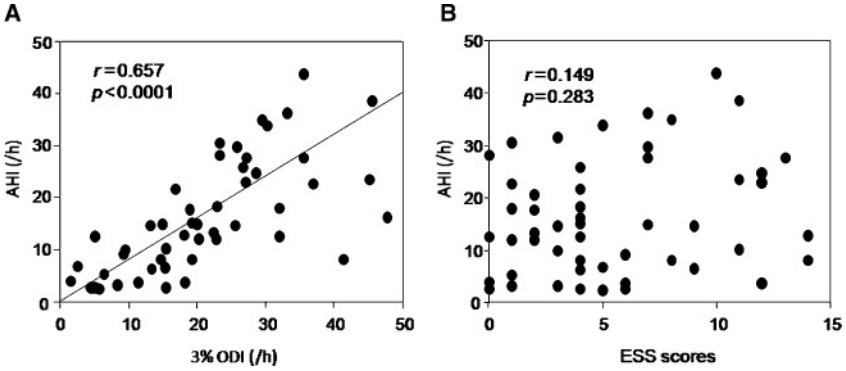

Fig. 1. Correlation between AHI and 3% ODI (**A**)/ESS scores (**B**) in dialysis patients ($n = 54$).

Table 1. Sensitivity and specificity of pulse oximetry/ESS scores screening for SAS in dialysis patients ($n = 54$)

		Mean value[a]	AHI cutoff	ODI or ESS cutoff	Sensitivity (%)	Specificity (%)
Pulse oximetry	3% ODI	23.4 $\pm$ 15.6	$\geq$15	$\geq$15	100	55.2
	4% ODI	15.7 $\pm$ 12.0		$\geq$15	76.0	93.1
ESS scores		5.9 $\pm$ 4.0		$\geq$11	20.0	82.8

[a]Data are presented as mean $\pm$ SD.

AHI: apnoea–hypopnoea index; ODI: oxygen desaturation index; ESS: Epworth Sleepiness Scale.

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Cinacalcet in HIV haemodialysis patients

Sir,

Cinacalcet HCL (MIMPARA®), a positive allosteric modulator of the calcium-sensing receptor (CaR) on the surface of the parathyroid glands, reduces serum parathyroid hormone (PTH) levels in more than 80% of haemodialysis (HD) patients [1]. The efficacy and safety of cinacalcet has been demonstrated in several studies [1,2], but its use in HIV patients on chronic dialysis is not described. We report two HD patients with HIV infection treated simultaneously with anti-retroviral therapy and cinacalcet.

A 24-year-old black woman was admitted in July 2002 for end-stage renal disease (ESRD) of unknown origin that required chronic HD. Simultaneously, HIV-1 infection was diagnosed. A tritherapy with efavirenz 600 mg, lamivudine 25 mg and didanosine 100 mg per day was initiated in January 2004, resulting in sustained undetectable HIV plasma viral load and stable T4 levels ($>550/mm^3$). Cinacalcet was started in May 2007 at 30 mg/day and progressively increased to 90 mg without any efficacy (intact parathyroid hormone (iPTH) > 1000 pg/ml). In December 2007, cinacalcet was stopped and a parathyroidectomy was performed. Histological examination revealed a bilateral parathyroid adenoma. Efavirenz residual serum concentration after surgery and cinacalcet withdrawal was 1.5 μg/ml (normal range: 1.1–4 μg/ml).

A 45-year-old Caucasian man was treated by chronic HD for ESRD of unknown aetiology since July 2003. HIV-1 and hepatitis B virus (HBV) co-infection was discovered at the time of dialysis initiation. A combination of efavirenz 600 mg, lamivudine 50 mg, didanosine 125 mg per day and tenofovir 245 mg per week resulted in undetectable HBV and HIV plasma viral load with sustained stable T4 levels ($>600/mm^3$). Because of high serum iPTH (>1000 pg/ml), cinacalcet was initiated in May 2007 at 30 mg per day and further increased to 120 mg in November 2007 without efficacy. Efavirenz mean residual serum concentration on three consecutive measurements under cinacalcet therapy (120 mg) was 1.3 ± 0.5 (SD) μg/ml.

The two patients received concomitant treatment with sevelamer, calcium carbonate and vitamin D_3 during cinacalcet therapy. In both the cases, tolerance of cinacalcet and anti-retroviral treatment was good. Monthly monitoring of pancreatic and liver enzymes and serum calcium levels was not modified.

Analysis of the literature shows that more than 80% of HD patients on cinacalcet therapy achieve an ≥30% reduction in iPTH level from the baseline over 6 months [1]. In our cases, whereas cinacalcet was administered for more than 6 months, no effect on iPTH was observed despite increased cinacalcet dosage.

Little is known about the pathophysiology of resistance to cinacalcet. A role for non-compliance to the drug was excluded in both the cases. Defective sensitivity of the parathyroid cell to the calcimimetic drug has been proposed. Additionally, a relative resistance to cinacalcet was demonstrated in the case of severe decreased expression of CaR in parathyroid glands [3]. In our cases, resistance to cinacalcet was likely the result of drug interaction.

Cinacalcet is metabolized through cytochrome P450 (CYP) isoenzymes 3A4, 2D6 and 1A2. *In vitro* studies have demonstrated that cinacalcet is a potent inhibitor of CYP2D6. Additionally, data suggest that during concomitant treatment with cinacalcet, dose adjustment may be necessary for CYP3A4 and CYP1A2 inductors or inhibitors [4].

As the metabolism of lamivudine, didanosine and tenofovir do not involve CYP450, the culprit drug seems to be efavirenz. Efavirenz is metabolized via CYP450, particularly by 3A4 and 2B6 isoenzymes. Although efavirenz is an *in vitro* inhibitor for 2C9, 2C19, 3A4, 2D6 and 1A2 isoenzymes, it has been demonstrated in humans that efavirenz can be inductor for CYP450 enzymes and can also induce its own metabolism by this mechanism [5,6]. This enzymatic induction, especially for CYP3A4 isoenzyme, is probably responsible for most drug interactions with efavirenz. Despite the absence of a known pharmakokinetics interaction between cinacalcet and efavirenz, enzymatic induction of CYP3A4 metabolism by efavirenz is probably responsible for therapeutic failure of cinacalcet in the present cases. Unfortunately, this hypothesis could not be verified, as the measurement of the serum cinacalcet level is not currently available. However, a role for decreased numbers of CaR or defective sensitivity of parathyroid cells cannot be excluded.

In summary, cinacalcet in HD patients with chronic HIV infection treated by efavirenz seems inappropriate. Nephrologists need to be aware of this rare potential interaction. Surgical parathyroidectomy should be recommended.