Profil Kadar Heparan Sulfat dan Dermatan Sulfat Urin Berdasarkan Jenis Mutasi Gen Iduronat-2-Sulfatase Pasien Mukopolisakaridosis Tipe II di Indonesia = Profile of Urinary Heparan Sulfate and Dermatan Sulfate Concentration Based on Type of Iduronate-2-Sulfatase Gene Mutation of Mucopolysaccharidosis Type II Patients in Indonesia.

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Abstrak

Mukopolisakaridosis tipe II (MPS II) merupakan penyakit kelainan lisosomal langka yang disebabkan oleh mutasi pada gen iduronat 2-sulfatase (IDS) dapat menyebabkan disfungsi dari enzim I2S yang dihasilkan sehingga molekul heparan sulfat (HS) dan dermatan sulfat (DS) terakumulasi pada jaringan. Penelitian ini dilakukan untuk mengetahui dan menganalisis hubungan kadar HS dan DS urin dengan jenis mutasi gen IDS pada penderita MPS II di Indonesia. Data susunan nukleotida gen IDS dari tujuh pasien MPS II dianalisis untuk melihat jenis mutasi dan dibuat model 3D proteinnya. Analisis 3D protein akan dikorelasikan dengan kadar HS dan DS urin pasien tersebut yang diukur menggunakan metode Enzyme-Linked Immunosorbent Assay (ELISA). Hasil analisis mutasi ditemukan beberapa jenis mutasi, seperti mutasi nonsense (1/7), delesi (2/7), insersi (1/7), dan missense (3/7). Dari ketujuh pasien tersebut, tiga diantaranya (P2, P6, P7) telah menjalani terapi ERT. Kadar HS urin dari ketujuh pasien menunjukkan peningkatan yang beragam dibandingkan dengan kadar HS normal. Berbeda dengan HS, kadar DS urin sampel pasien ada yang mengalami sedikit peningkatan (P1, P2, P7) dan ada pula yang tetap berada pada rentang kadar DS normal (P3, P4, P5, P6). Keragaman kadar HS dan DS sampel pasien tersebut sangat dipengaruhi oleh letak mutasi, jenis mutasi, diagnosis dan prognosis yang ditegakkan sedini mungkin, terapi ERT yang telah dilakukan pasie, durasi ERT, dan respon masing-masing pasien terhadap pengobatan yang telah diberikan.

.....Mucopolysaccharidosis type II (MPS II) is a rare lysosomal disorder caused by mutations in the iduronat 2-sulfatase (IDS) gene that can cause dysfunction of I2S enzyme so that the heparan sulfate (HS) and dermatan sulfate (DS) molecules accumulate in the tissue. This study was conducted to determine and analyze the relationship of urinary HS and DS levels with the type of IDS gene mutation in MPS II patients in Indonesia. The nucleotide of IDS genes sequences from seven MPS II patients were analyzed to see the type of mutation and the 3D protein model was made. 3D protein analysis will be correlated with urinary HS and DS levels of the patients measured by using the Enzyme-Linked Immunosorbent Assay (ELISA) method. Results of mutation analysis results found several types of mutations, such as nonsense mutations (1/7), deletions (2/7), insertions (1/7), and missense (3/7). From the seven patients, three of them (P2, P6, P7) had undergone ERT therapy. The urine HS level of the seven patients showed a varied increase compared to normal HS levels. In contrast to HS, the urine DS level of the sample of patients had a slight increase (P1, P2, P7) and some remained in the normal DS level range (P3, P4, P5, P6). The diversity of HS and DS levels of the patient's samples is strongly influenced by the location of the mutation, type of mutation, diagnosis and prognosis that is enforced as early as possible, ERT therapy has been carried out, ERT duration, and each patient's response to the treatment given.