Efek samping pengobatan antiepilepsi jangka panjang terhadap tubulus ginjal = Side effect of long term antiepileptic drugs on kidney tubules

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Abstrak

[ABSTRAK
  Latar belakang: Obat antiepilepsi (OAE), seperti asam valproat (valproic acid, VPA) dan karbamazepin (carbamazepin, CBZ) sering digunakan dalam jangka waktu panjang. Obat-obatan tersebut dapat mengganggu fungsi tubulus ginjal. N-acetylbeta-D-glucosaminidase

(NAG) urin merupakan enzim yang dapat dipakai sebagai marka fungsi tubulus sehingga diharapkan dapat mendeteksi jejas tubulus. Penelitian mengenai efek nefrotoksik VPA dan CBZ terhadap tubulus menggunakan penanda NAG urin ini belum pernah dilakukan di Indonesia.

Tujuan: Mengukur indeks NAG (iNAG) urin pada anak epilepsi yang mendapat VPA dan atau CBZ jangka panjang untuk mendeteksi efek nefrotoksik kedua OAE tersebut pada tubulus ginjal.

Metodologi: Penelitian ini menggunakan studi potong lintang yang dilakukan pada Januari-Maret 2015. Subjek penelitian ini adalah 36 anak epilepsi dengan monoterapi VPA, 14 dengan monoterapi CBZ, 14 dengan kombinasi VPA dan CBZ, rentang usia 3-16 tahun. Pada seluruh subjek dilakukan pemeriksaan kadar kreatinin urin dan kadar NAG urin. Sebagai nilai acuan kadar NAG urin, dipilih 30 anak sehat dengan usia yang disesuaikan dengan subjek penelitian. Untuk menghilangkan variabilitas harian, maka NAG urin dibagi dengan kreatinin urin, menjadi iNAG (satuan U/g kreatinin). Indeks NAG dikategorikan meningkat bila nilainya lebih dari rerata NAG + 2 SD kelompok anak sehat.

Hasil: Rerata iNAG urin pada kelompok anak sehat, monoterapi VPA, monoterapi CBZ dan kombinasi VPA dan CBZ berturut-turut adalah 3,01; 5,9; 4,07; 6,9. Tiap kelompok kasus memiliki rerata iNAG urin lebih tinggi dibandingkan anak sehat. Proporsi kenaikan iNAG urin ditemukan pada 11/ 36 anak dengan monoterapi VPA, 2/14 pada kelompok monoterapi CBZ, dan 9/14 pada terapi kombinasi VPA dan CBZ.

Simpulan: Pemberian VPA jangka panjang dapat menyebabkan jejas pada tubulus ginjal dengan parameter kenaikan iNAG urin, dan jejas tubulus ini meningkat dengan pemakaian VPA dan CBZ secara kombinasi.ABSTRACT Background: Antiepileptic drugs such as valproic acid (VPA) and

carbamazepine
(CBZ) are often used in the long term manner. These drugs may disrupt the function of the kidney tubules. Urinary N-acetyl-beta-D-glucosaminidase (NAG) is an enzyme that can be utilised as marker of tubular function and is therefore expected to be useful in detecting kidney tubular injuries. There have been no studies conducted in Indonesia on the nephrotoxic effect of VPA and CBZ to tubules using urinary NAG as marker.

Objectives: To measure urinary NAG index (iNAG) in epileptic children with longterm

use of VPA and CBZ in order to detect their nephrotoxic effects on kidney tubules.
Methods: This is a cross-sectional study performed on January to March 2015. The subject includes 36 patients on VPA monotherapy, 14 patients on CBZ monotherapy, and 14 patients on VPA-CBZ combination therapy with age ranging from 3 to 16 years old. Urine creatinine concentration and urinary NAG values of all the patients are measured. Thirty age-adjusted healthy children are included in the study for NAG value reference. To eliminate NAG diurnal variability, iNAG is calculated by dividing urinary NAG value and urine creatinine concentration. Urinary iNAG values that fall above the +2 standard deviations from the mean of healthy children are considered elevated.
Results: Urinary iNAG values of the healthy children, VPA monotherapy, CBZ monotherapy, and VPA-CBZ comination therapy groups are 3.01; 5.9; 4.07; 6.9 U/g respectively. Each case group has higher urinary iNAG mean value than the control group. Urinary iNAG urine increased proportion is found in 11/36 children on VPA monotherapy, 2/14 children on CBZ monotherapy, and 9/14 children on VPA-CBZ combination therapy.
Conclusions: Long-term VPA use may cause renal tubular injuries with increased urinary iNAG value as parameter. Tubular injury is increased with the use of VPA and CBZ in combination. ;Background: Antiepileptic drugs such as valproic acid (VPA) and carbamazepine
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