Mekanisme terjadinya hiperaldosteronisme primer pada penderita obstructive sleep apnea: peranan neuroglobin, cryptochrome-1 dan cryptochrome-2 = Mechanism of primary hyperaldosteronism in obstructive sleep apnea: the role of neuroglobin cryptochrome 1 and cryptochrome 2

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Abstrak

ABSTRAK
Latar belakang: Obstructive Sleep Apnea OSA berkorelasi dengan hipertensi. Pada OSA dengan hipertensi resisten ditemukan hiperaldosteronisme primer. Disfungsi gen Cryptochrome-1 Cry1 dan Cry2 menyebabkan peningkatan aldosteron dan hipertensi pada mencit. Neuroglobin Ngb diketahui mempengaruhi gen Per. Peneliti menduga penurunan kadar Cry pada OSA menyebabkan peningkatan aldosteron dan hipertensi, dan kadar neuroglobin serum mempengaruhi Cry.Metodologi: Subyek dikumpulkan secara konsekutif dari survei populasi Jakarta berusia 30-65 tahun yang menderita OSA sedang-berat dan hipertensi. OSA didiagnosis menggunakan portable monitor tipe 2 Alice Pdx unattended. Subyek didiagnosis hipertensi bila tekanan darah pagi hari lebih dari 140/90 mmHg atau minum obat anti hipertensi. Konsentrasi aldosteron, renin, neuroglobin, Cry1 dan Cry2 serum ditentukan dengan metode ELISA. Hiperaldosteronisme ditentukan dengan Aldosterone Renin Ratio ARR >20.Hasil Penelitian: Terdapat 40 subyek yang memenuhi kriteria, 26 laki-laki dan 14 perempuan dengan median usia 52,5 tahun, BMI 27,46 kg/m2, AHI 34.8 kali/jam. Ditemukan 16 subyek dengan hiperaldosteronisme primer HP dan 24 subyek nonHP. Tidak ditemukan perbedaan bermakna Cry1, Cry2 dan Ngb pada kedua kelompok. Walaupun secara statistik tidak bermakna terdapat kecenderungan penurunan kadar Cry1 dan Cry2 pada ARR tinggi pada HP, terutama Cry1. Ditemukan korelasi positif antara kadar Ngb dengan Cry1 pada HP Spearman rsquo;s rho= 0.455, p= 0.038 . Selain itu ditemukan hubungan bermakna antara Cry1 dan O2 nadir p= 0.026 . Cry1 menurun pada hipoksia berat. Pada HP terdapat kecenderungan penurunan Ngb pada kadar O2 nadir rendah, walaupun secara statistik tidak bermakna.Kesimpulan: Penurunan kadar Cry1 mungkin berhubungan dengan terjadinya kelebihan aldosteron pada OSA. Ngb tampak berperan pada penurunan Cry1.
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ABSTRACT
Background Obstructive Sleep Apnea OSA patients with resistant hypertension also had primary hyperaldosteronism. Cryptochrome 1 Cry1 and Cry2 dysfunction were associated with increased aldosterone and hypertension. Neuroglobin Ngb is known to influence Per gene. In this study we want to investigate whether Cry decrease in moderate to severe OSA causes aldosterone increase and hypertension, also the possible role of Ngb on Cry expression.Methods Subjects were recruited consecutively from a population study of OSA in Jakarta, subjects aged 30 65 years with moderate to severe OSA and hypertension. OSA was diagnosed using unattended type 2 portable monitor Alice Pdx , hypertension was established when morning blood pressure exceed 140 90 mmHg or on anti hypertensive drugs. Serum aldosterone, renin, neuroglobin, Cry1 and Cry2 were determined using ELISA method. Primary hyperaldosteronism was

determined by Aldosterone Renin Ratio ARR 20.Results Of the 40 subjects recruited, there were 26 males and 14 females, with median age 52.5 years, BMI 27.46 kg m2, and AHI 34.8 times hour. We found 16 subjects with primary hyperaldosteronism PH and 24 nonPH. No difference in Cry1, Cry2 and Ngb levels was found in these groups. Although statistically not significant Cry1 and Cry2 concentration decrease with higher ARR in PH, especially Cry1. There was a positive correlation between Ngb and Cry1 in PH Spearman rsquo s rho 0.455, p 0.038 . There was relationship between Cry1 and nadir O2 p 0.026 . Cry1 was decreased in severe hypoxia. Although statistically not significant, serum Ngb decreased in severe hypoxia.Conclusions Cry1 decrease might be the cause of increased aldosterone in OSA. Ngb decrease is associated with Cry1 decrease.