Clinical Pharmacology

36. Efficacy and Tolerability of Topiramate as an Early Add-on Therapy

AM Verma, AK Thacker, S Dhawan, AK Mall, MJ Khan, M Misra
BRD Medical College, Gorakhpur.

Purpose: To evaluate the use of Topiramate as an early add-on therapy.

Method: Prospective open label observational study. Patients with established partial or generalised tonic-clonic seizures with difficult to control seizures with one or two primary anticonvulsants.

Result: Eighty eight patients (56%) males), age of onset of seizures < 20 years in 72% cases and duration of epilepsy > 5 years in 86% (>10 years in 30%). Forty seven percent had complex partial seizures, 33% had generalised seizures with 3% having simple partial seizures.

On investigations, localization related epilepsy was seen in 45 patients, generalised epilepsy in 33 and 10 had undetermined cause.

Addition of Topiramate (Range 100-400 mg/day) after base line period of 8 weeks led to significant reduction in fit frequency (> 50% reduction in mean seizure frequency and response ratio < 0.33%) in 87.1% patients with partial seizures and 76.9% patients with multiple seizures type (p< 0.001).

Adverse events were reported in 30 patients predominantly being anorexia, loss of weight, asthenia and dizziness. Nine patients complained of behavioural problems. Two patients discontinued treatment due to psychosis.

Conclusion: Topiramate add-on was effective but mild side effects were common.

657. Randomised, Double Blind, Cross Over Comparison Between Two Levocetirizine Formulations on Histamine-Induced Cutaneous Response in Healthy Male Human Adult Volunteers

PR Usha, MUR Naidu, T Ramesh, KLN Reddy, BSP Reddy
Nizam’s Institute of Medical Sciences, Panajagutta, Hyderabad, Andhra Pradesh - 500 045.

Objective: The aim of this study was to compare the effect of levocetirizine (Indian formulation) versus International brand of levocetirizine in twelve healthy male human volunteers under fasting conditions, using pharmacodynamic measure of inhibition of histamine induced wheal and flare response.

Methodology: Twelve healthy male volunteers were enrolled in this study. All volunteers gave written informed consent to protocol approved by the ethics committee of NIMS. This was a balanced, randomised, double-blind, single oral dose, cross over study, where the subjects were randomized to receive either 5 mg levocetirizine reference or test formulation after overnight fast. Ten days period was wash out period. Wheal and flare were induced on the forearm of the trial subjects, by injecting freshly prepared histamine (0.1 ml containing 2 micrograms) intradermally while the subject was lying comfortably with arm resting on the bed. Ten minutes later, wheal and flare were visualized under a bright lamp. Histamine induced wheal and flare skin test was performed before and at 2, 4, 6, 8, 12 and 24 hours after drug administration.

Results: Ten minutes after intradermal injection, 2 mcg of histamine produced significant wheal and flare cutaneous response in all subjects. Reference and test formulations of levocetirizine, significantly inhibited the histamine induced cutaneous response in all the subjects. Maximum inhibition of histamine induced wheal response (Iw max%) with reference was 82.45 ± 8.8% and 77.9 ± 12.9% with test formation. Maximum inhibition of histamine induced flare response (If max%) was 80 ± 4.4% and 81.58 ± 6.7% with reference and test formulations respectively. The AUC for wheal was 2211 ± 270 mm sq/hr and 2482 ± 368 mm sq/hr with reference and test formulations respectively and was found to be comparable.

Conclusion: It can thus be concluded that the test formulation of levocetirizine tablet is bioequivalent to reference levocetirizine tablet and both formulations are equally effective and well tolerated.

698. To Study the Effect on Serum Magnesium Levels after Magnesium Sulphate Infusion in Acute Stroke

H Singh, JK Jalodia, MS Gupta, R Singh
Pt. BDS PGIMS and MDU Rohtak.

Object of Study: Dose optimization of intravenous magnesium sulphate to achieve neuroprotective levels after acute stroke has been a subject of interest but only limited clinical reports are available. The present study was done with object to see the effect on serum magnesium levels after 20 gms of magnesium sulphate infusion in acute stroke.

Methodology: Sixty consecutive clinical cases of acute stroke were randomly divided into two groups (I and II) of 30 each. Group I received intravenous magnesium sulphate as 4 grams bolus dose over 15 minutes followed by 16 grams of infusion over 24 hours. Group II was made control. Serial serum magnesium levels were estimated on at time of admission (day 0), day 1 and day 2 using atomic absorption spectrometer.

Summary of Results: The mean age was 56.47 ± 14.55 years in Group I and 55.93 ± 15.59 in group II (p-value NS). In group I the serum magnesium levels (in mg/dl) were 2.22 ± 0.43, 5.63 ± 0.65 and 3.69 ± 0.35 on day 0, day 1 and day 2 respectively while in Group II these were 2.23 ± 0.47, 2.18 ± 0.34 and 2.16 ± 0.39 on respective days of estimation. The serum magnesium levels were statistically higher (p-value > 0.05) on day 0 between the two groups but thereafter Day 1 and Day 2 the values of serum magnesium were statistically higher (p-value <0.001) in Group I. All patients in Group I achieved serum magnesium levels of ≥ 3.57 mg/dl i.e. neuroprotective levels. No adverse effect was seen in any subject during infusion.

Conclusion: The present study highlights that 20 gms dosage over 24 hours of magnesium sulphate in Acute Stroke is well tolerated by Indian patients (no other study available) and is effective to cause significant sustained rise in serum magnesium levels.

*Adjudged Best Papers and got an award of Rs. 1000/- each from Chairman Scientific Committee, Diamond APICON 2005.