

## ABSTRAK

### PERBANDINGAN HUBUNGAN POLIMORFISME GEN ENDOTELIAL NITRIT OKSIDA SINTASE DENGAN EDEMA PERIFOKAL BERDASARKAN CT SCAN ANTARA STROKE PERDARAHAN INTRASEREBRAL DENGAN STROKE ISKEMIK

**Latar belakang:** Kematian akibat Stroke perdarahan menempati urutan ketiga setelah penyakit kardiovaskular dan *outcome* memburuk jika volume edema perifokal meningkat. Mekanisme edema perifokal yang meningkat belum diketahui secara sempurna, diduga ada kaitan dengan genetik. Polimorfisme gen eNOS diyakini dapat menurunkan kadar Nitrit Oksida (NO) darah. Akibat kadar NO yang rendah terjadi vasokonstriksi, agregasi trombosit, adhesi leukosit dan proliferasi otot polos dinding vaskuler, akhirnya terjadi gangguan hemodinamik menyebabkan edema.

**Tujuan :** Mengetahui hubungan antara polimorfisme gen endotelial nitrit oksida sintase (eNOS) dengan volume edema perifokal berdasarkan pemeriksaan CT scan pada stroke perdarahan intracerebral dibanding stroke iskemik. Hubungan polimorfisme gen eNOS dengan kadar NO dan hubungan antara kadar NO dengan volume edema perifokal.

**Metode :** Penelitian dilakukan terhadap 92 pasien stroke dengan desain *cross-sectional*. Pengambilan sampel secara *consecutive sampling*. Polimorfisme gen eNOS ditentukan dengan metode PCR-RFLP. Volume edema diukur dengan CT scan secara *semi-automatic CT volumetry*. Pemeriksaan kadar NO diperiksa dengan kit *Cayman Systems* mengikuti protokol Griess. Uji Chi Square digunakan untuk menilai hubungan dua variabel dan uji korelasi Spearman untuk menilai hubungan antara NO dengan luas edema. Bermakna jika  $p < 0,05$ .

**Hasil penelitian :** Volume edema perifokal lebih besar pada stroke perdarahan intracerebral dengan mutan baik untuk polimorfisme T-786C maupun G894T ( $p=0,016$  dan  $p= 0,038$ ) dengan distribusi frekwensi 90,3% dan 9,7%. Kadar NO menurun jika ada polimorfisme ( $p=0,001$ ). Ada korelasi bermakna antara kadar NO yang rendah dengan besar volume edema ( $p=0,040$ ).

**Simpulan :** 1. Terdapat perbedaan hubungan polimorfisme gen eNOS dengan volume edema antara stroke perdarahan intracerebral dengan stroke iskemik. Apabila terdapat polimorfisme gen eNOS maka volume edema menjadi besar pada stroke perdarahan intracerebral dan secara statistik berbeda bermakna, sedangkan pada stroke iskemik tidak berbeda bermakna. 2. Terdapat perbedaan hubungan polimorfisme gen eNOS dengan kadar NO yang rendah antara stroke perdarahan intracerebral dengan stroke iskemik. 3. Terdapat korelasi yang lemah antara kadar NO yang rendah dengan edema yang meningkat.

**Kata kunci :** Polimorfisme, Nitrit Oksida, Edema perifokal, Stroke.

## ABSTRACT

### COMPARITION BETWEEN ENDOTHELIAL NITRIC OXIDE SYNTHASE GENE POLYMORPHISM WITH PERIFOVAL EDEMA BASED ON CT EXAMINATION IN INTRACEREBRAL HEMORRHAGE AND ISCHEMIC STROKE

**Background:** Mortality rate of hemorrhagic stroke are leading third ranks after cardiovascular disease and worsen outcome in case extensive perifocal edema. Mechanism of extensive perifocal edema completely unknown, suspected genetics factor. eNOS gene polymorphism is believed to reduce levels of nitric oxide (NO) in blood. Due to low levels of NO occurs vasoconstriction, platelet aggregation, leukocyte adhesion and proliferation of vascular smooth muscle wall. Finally occur hemodynamic disturbances cause edema.

**Objective:** To prove the relationship between polymorphisms of endothelial nitric oxide synthase gene with extensive perifocal edema based on CT scan on intracerebral hemorrhage and ischemic stroke.

**Methods:** A cross-sectional study for 92 subject with consecutive sampling collected. eNOS gene polymorphism was determined by PCR-RFLP method. Edema volume was measured by CT scan in semi-automatic CT volumetry. The levels of NO checked with Cayman Systems kit following the protocol Griess. Chi-square test was used to assess the relationship in the two variables and Spearman correlation test to assess the correlation between NO and extensive edema. Significant if  $p < 0.05$ .

**Result:** Perifocal edema increase on intracerebral haemorrhagic stroke in both mutant for the T-786C polymorphism and G894T ( $p = 0.016$  and  $p=0.038$ ) with frequensi distribution are 90.3% and 9.7%. NO levels decreased if there polymorphism ( $p = 0.001$ ). There is a significant correlation between low levels of NO and extensive edema ( $p = 0.040$ ).

**Conclusion:** 1. There are differences in eNOS gene polymorphism relationship with edema volume between intracerebral hemorrhage stroke with ischemic stroke . If there is a gene polymorphism of eNOS then becomes a large volume of edema in intracerebral hemorrhage stroke and statistically significant, whereas in ischemic stroke did not differ. 2. There are difference eNOS gene polymorphism relationship with the levels of NO were lower among of intracerebral hemorrhage stroke with ischemic stroke. 3. Less correlation between low levels of NO with increased edema.

**Keywords:** Polymorphism, Nitric Oxide, Perifocal edema, Stroke.