Role of Permeability glycoprotein (P-gp) and Multidrug resistance protein 1 (MRP-1) in drug-resistance in mesial temporal lobe epilepsy

Mandeep Kaur[1], Tulika Gupta[1], Mili Gupta[2], Navneet Singla[1], Parampreet Singh[1], Yogendra Bansal[1], B.D. Radotra[1], and S.K. Gupta[1]

[1]Post Graduate Institute of Medical Education and Research
[2]Panjab University

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Abstract

About 30% of patients with epilepsy do not respond to anti-epileptic drugs leading to refractory seizures. The pathogenesis of drug-resistance in Mesial Temporal Lobe Epilepsy (MTLE) is not completely understood. Increased activity of drug-efflux transporters might be involved, resulting in subclinical concentrations of the drug at the target site. The major drug-efflux transporters are permeability glycoprotein (P-gp) and multidrug-resistance protein-1 (MRP-1). We have studied these two transporters in the sclerotic hippocampal tissues resected from the epilepsy surgery and compared their expression profile with the tissues resected from non-epileptic autopsy cases. Statistically significant over expression of both P-gp (p-value<0.0001) and MRP-1 (p-value 0.01) at gene and protein levels was found in the MTLE cases. The fold change of P-gp was more pronounced than MRP-1. Immunohistochemistry of patient group showed increased immunoreactivity of P-gp at blood brain barrier and increased reactivity of MRP-1 in parenchyma. The results were confirmed by confocal immunofluorescence microscopy. This suggested that P-gp in association with MRP-1 might be responsible for the multi-drug resistance in epilepsy.

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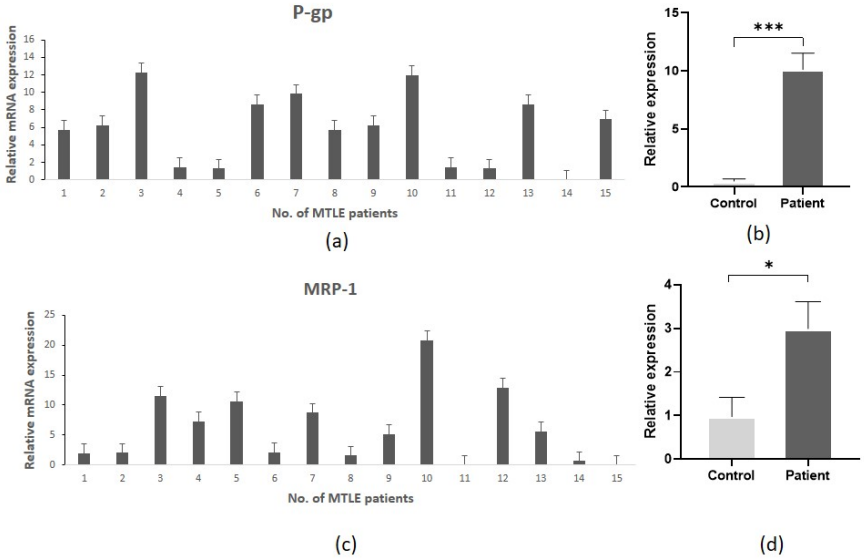

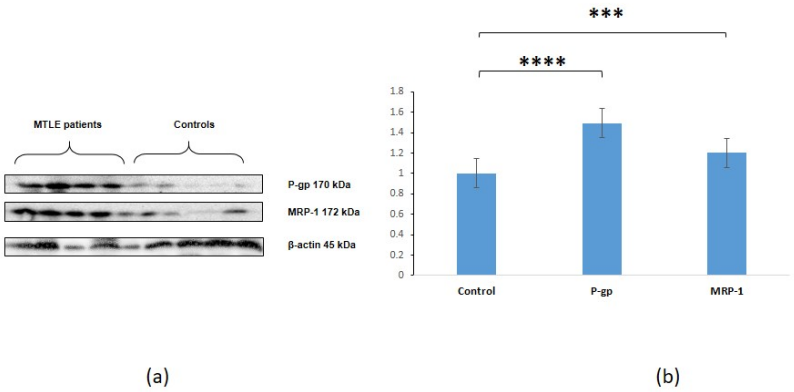

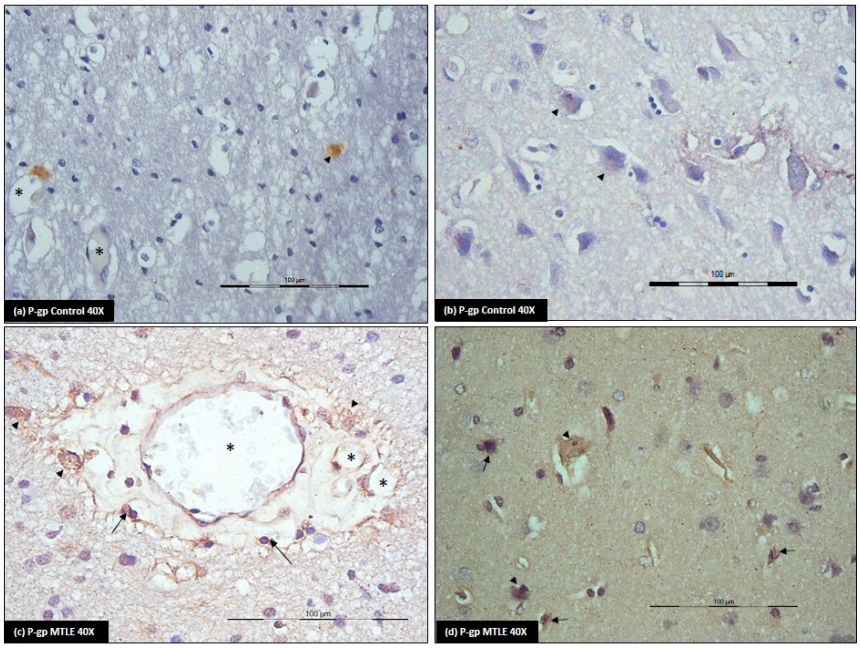

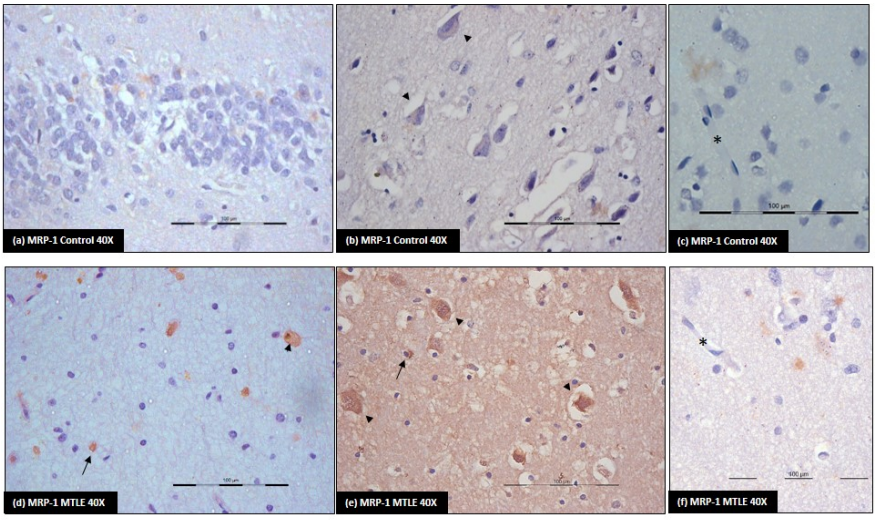

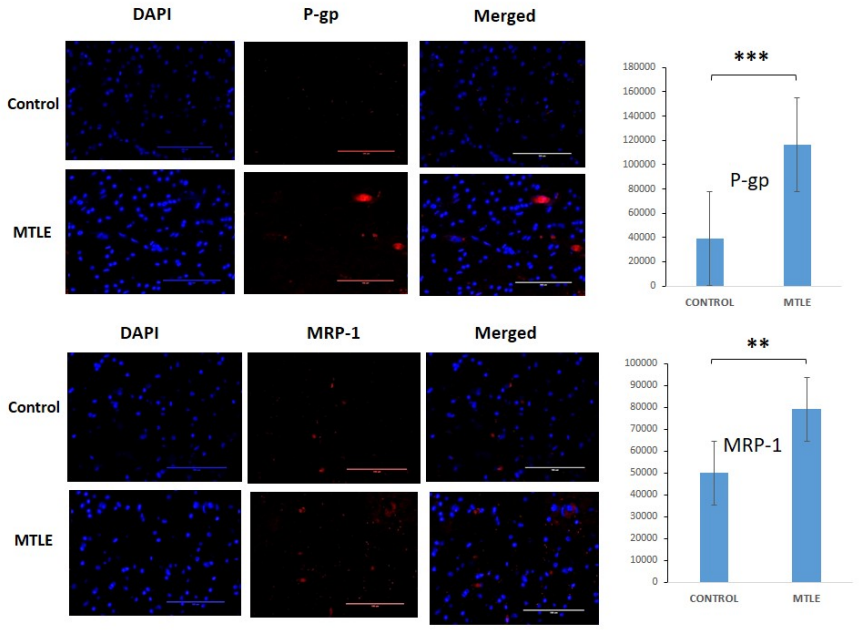

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