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Correspondence

Observational studies versus controlled clinical trials for efficacy & effectiveness of a drug

Sir,

This is regarding an article on effect of clobazam (CLB) as add-on antiepileptic drug in patients with epilepsy published recently[1]. The authors have done a commendable job to evaluate usage pattern, retention rate, effectiveness and tolerability of clobazam during routine practice in an outpatient epilepsy clinic of a tertiary care hospital in north India. They have conducted an observational study by taking consecutive sample of consenting PWE (patients with epilepsy) attending the OPD. Patients of all age and either gender taking CLB were included in the evaluation in the present study[1].

We have a few concerns regarding the methodology adopted in this study. It would have been more appropriate to conduct an observational study with a nested case-control group to evaluate the efficacy of clobazam. The authors could have taken the patients on clobazam as the case group and those who were on some other antiepileptic drug except clobazam as controls. Further, the cases and controls should have been matched for age and gender.

Except in specific circumstances, the aim of observational post-authorisation efficacy studies is not to demonstrate the efficacy of a drug; this is the role of randomized clinical trials (RCTs). Once efficacy has been demonstrated, observational studies are useful to study effect modifiers, namely variables that may influence the level of efficacy of the drug and have been controlled for in the RCTs[2]. To assess strengths and weaknesses of different design options to study efficacy in the conditions of the everyday medical practice, recommendations have been issued for the improvement of methods[2]. Further, the aim of the study was to evaluate effectiveness of clobazam during routine practice in an outpatient epilepsy clinic. Efficacy and effectiveness exist on a continuum and RCTs are considered the gold standard in evaluating the effects of treatments. Controlled clinical trials can be efficacy trials (explanatory trials) which determine whether an intervention produces the expected result under ideal circumstances and effectiveness trials (pragmatic trials) which measure the degree of beneficial effect under "real world" clinical settings[3].

A nested case-control study would have helped to determine if an exposure is associated with an outcome (*i.e*. disease or condition of interest), for example, as given by the authors in the results; *viz*. seizure free period in patients, improvement in seizure control, change in disease severity without change in seizure frequency and the causes for discontinuation of CBZ. The authors could have given the results in comparison with the control group by calculating the frequency of each of the measured variables in the two groups and as a measure of the strength of the association between an exposure and the outcome, the odds ratio should have been calculated.

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References

1. Joshi R, Tripathi M, Gupta P, Gupta YK. Effect of clobazam as add-on antiepileptic drug in patients with epilepsy. *Indian J Med Res* 2014; *140* : 209-15.
2. Highlights from the "Workshop on methods for efficacy studies in the everyday practice". Available from: *http://www.ema.europa.eu/docs/en_GB/document_library/Minutes/2013/11/WC500155692.pdf,* accessed on October 9, 2014.
3. Godwin M, Ruhland L, Casson I, MacDonald S, Delva D, Birtwistle R, *et al*. Pragmatic controlled clinical trials in primary care: the struggle between external and internal validity. *BMC Med Res Methodol* 2003; *3* : 28.