ABSTRACT

APOPTOSIS MECHANISM OF RETINAL GANGLION CELLS RATTUS NORVEGICUS INDUCED BY ETHAMBUTOL
(A True Experiment in Animal Model)

Purpose : Ethambutol is still the first-line drug for tuberculosis management. Toxic optic neuropathy is the most frequent side effect of ethambutol which is reversible if it can be identified early and can be irreversible if it is too late to detect and can cause permanent visual loss.The purpose of this study is to explain the mechanism of apoptosis in RGCs which is thought to underlie the occurrence of ethambutol toxic optic neuropathy.

Materials and methods : This study was a true experiment in animal model with a randomized control group design with time series test. A total of 42 male, adult *Rattus norvegicus* were divided into 6 groups with 3 control groups and 3 treatment groups. The treatment groups were given ethambutol at a dose of 15 mg / kg / day for each group within 5, 10 and 15 days orally using gauge. The rats in the control and treatment groups then sacrificed using cervical dislocation method under rat cocktail anesthesia and then the eye is enucleated for the sake of tissue examination. Expressions of SOD_2, MDA, PKC δ, p53, Cyt c, Caspase 3 and apoptosis were examined by immunohistochemical methods. The collected data was analyzed statistically with the R program. Bivariate analysis was tested with Kruskal Wallis test and then with Mann-Whitney test or t_2-free sample test. Multivariate analysis was tested with gradual correlation using Spearman test.

Results : Ethambutol affected in significant decreased expression of SOD_2 with p=0,002 in 5 days, p=0,013 in 10 days and p=0,018 in 15 days; significant increased MDA in 5 days with p =0,05 , 10 days with p = 0,017, 15 days with p= 0,002 ; not significant increased PKCδ in 5 days with p= 0,881, 10 days with p= 0,160, 15 days with p=0,100 ; significant increased p53 in 5 days with p= 0,012, 10 days with p= 0,002, 15 days with p=0,001; significant increased Cyt c in 5 days with p=0,004 , 10 days with p =0,001, 15 days with p=0,001; significant increased Caspase 3 in 5 days with p=0,001, 10 days with p= 0,003, 15 days with p= 0,001 and apoptosis in 5 days with p=0,001, 10 days with p=0,001, 15 days with p=0,001. The result of causalystic path analysis used Spearman test. Ethambutol caused significant decreased expression of SOD_2 with p=0,001rs =-63%, signicant correlation between SOD_2 to MDA with p=0,003 rs=-45%, MDA to Cyt c with p=0,001 rs=66%, Cyt c to apoptosis p=0,001 rs=79% and between p53 to Cyt c with p 0,001 rs71%

Conclusion : The mechanism of apoptosis of RGCs caused by ethambutol was showed by decreased of expression SOD_2, increased expression of MDA, p 53, Cyt c, Caspase 3 and apoptosis . These biomarkers are essensial to detect apoptosis as one of mechanism in cell death.

Keywords : Apoptosis, ethambutol, toxic, rattus, mechanism, SOD_2