Profil Kadar Glikosaminoglikan dan Aktivitas Enzim N-Acetylgalactosamine Sulfatase (GALNS) Berdasarkan Jenis Mutasi Gen GALNS pada Pasien MPS-IVA di Indonesia = Profil of Glycosaminoglycans Level and Activity of N-Acetylgalactosamine Sulfatase (GALNS) Based on Type of GALNS Gene Mutation of Mucopolysacchariosis IVA Patients

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Abstrak

Introduksi. Mukopolisakaridosis tipe IVA (MPS IVA; Morquio A) merupakan kelainan genetik ditandai dengan adanya gangguan aktivitas enzim N-acetylgalactosamine-6-sulfatase (GALNS). Defisiensi enzim GALNS menyebabkan kegagalan degradasi KS dan C6S sehingga terakumulasi di urin.
Metode. Data varian gen GALNS diperoleh dari Database Human Genetic Research Center IMERI FK UI. Perubahan struktur protein berdasarkan varian yang telah teridentifikasi divisualisasi menggunakan BIOVIA Discovery Studio. Pengukuran aktivitas enzim GALNS menggunakan sampel leukosit dengan metode fluorosensi 4-metilumbelliferone (4-MU). Pengukuran kadar KS dan C6S menggunakan sampel urin dengan metode ELISA kompetitif.
Hasil. Varian missense yang teridentifikasi menyebabkan perubahan hilangnya ikatan hidrogen, jembatan disulfida, struktur hidrofobik dan salt bridge, sedangkan varian delesi mereduksi basa nukleotida yang mengakibatkan perubahan pemetaan asam amino Rerata nilai aktivitas spesifik GALNS pada pasien MPS IVA adalah 1,81 nmol/h/mg. Rerata kadar KS dan C6S pasien MPS IVA di Indonesia secara berturut-turut adalah 15,90 ng/mg kreatinin dan 2,14 ng/mg kreatinin.
Kesimpulan. Pada keenam pasien MPS IVA varian yang telah teridentifikasi adalah varian missense dan delesi. Kedua tipe varian memengaruhi rendahnya nilai aktivitas spesifik GALNS (1,81 nmol/h/mg) dan meningkatnya kadar GAG urin pada pasien MPS IVA
.....Introduction. Mucopolysaccharidosis type IVA (MPS IVA; Morquio A) is a genetic disorder characterized by impaired activity of enzyme N-acetylgalactosamine-6-sulfatase (GALNS). Impaired activity of enzyme GALNS caused by failure degradation of glycosaminoglycans (GAG) including Keratan Sulfate (KS) and Chondroitin 6-Sulfate (C6S) and it leads to accumulating GAG in urine.
Methods. Data on GALNS gene variants was obtained from Human Genetic Research Center IMERI Universitas Indonesia. Changes in protein structure based on identified variants were visualized using BIOVIA Discovery Studio. Measurement of GALNS enzyme activity using leukocyte samples with the 4-methylumbelliferone (4-MU) fluorescence technique. KS and C6S levels were measured using urine samples using ELISA.
Results. The identified missense variant causes changes interaction of amino acid GALNS including loss of hydrogen bonds, disulfide bridges, hydrophobic structures, and salt bridges, while the deletion variant reduces nucleotide bases which results in changes in amino acid mapping. Mean specific activity of GALNS in MPS IVA patients is 1.81 nmol/h/mg. The mean levels of KS and C6S in MPS IVA patients in Indonesia were 15.90 ng/mgcreatinine and 2.14 ng/mgcreatinine, respectively.
Conclusions. Among six MPS IVA patients, the variants that were identified were missense and deletion

variants. Both types of variants affected low value of GALNS specific activity (1.81 nmol/h/mg) and increased urinary GAG levels in MPS IVA patients.