pharmacokinetics. Adverse effects with zanamivir comprise nasal and throat discomfort, headache and cough.

Conclusion

Chronic renal disease is frequent in the general population. In the case of epidemia or pandemia of avian influenza A (H5N1), the two neuraminidase inhibitors, oseltamivir and zanamivir will therefore be used in patients with renal impairment. Although zanamivir does not necessitate any adjustment of its dosage in patients with renal failure, because it is not absorbed after oral inhalation, oseltamivir dosage must be reduced by half in patients with CrCl between 15 and 30 ml/min and may be used at the usual dose when CrCl is higher.

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ICAR, Department of Nephrology
Pitié-Salpêtrière Hospital
Paris
France
Email: svetlana.karie@psl.aphp.fr

Svetlana Karie
Vincent Launay-Vacher
Nicolas Janus
Hassane Izzedine
Gilbert Deray

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Nephrotoxicity of vancomycin in patients with normal serum creatinine

Sir,
The reported rate of nephrotoxicity of vancomycin (VCM) has been 7–16%. It can reach 35% with concurrent aminoglycosides and is associated with serum concentration >40 μg/ml [1]. However, in patients with normal serum creatinine (SCr), monitoring of VCM–serum concentrations is disputable [2]. We retrospectively studied 19 patients (age 51 ± 19 years, 12 women) who had a 50% increase of their normal baseline SCr (ARF) during VCM therapy. Trough serum concentration of VCM was monitored once the ARF diagnosis was made and it was >40 μg/ml in all patients (VCMmax). Initial VCM dosing regime was unchanged up to ARF, when VCM administration was stopped. Spearman's correlations between VCMmax and age, duration of therapy (△T), peak SCr, albumin and bilirubin were calculated. Results (mean ± SD): VCMmax, 83 ± 12 μg/ml (range 50–289); △T, 12 ± 9 days; baseline SCr, 1.0 ± 0.3 mg/dl; peak SCr, 3.6 ± 2.1 mg/dl; albumin, 2.1 ± 0.6 g/dl; bilirubin, 3.8 ± 7.2 mg/dl. Oliguria was present in nine patients (47%) and seven (37%) needed dialysis. Twelve patients worsened and were admitted to ICU. Concurrent with VCM, eight patients (42%) received another nephrotoxic drug (amphotericin in five). All the patients had other cause for ARF besides VCM [severe sepsis in 16 (84%)]. Survivors were six (47%), and in two of them SCr did not return to baseline. There was no correlation between VCMmax and any of the evaluated parameters. In conclusion, in order to avoid nephrotoxic levels, even in patients with normal SCr, VCM–serum concentration monitoring should be started and its dose appropriately adjusted as soon as any potential factor for ARF superimposes.

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Hospital das Clínicas
Nephrology Division
University of São
Paulo Medical School
São Paulo, SP
Brazil
Email: kader@usp.br

Vinícius S. Colares
Rodrigo B. Oliveira
Regina C. R. M. Abdulkader

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Associations of chronic kidney disease with the metabolic syndrome in non-diabetic elderly

Sir,
Chronic kidney disease (CKD) and the metabolic syndrome are worldwide public health problems. Few studies have reported that persons with mildly reduced kidney function are at greater risk for cardiovascular disease [1], but it remains unclear whether CKD contributes to prevalent metabolic syndrome in non-diabetic population. In addition, there are no studies that have focused on the elderly to evaluate the relationship between level of kidney function and prevalent metabolic syndrome.

Table 1. Multivariate, adjusted odds ratio and 95% confidence interval (CI) of reduced kidney function for the prevalent metabolic syndrome

Stage	Normal kidney function ($n=92$)	Mildly decreased kidney function ($n=170$)	Chronic kidney disease ($n=53$)
Description	Estimated GFR $\geq$90 ml/min per 1.73 m^2 (the reference group)	Estimated GFR 60–89 ml/min per 1.73 m^2 (corresponding to stage 2 CKD)	Estimated GFR $<$60 ml/min per 1.73 m^2 (corresponding to stages 3–4 CKD[b])
Odds ratio[a](95%CI)	1.00	2.26 (1.04–4.89)	4.55 (1.69–12.25)
P-value		0.040	0.003

[a]Adjusted for age, sex, smoking habit, total cholesterol, prior cardiovascular disease, area under the response curve of plasma glucose (AUC-G), area under the response curve of plasma insulin (AUC-I) and the homoeostasis model assessment of insulin resistance (HOMA-R).
[b]Subject with kidney failure of an eGFR $<$15 ml/min per 1.73 m^2 (stage 5 CKD) was absent in the current analysis.

The study sample was drawn from a database of 954 Japanese who had undergone a 75 g oral glucose tolerance test (OGTT) as part of an evaluation for glucose intolerance. Only older individuals, $\geq$65 years of age, were included in the present analysis. Exclusion criteria were overt diabetes; fasting hyperglycaemia $\geq$7.0 mmol/l or 2 h plasma glucose $\geq$11.1 mmol/l; or those with signs of serious diseases which affect insulin sensitivity. Hence, a total of 315 non-diabetic elderly were included in the present analysis. Estimated glomerular filtration rate (eGFR) was calculated by using the equation developed by the Modification of Diet in Renal Disease (MDRD) study [2]. We calibrated eGFR values for smaller Japanese subjects ($\times$0.881) recommended by the Japanese Society of Nephrology. The metabolic syndrome was defined according to the revised criteria of the National Cholesterol Education Program Adult Treatment Panel III (ATPIII), recently recommended from the American Heart Association/National Heart, Lung, and Blood Institute [3]. Insulin sensitivity was measured by the homoeostasis model assessment of insulin resistance (HOMA-R) [4].

Of the 315 subjects included in the analysis, the mean age was 71.5 $\pm$ 5.2 year, 36.8% were female and mean body mass index was 23.4 $\pm$ 3.1 kg/m^2. The mean serum creatinine was 79.7 μmol/l with a range of 38.9–213.9 μmol/l, and the eGFR was 77.6 ml/min per 1.73 m^2, with a range of 23.4 to 144.5 ml/min per 1.73 m^2. Age tended to increase and total cholesterol tended to decrease in the groups with lower eGFR. By logistic regression analysis adjusted for potential confounding factors, reduced kidney function was independently associated with an increased risk for prevalent metabolic syndrome (Table 1).

Prior study has been consistent in showing an association between decreased kidney function and increased insulin resistance even in patients with incipient kidney disease [1]. In the Third National Health and Nutrition Examination Survey, insulin resistance estimated by HOMA-R was associated with an increased risk for CKD in non-diabetic participants [5]. But, it remains unknown whether CKD is associated with the metabolic syndrome in non-diabetic elderly. Our study has several strengths, including the large number of subjects who had undergone 75 g OGTT, exclusion of individuals with diabetes and adjustment for a number of potential confounding factors, such as insulin resistance (HOMA-R). But, several limitations may affect the interpretation of our results. First, we selected a relatively high-risk population who had undergone 75 g OGTT. Second, we applied the revised ATPIII criteria in this study. When applying the revised criteria (as a glucose cutoff point of 5.6 mmol/l and a lower threshold of waist) instead of the original ATPIII criteria, the prevalence of the metabolic syndrome might be overestimated in our subjects compared with those in non-institutionalized population. Third, we used the MDRD equation to estimate GFR. The MDRD equation was validated in both White and Black population, but the precise calibration of this equation for Japanese has not been established. Because Japanese have smaller body mass for whites, we calibrated eGFR values using a recommendation by the Japanese Society of Nephrology. On the basis of our results, the mildly decreased kidney function as well as chronic kidney disease might be an important factor for the metabolic syndrome even after adjusting for insulin resistance in non-diabetic elderly Japanese.

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[1]First Department of Internal Medicine
Nara Medical University
Kashihara, Nara
[2]Health Care Unit
SHARP Corporation, Japan
Email: kanauchi@nmu-gw.naramed-u.ac.jp

Masao Kanauchi[1]
Kimiko Kanauchi[2]
Kuniko Kimura[1]
Tomoko Inoue[1,2]
Yoshihiko Saito[1]

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Progression of vascular calcification increases QT interval in haemodialysis patients

Sir,

Vascular calcifications are now recognized as an important determinant of cardiovascular mortality in patients on