JPPS 2008; 5(1): 1-2 EDITORIAL

PSYCHOSIS ASSOCIATED WITH EPILEPSY: CHALLENGES AND OPPORTUNITIES

IN DEVELOPING COUNTRIES

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Developing countries bear more than 90% of the total burden of disease caused by epilepsy worldwide as estimated by Disability Adjusted Life Years1. About 80-98% of patients suffering from epilepsy in the devel- oping countries are untreated1,2. The discrimination, stigma and ignorance about the disorder are widely prevalent in developing countries. A recent survey from Turkey showed that 70% of people thought that epilepsy resulted from supernatural causes2. The prospects of marriage for a girl suffering from epilepsy are often bleak in our country.

Now consider someone having two disorders epi- lepsy and psychosis, both associated with the worst stigma. People suffering from epilepsy have an in- creased risk of suffering from psychotic symptoms3,4. The prevalence of schizophrenia in people with epilepsy varies between 3% and 7% (prevalence in the general population is 1%)4. In Iceland a case controlled study found that although there was no excess of psychiatric illness in people with epilepsy, among those who were psychiatrically ill a disproportionate number were suf- fering from psychotic disorder5. Two national inpatient registers for epilepsy and for psychosis respectively were used to compare the subsequent incidence of schizo- phrenia in people who had at some point undergone admission to hospital for epilepsy with that in the gen- eral population6. A standardized incidence ratio of 1.48 for all epilepsy and 2.35 for temporal lobe epilepsy was found which suggests epilepsy as a risk factor for schizo- phrenia. These studies have many methodological limi- tations, such as a failure to use strictly defined and inter- nationally recognized diagnostic criteria for schizophre- nia and samples drawn from the neurology facilities which are not representative of the prevalent population with epilepsy. However, the results do indicate the con- siderably heightened risk for psychosis in patients with epilepsy.

Since clinical seizures are the outstanding fea- ture of epilepsy, psychotic syndromes have generally been classified in the literature according to their tem- poral relationship to seizure itself, as ictal, postictal and interictal psychosis. An ictal psychosis can result from status epilepticus of a non-convulsive nature. The psy- chosis usually lasts for hours to days and conscious- ness is invariably impaired 3,4. The most common asso- ciation is with partial complex status. In the interictal psychosis the presence of psychotic episodes is not

directly related to the occurrence of seizures. This can be either brief or chronic3. Chronic interictal psychosis closely resembles schizophrenia. Nearly half (45%) of the participants in the Slater study had a chronic psy- chosis7. In a 10-year follow-up study in Japan, 64% of the participants had a chronic psychosis8. Postictal psy- chosis is the most common form of psychosis found in people with epilepsy4. The psychosis, which comprises affective, schizophrenic, and organic symptoms, may last for up to a week. The psychotic symptoms are pleo- morphic (persecutory, grandiose, referential, somatic, and religious delusions, catatonia, hallucinations, etc.). The affective symptoms (manic or depressive) are often prominent9.

The treatment of epilepsy as well as psychotic symptoms is very challenging. In patients treated with therapeutic doses of the more commonly used antide- pressants and antipsychotics, seizure incidence rates have been reported to range from approximately 0.1% to approximately 1.5% (incidence of the first unprovoked seizure in the general population is 0.07 to 0.09)10. Amongst the antipsychotics, clozapine is the most epi- leptogenic. Seizures are reported in 0.3% to 5% of people treated with therapeutic doses11. To complicate matters further the anticonvulsant drugs have been reported to precipitate psychosis. There are reports that zonisamide, the most commonly used add-on treatment in Japan, is associated with psychoses12. Several cases of psycho- sis have also been reported during add-on therapy with newer antiepileptic drugs such as vigabatrin, felbamate, lamotrigine, tiagabine, and topiramate. In addition psy- chosis has also been reported in association with clobazam, phenytoin, carbamazepine, barbiturates, ethosuximide and benzodiazepines13-14.

Surprisingly, however there is little reliable objec- tive evidence for the efficacy of antipsychotic in those suffering from psychosis concomitant with epilepsy. On a systematic search of literature we could find only one randomized trial evaluating the effectiveness of an an- tipsychotic (Olanzapine) in patients suffering from epi- lepsy which enrolled only 16 patients15.

The need for RCTs in this area is much more than realized in view of the general impression that anti- psychotics are generally epileptogenic drugs. This how- ever does not seem to be born out by clinical studies, especially in those suffering from psychosis. It is reported that the use of Clozapine, arguably most epileptogenic

antipsychotic was not associated with increased risk of epileptic seizures11. The use of Clozapine in six patients with epilepsy and severe psychosis suggested that none of the reported patients had an increase of their seizure frequency; in contrast, three patients had a substantial reduction of seizures12. Similarly, another descriptive study with Thioridazine in 100 institutionalized patients with epilepsy and behavioral symptoms reported that 41% of patients had reduction in seizures after the improvement of their behavioral symptoms16. It is possible that improvement in sleep, decreased stress and possible interaction of psychotropic drugs with antiepileptic increasing the levels of later could re- sult in improvement in the seizures. These assertions however need to be tested in randomized controlled trials.

It should be possible to conduct the pragmatic ran- domized controlled trials recruiting those exhibiting psy- chotic symptoms in a specified temporal relationship with epilepsy in developing countries in view of the high prevalence of epilepsy in many developing countries. The feasibility of such trials is further enhanced by the fact that in many developing countries including Paki- stan psychiatrists treat a substantial number of people suffering from epilepsy. These trials need to include the outcome measures related to seizure control such as change in the frequency and duration of seizures which remain as matter of primary concern in the clinical prac- tice in addition to the outcome of psychotic symptoms. A recent trial from Bangladesh addressing the complex issue of treatment of childhood epilepsy with pheno- barbitone is an illustration of what can be achieved in a developing country setting with limited resources but creative thinking17. Psychosis associated with epilepsy is a major challenge for clinicians and researchers. This also provides a unique opportunity for gaining insights in two complex disorders which must be taken up by clinicians and academicians in the developing coun- tries.

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