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 Years[1]. About 80-98% of patients suffering from epilepsy in the developing countries are untreated[1,2]. 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 causes[2]. The prospects of marriage for a girl suffering from epilepsy are often bleak in our country.

Now consider someone having two disorders epilepsy and psychosis, both associated with the worst stigma. People suffering from epilepsy have an increased risk of suffering from psychotic symptoms[3,4]. 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 suffering from psychotic disorder[5]. Two national inpatient registers for epilepsy and for psychosis respectively were used to compare the subsequent incidence of schizophrenia in people who had at some point undergone admission to hospital for epilepsy with that in the general population[6]. 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 schizophrenia. These studies have many methodological limitations, such as a failure to use strictly defined and internationally recognized diagnostic criteria for schizophrenia and samples drawn from the neurology facilities which are not representative of the prevalent population with epilepsy. However, the results do indicate the considerably heightened risk for psychosis in patients with epilepsy.

Since clinical seizures are the outstanding feature of epilepsy, psychotic syndromes have generally been classified in the literature according to their temporal relationship to seizure itself, as ictal, postictal and interictal psychosis. An ictal psychosis can result from status epilepticus of a non-convulsive nature. The psychosis usually lasts for hours to days and consciousness is invariably impaired [3,4]. The most common association 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 chronic[3]. Chronic interictal psychosis closely resembles schizophrenia. Nearly half (45%) of the participants in the Slater study had a chronic psychosis[7]. In a 10-year follow-up study in Japan, 64% of the participants had a chronic psychosis[8]. Postictal psychosis is the most common form of psychosis found in people with epilepsy[4]. The psychosis, which comprises affective, schizophrenic, and organic symptoms, may last for up to a week. The psychotic symptoms are pleomorphic (persecutory, grandiose, referential, somatic, and religious delusions, catatonia, hallucinations, etc.). The affective symptoms (manic or depressive) are often prominent[9].

The treatment of epilepsy as well as psychotic symptoms is very challenging. In patients treated with therapeutic doses of the more commonly used antidepressants 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 epileptogenic. Seizures are reported in 0.3% to 5% of people treated with therapeutic doses[11]. 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 psychoses[12]. Several cases of psychosis have also been reported during add-on therapy with newer antiepileptic drugs such as vigabatrin, felbamate, lamotrigine, tiagabine, and topiramate. In addition psychosis has also been reported in association with clobazam, phenytoin, carbamazepine, barbiturates, ethosuximide and benzodiazepines[13-14].

Surprisingly, however there is little reliable objective 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 antipsychotic (Olanzapine) in patients suffering from epilepsy which enrolled only 16 patients[15].

The need for RCTs in this area is much more than realized in view of the general impression that antipsychotics are generally epileptogenic drugs. This however 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 seizures[11]. 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 seizures[12]. 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 symptoms[16]. It is possible that improvement in sleep, decreased stress and possible interaction of psychotropic drugs with antiepileptic increasing the levels of later could result in improvement in the seizures. These assertions however need to be tested in randomized controlled trials.

It should be possible to conduct the pragmatic randomized controlled trials recruiting those exhibiting psychotic 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 Pakistan 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 practice in addition to the outcome of psychotic symptoms. A recent trial from Bangladesh addressing the complex issue of treatment of childhood epilepsy with phenobarbitone is an illustration of what can be achieved in a developing country setting with limited resources but creative thinking[17]. 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 countries.

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