
ANTIEPILEPTIC DRUGS IN PSYCHIATRY

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Slide 1& 2 : introduction. Glossary of abbreviations of antiepileptic drugs used. Throughout this lecture the term antiepileptic drug (AED) would be used rather than anticonvulsant drug (ACD). The former is more accurate since epileptic seizures are not necessarily convulsive seizures.

SECTION 1

EPILEPSY & PSYCHIATRY

Slide 3: There is a complex relationship between epilepsy and Psychiatry. In the past both groups ended in asylums, and probably till now there are stigmas attached to epilepsy as well as psychiatry. Furthermore, we know that mental disorders are more common in Epilepsy, which could be nonspecific due to the chronicity of the disease or specific to epilepsy itself. More complex relationship which I shall address today is the use of AED in psychiatry. It is not an exaggeration to state that Epilepsy is the perfect illness to study all the models of mental disorders.

Slide 4: Models of mental health problems as we call them today have been identified and studied for decades. The Social model prevailed in the early 80s and followed by Cognitive Behavioural models later. However, we may look at these models and relate them to our clinical practice. Social Adversity often leads to emotional change, while psychodynamic factors which colonize the human mind would give rise to symptoms. The resulting Cognitive schema of the individual would result in behaviours that will propel him towards a change in his functioning and personality. Finally, the medical model prevails with change in circuitry and neurotransmission and this is when the person disintegrates.

Slide 5: There is always a hypothesis of common pathophysiology that is operative in Epilepsy and and psychiatry. Organic Disorders whether chronic or acute, Ictal or Peri-Ictal. The relationship between schizophrenia and Epilepsy is well established specifically in relation to temporal lobe focus and chronicity of the epilepsy itself. The same applies to mood disorders, OCD, anxiety and Personality Disorders. There is no epileptic personality, but the most common type of PD seen in Epilepsy is Borderline Personality Disorder.

Slide 6: The entry to the relationship between behavioural disturbance and epilepsy started with the famous observation of Kaplan about the psychic reflex, which he presumed is due to some kind of epileptic Disturbance.

Slide 7: That issue of the relationship between Aggression and limbic system was covered over a long period by several authors.

Slide 8: It was later reformulated as a triangle of brain damage, poor impulse control, and Aggression.

Slide 9: Later on, it was refined as a relationship between Epilepsy and aggression and Dyscontrol Syndrome.

Slide 10: The concept of Dyscontrol Syndrome was hypothesised by Monroe 1970, and this hypothesis opened the gate to using AED in Behavioural disturbance with or without evidence of seizure activity. The definition per se is rather vague presuming that there are paroxysmal discharges in subcortical structures . The other vague criterion is the absence of a personality Disorder. One may conclude that this concept medicalised anger outbursts, and as result we often hear about using CZB, VAL , Risperidone and Trazadone to treat such state.

Slide 11: But in reality Dyscontrol states in practice we observe a history of multi-impulsive behaviour, history of psychiatric disorder, no specific brain pathology. Most Controversial is : Do AEDs help? In my experience their effect is not better than anger management course that are non evidence based.

Slide 12, 13: To finish this section of our discussion I shall conclude with two slides. The first relates to people who do not have Epilepsy and sent for an EEG resulting in Over interpretation of results by physicians. The second slide relates to a syndrome rarely observed in patients with history of Epilepsy who might well be controlled by AEDs illustrating the remarkable change in personality.

¹SECTION 2

AEDS

Slide 15: There are no classifications of AEDS like antidepressant or antipsychotics but for clarification I may say that there are four groups. The Benzodiazepines are the most commonly shared drugs between Epilepsy and Psychiatry. Then we have the first and older generation of AEDs that are effective and remains the most commonly used drugs till now.

Slide 16: There is also another classification relating to narrow and broad spectrum just like antibiotics. As a rule CBZ does not help with Generalised seizures while Valproate is effective in all types of seizures.

SECTION 3

BENZODIAZEPINES

Slides 18, 19: The mechanism of action of BZD is most interesting for Neurologists and Psychiatrists. They are unique drugs because the human body has specific receptors for them. These receptors are close to the GABA receptors and Chloride gate. Once stimulated they lead to release of GABA which opens the gates for Chloride to hyperpolarize the neurone resulting in sedation and muscle relaxation.

Slide 20: Diazepam is a powerful antiepileptic drug that has changed the management of status epilepticus. However, as with all BZD Tolerance developed to its antiepileptic activity within 3 - 6 months. It is a useful anxiolytic through its action on Alpha 2 receptors in the Limbic system. In higher doses it acts on Type 2 receptors leading to problems with anterograde amnesia.

Slide 21: CLN is the most commonly used AED to treat myoclonic Epilepsy. However, its use proliferated in psychiatry in recent years to control agitation in inpatient and outpatient settings. There is an important clinical point that is relevant to CLN and PRM which is referred to as First dose effect. Always make sure to start treatment with 0.25 mg because some patients react to it by going into deep sleep for 72 hours with higher doses.

Slide 22: Midazolam is used extensively in clinical practice and most useful in treating serial convulsions. It can be administered SL and helps with rapid tranquilization.

Slide 23: Clobazam is 1,5 BZD unlike all others that are 1,4 benzodiazepines. It was marketed as antiepileptic drug, and often used as an add on therapy. It is also used to treat anxiety sometimes and specifically used to treat catamenial epilepsy.

Slide 25: There is a lot to talk about the neuropsychiatric aspects of BZD. Disinhibition is a real problem in some patients in Clinical practise ; so avoid prescribing the drug with patients known to have low impulse threshold.

Slide 26, 27: The other aspect is that of memory. We need to remind ourselves of the a simple classification of short term and long term memory . Only anterograde memory is affected by BZD. It is always a myth to state that using BZD would help patients recall suppressed memory.

SECTION 3

CONVENTIONAL AEDS IN PSYCHIATRY

Slide 29: The first reference to using AEDs in Psychiatry started with a paper describing the usefulness of DPH in the treatment of non-epileptic emotional disorder. However, the case series was just an observational non controlled study, and what we know now is that DPH has no use in Clinical Psychiatry. Then CZB and VAL use in Bipolar Disorder followed by using other AEDs in Mood disorder, anxiety and Chronic pain.

Slide 30: The simple model that explains the use of AEDs in Psychiatry simply relates to the overactivity of hyperexcitable neurons in both. As a result, we get better sleep, better mood regulation, and reduced inhibition.

Slide 31: A more interesting theory that covers both is that of Kindling which explains lowering of threshold to have epileptic seizures in Chronic epilepsy and we know that Amygdala Kindling explains lowering threshold to have anxiety, recurrence of mood disorder and relapse with alcohol and illicit drug abuse.

SECTION 4

AEDS & BIPOLAR DISORDER

Slide 33: The use of AEDs in Bipolar Disorder is well established but nevertheless Lithium remains the gold standard in managing acute mania and prophylaxis. There is no trial yet that demonstrated either VAL or CBZ are more effective than Li, and in challenging cases they are an add on therapies to Lithium. Goals of treatment are well known, and Li is proven to prevent suicidal behaviour.

Slide 34: lamotrigine emergence as a useful drug for mood disorder started with the observation of improving Quality of Life measures in clinical trials in patients with epilepsy. However, it is not antimanic and useful only to treat Bipolar Depression. Probably trying LTG in Bipolar depression and avoiding the use of antidepressant is worth remembering. CZB has the best evidence in acute and prevention. VAL treats mania and has rapid onset compared to CZB that needs slow titration. Others are NOT effective.

Slide 35: The summary of use of AEDS is None of them is superior to Lithium. The guidelines for their use varies from one place to another because of conflicting outcomes of Clinical Trials.

SECTION 5

AEDS & ANXIETY

Slide 37: BZD are useful in anxiety to use when required. Lorazepam is the most commonly used drug in inpatient setting, and it is also an AED.

Slide 38: Pregabalin as well as BZD better not be used to treat Chronic anxiety before using antidepressant. They are not always effective, and the dose should not exceed 600 mg daily. PRG is a drug of misuse, and probably there are some pharmacokinetic as well as pharmacodynamic issues that we need to keep in mind.

SECTION 6

INDIVIDUAL AED IN PSYCHIATRY

Slide 40: CZB should be introduced slowly, and its levels monitored regularly. It is a powerful enzyme inducer and also unique in being an autoinducer. It is used in treating Neuropathic pains, and there are case reports about its usefulness in Kluver Bucy Syndrome. Rapid increase of the dose initially might result in a rash in around 20% of patients.

Slide 41: Lamotrigine is licensed for use in Bipolar Depression. It needs very slow titration, and toxic levels might lead to behavioural side effects. Do not combine with CZB because of headaches. Also remember NOT to prescribe at night because of Insomnia.

Slide 42: VAL has bad name nowadays, but it is one of the most effective AEDs. It is an enzyme inhibitor, and as result it may increase the levels of other psychotropic when used in combination. Polycystic ovary and Obesity are the main issues. Alopecia often followed by regrowth of thickened hair.

Slides 43 and 44: Both drugs are used in Chronic Pain, and they both prone to tolerance.

Slide 45: There are AEDs that are prescribed for use because of their side effect which is Weight Loss. This is not a very good practice since both are devoid of useful psychotropic effects. Furthermore, TPR has been associated with auditory hallucinosis and neuropathy.

Slide 46: Summary of current uses of AEDS. They are useful in Bipolar, pain and anxiety BUT are not first line treatment.

SECTION 7

PSYCHIATRIC ADVERSE EFFECTS OF AEDS

Slide 48: These are referred to as Psychiatric and Behavioural Side effects which could be summarised as outlined.

Slide 49: VGB is one of the most powerful AEDs but its use is curtailed because of neurotoxicity and effects on visual field. It is linked to psychosis in case reports. LVT is also a very powerful AED and has been associated with suicidal tendencies.

Slide 50: Chronic Behavioural Toxicity is dose related and may lead to personality change, and there is no reason to believe that it may occur only with PB and PRM. This is why it is essential to monitor the use of medication.

Slide 51: Forced Normalization and alternate psychosis refers to onset of Behavioural symptoms following normalization of the EEG in

patients with Epilepsy. Remember you may not diagnose it without an EEG.