



POST TRAUMATIC EPILEPSY AND COMORBIDITIES: AN OVERVIEW

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Abstract:

Post-traumatic epilepsy (PTE) is one of the most destructive long-term, recurrent seizure disorder in network consequences of traumatic brain injury following head trauma. PTE is not a homogeneous Condition and can appear several years after the head injury. Severe TBI, after a period of time, causes numerous neuropsychiatric and neurodegenerative problems or neurological impairments with varying comorbidities, and brain homeostasis may never be restored. The anti-epileptic drugs (AEDs) are used as preventive strategies to manage TBI, control the frequency of acute Seizures and prevent development of PTE their efficacy in PTE remains controversial. Simultaneously, there have been repeated recommendations by radiologists and neuroimaging experts for the incorporation of localization based on electroencephalography (EEG) into the Process of clinical decision-making regarding PTE patients. While seizure or prophylaxis can prevent early onset seizures, there are no available treatments effectively prevent late-onset seizure. The purpose of this review is to discuss the current state of knowledge pertaining to neuroprotection in epileptic conditions, by increasing understanding about post-traumatic epilepsy and injury expansion over time, it will be possible to design better treatments with specific molecular targets to prevent late-onset seizure occurrence following traumatic brain injury. to investigate the epidemiology and the risk factors for post-traumatic epilepsy (PTE) in a large cohort of patients after severe non-penetrating civilian traumatic brain injury (TBI). Finally describe current and novel treatments and management strategies for preventing PTE. The review provides an opportunity for researchers and health service professionals to better understand the underlying pathophysiology of PTE to develop novel, more effective therapeutic targets and to improve the quality of life of people with this condition.

Keywords: -posttraumatic epilepsy, seizures, comorbidities, Traumatic Brain Injury, antiepileptic drugs Prophylaxis.

Introduction: -

In whole world about 6% of patients with epilepsy, seizures are idea to be the end result of preceding head trauma; regularly, seizures in those sufferers are hard to govern with trendy antiepileptic drugs (AEDs). The presence of early and past due seizures has great impact on next outcomes, such as medicine use, great of life, employment, and psychosocial adjustment. In those sufferers, the authentic insult is regularly diagnosed from the history, however the severity of the damage can be hard to judge. Based on research carried out during the last numerous decades, sufferers who've suffered mild or excessive disturbing mind damage (TBI) are usually positioned on an AED proper after the preliminary trauma, commonly phenytoin (PHT), however greater currently additionally on levetiracetam (LEV), that allows you to regulate the development of epileptogenic to past due seizures and epilepsy. If seizures aren't gift with inside the first 7 days after trauma, the AED is weaned, with an expectation that seizures will now no longer arise with inside the future. Since the idea of seizure and epilepsy prevention after TBI is nicely established, it's far incumbent upon us to decide now no longer handiest which factors, while gift or absent in the latent period (time among trauma and past due seizures), are essential for starting up and finishing the cascade of activities that ultimately cause seizure occurrence [1]

As proposed via way of means of the International League Against Epilepsy and the International Bureau for Epilepsy in 2005, epilepsy is a disease of the mind characterized via way of means of a long-lasting predisposition to generate epileptic seizures, and via way of means of the neurobiology, cognitive, mental and social results of this condition. Epilepsy is similarly described as recurrent unprovoked seizures taking place at the least 24 h apart. Post-disturbing epilepsy (PTE) is a life-lengthy worry of disturbing mind damage (TBI). PTE is described as one or greater unprovoked seizures that arise at the least every week after TBI .These aren't universally universal definitions, as a few research have allowed as much as four weeks after head damage for early PTS. [2]While damage kind and severity seem to partly expect PTE susceptibility, comparable accidents in human beings do now no longer cont Penetrating lesions in motor regions and the parietal lobe also are related to an improved threat of PTE Importantly, some risk factors have been suggested to be neuropathological relevant in PTE development in humans, such as age, early seizures after TBI, and trauma severity.[3]

post-traumatic epilepsy refers to the condition where recurrent spontaneous seizures occur more than 1 week after TBI. These seizures are often called "late seizures" to differentiate them from "early seizures," which occur within 1 week after TBI, or "immediate seizures," which occur within the first 24 h). Early seizures occur in up to 25% of patients with moderate to severe TBI, and in 6% of patients the seizures present. Immediate and early seizures are most likely due to the physical trauma itself, and should not be considered as an end product of the reorganization of neuronal circuits that results in PTE. [4]Epilepsy complicates head trauma in approximately 7% of patients in a civilian population and 34% of patients injured in combat. The severity of brain injury appears to correlate with the incidence of post-traumatic epilepsy.[5] the neurophysiological and structural abnormalities believed to underlie the increased propensity of the injured brain to generate spontaneous seizures. Emphasis is placed on modifications of synaptic networks in the injured dentate gyrus

that are associated with post-traumatic palatogenesis. The hippocampus has long been recognized as an important structure in epilepsy.[6]Traumatic brain injury (TBI) is defined as a disruption of brain functioning, or other brain pathology, caused by an external force The TBI is typically accompanied by one or more clinical signs immediately following the injury; including lost or altered consciousness, amnesia, neurologic deficit, intracranial lesion, and seizures.[7]

Traumatic brain injury (TBI) has been emerging as a significant concern recently due to the rising number of cases leading to long-term disability, impacting the healthcare system. TBI can lead to numerous adverse effects ranging from simple seizures to debilitating chronic epilepsy.

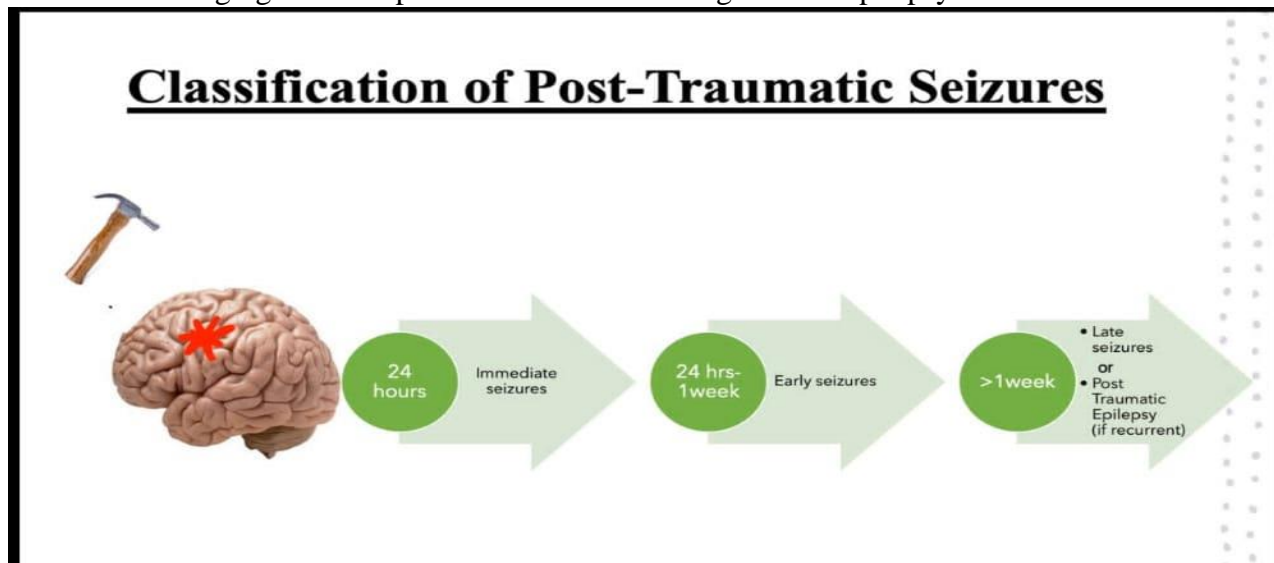


Fig1: - classification of post traumatic epilepsy

It has been classified based on the time of onset after injury. The ones occurring within 24 hours are called "immediate." "Early seizures" appear between 24 hours and one week. Those after one week are "late seizures." In some cases, these are different from acute episodes (< 1 week), The PTE can lead to a detrimental effect on the quality of life. [8]

Traumatic brain injury (TBI) is a most common cause of epilepsy. Acquired epilepsy in general increases mortality to a median standardized mortality ratio of 2.3. In post-traumatic epilepsy (PTE), mortality varies in the literature. A US study determined a nearly 3 instances elevated mortality in PTE and an elevated danger of dying in more youthful age groups. A Taiwanese study mentioned a twofold elevated mortality in PTE, additionally after adjustment for age, sex, and comorbidities. In addition, large-scale studies of American-style football players and military veterans have demonstrated that prior TBI is associated with multi system chronic conditions, suggest in that recurrent severe head injuries may be associated with long-term health and functional status. The development of chronic medical comorbidities after TBI can complicate the course of recovery and increase health care costs and mortality. [9]

Set of definitions of subthreshold epilepsy were adopted through many researchers in defining subthreshold seizures (PTs). subthreshold harm is located as foremost not unusual place reason of received epilepsy. The foremost chance elements for PTE in preceding research were located as: male sex, cranium fracture, mind contusion, intracranial Hematoma, a depressed degree of attention on the time of admission, And

the prevalence of early PTSs, etc. [10]. TBI is described as a disruption with inside the ordinary feature of the mind that may be because of a bump, blow, or jolt to the head, or a penetrating Head harm. Common reasons of TBI encompass sports activities associated injuries, falls, vehicle accidents, and army incidents. These headaches encompass starting from Physical pressure and emotional strain of residing with someone whose abilities, behavior, and persona were altered, to extra needs at the caregivers for ongoing tracking and help with each day Furthermore, the weight of TBI can also additionally erratically fall on lower-profits households, dropping mild at the inequity of get entry to vital fitness care each withinside the United States and abroad.

Moreover, TBI places sufferers at better hazard of sleep disturbances and submit-disturbing seizures. Post-disturbing epilepsy (PTE) is characterized with the aid of using spontaneous recurrent seizures (SRSs) taking place due to TBI. Seizures were temporally labeled into immediate (inside 24 hour), early (1–7 days submit harm), and past due seizures (>7 days submit harm) Immediate and early seizures aren't taken into consideration to be "epileptic" and are idea tube provoked from the harm itself, in place of springing up from a large number of mobile and molecular changes. The cumulative hazard of growing PTE levels from 2%–50% pending at the region and severity of harm; It is well-installed that the occurrence of PTE will increase with severity off TBI; however, the mechanism with the aid of using which those seizures broaden continues to be unclear.

Many mechanisms had been diagnosed through research of reputation epilepticus and temporal lobe epilepsy. Acute or immediate seizures after TBI are treated symptomatic antiseizure medications (ASMs), but these drugs are ineffective at preventing long-term or epileptic seizure occurrence .Although there are more than 20 ASMs in clinical use, approximately 30% of patients with epilepsy still experience drug-refractory epileptic seizures .[11]

Comorbidities In Post-Traumatic Epilepsy:

A classification scheme for the different mechanisms of Association between epilepsy and comorbid conditions Has been presented Mechanisms, resultant mechanisms, shared risk factors, And bidirectional effects in figure.

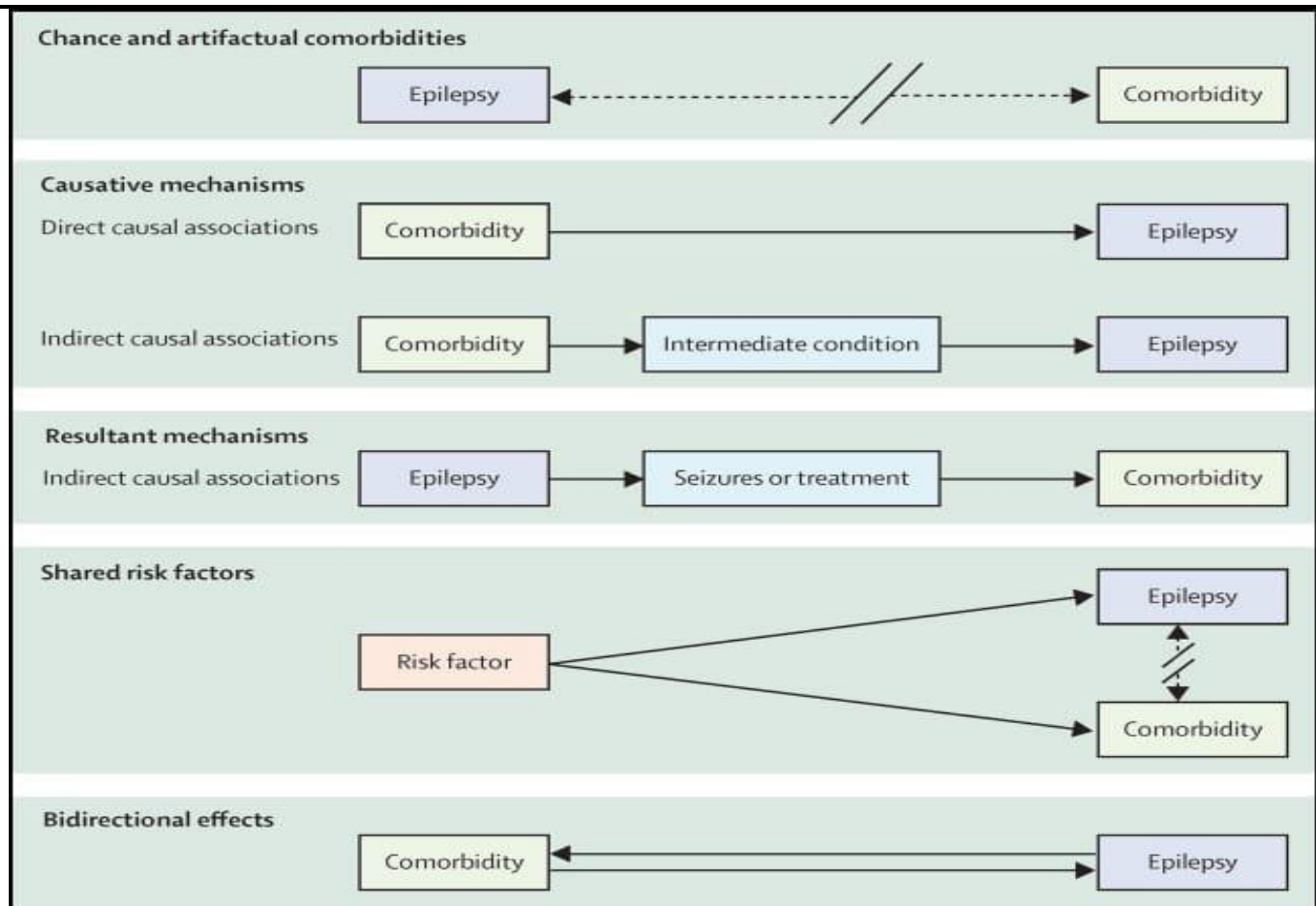


Fig2: -Mechanism of association between epilepsy and it's Comorbidities.

Each arrow with a strong line represents an informal association, with the motive main to the effect. Arrows with Dashed strains constitute non-causal associations.[12] Medical comorbidities have been located in fairly younger sufferers with TBI. Comorbidities going on after TBI have been related to better mortality.[13] Comorbidities are clinical situations that arise on the identical time which could affect a person's health. Comorbidities in PTE can consist of physical, cognitive and psychiatric disorders. The assessment and remedy of PTE wishes cautious attention of the viable co-morbid disease, the manner the comorbid sicknesses are being dealt with and the way those elements may affect seizures or the remedies used to govern seizures in PTE. [14]

History Of Epilepsy: -

The herbal records of PTE can contain an extended latency, frequently numerous decades, among the inciting trauma and the primary past due seizure. Although greater than 80% of PTE starts inside 2 years of TBI, the relative chance of growing PTE stays drastically accelerated after >10 years in adults and in children. Thus, vigilant long-time period neurologic follow-up is essential. The so-known as silent duration earlier than the onset of PTE additionally provides a completely unique possibility for prophylaxis in opposition to palatogenesis, and several interventions were explored,28, forty-two inclusive of antiepileptic drugs (AEDs), inhibitors of intracellular sign transduction, ketogenic diet, healing hypothermia, and exercise, even though all stay investigator trigonal at present. In addition to tracking for the onset of PTE, clinicians must be conscious that a rising idea of posttraumatic morbid genesis frames epilepsy as certainly considered one among numerous interconnected endophenotypes, which may also every require unique attention. Prolonged durations of seizure

freedom arise in as much as ½ of sufferers with PTE, incredibly decrease than remission quotes within the epilepsy populace as a whole. Forty-seven Most early seizures after TBI are of the generalized tonic clonic type, forty-eight while past due seizures are much more likely to have focal onset. The frontal and temporal lobes are maximum typically affected in TBI, and that is pondered within the Distribution of posttraumatic focal epilepsies.[15]

PTE provides with special seizure frequency and might evolve into remission or become intractable seizures. The lifetime overall variety of seizures after TBI varies amongst sufferers. In the Korean battle study, 39 % of the veterans had 1 to a few seizures in the course of a 10-12 months follow-up duration, even as 38 percentage had >30 seizure. The seizure remission quotes in PTE have been approximately 25 to 40 percentage in nonpenetrating head harm. Frequent seizures within the first 12 months after penetrating head harm endorse a discounted danger of remission. An envisioned thirteen percentage of PTE sufferers emerge as refractory to AED therapy.[16]

Epidemiology: -

Though epidemiological estimates regarding the prevalence of PTE vary, it has been suggested that as many as 20% of acquired Epilepsy cases are due to TBI, with a 30 year cumulative incidence Of up to 16% in the case of severe injuries Some authors Have reported that the likelihood of developing epilepsy after TBIs as high as 30–50% and that PTE is among the most common Forms of acquired epilepsies Over half of all patients with Penetrating head injuries acquire PTE, which develops within 2 years in approximately 80% of all cases, though substantial risks For PTE onset extend for longer than 10 years post-TBI The latter condition is also the most frequent cause of remote symptomatic epilepsy in 15 to 34 year old's, and accounts for around 30% of Epilepsy cases in this age group. In the pediatric population, TBI is one of the most significant epilepsy risk factors, with a seven-fold increase in epilepsy risk in children Overall, Inpatients are almost 30 times more likely to develop epilepsy than the general population and the probability for PTE to be pharmacologically resistant is excessive in each focal in addition to generalized Cases of the disease. Intractable PTE is a prime scientific hassle for patients with penetrating head injuries, in which the chance for this situation stays very excessive even many years after injury. Although Over 20 AED are in not unusual place use today, about one-1/3 of epilepsy sufferers have drug-refractory seizures or even greater Have AED-associated unfavorable results which compromise lifestyles quality .Begin found that, in randomized clinical trials involving treatment using phenytoin, phenobarbital or carbamazepine, The difference between active treatment and placebo has lacking for the prevention of PTE. Based on a thorough review and analysis, Marks et al. concluded that seizure localization in TBI patients with uncontrolled Epilepsy was difficult at the very least, partly due to anatomical Changes induced by injury and partly due to the often-multifocal Nature of post-traumatic seizures.[17]

Causes Of Post Traumatic Epilepsy: -

TBIs can cause a seizure right after the injury happens or even months or years later PTE can be caused by internal or external mechanisms. When the damage is related to an external trauma, then the term

traumatic brain injury (TBI) is used. Commons include road traffic accidents, violence, falls, occupational hazards in the building and farming industries, domestic accidents and con-tact sports, Alcohol overindulgence seems to be a major risk factor³. The incidence of TBI seems to correlate with social development and the poorer the country the greater the number of fatal accidents. A recent development seems to be that the rapid deployment of two-wheeled vehicles in some resource-poor settings has led to local epidemics of TBI¹. In view of the most common causes, it is not surprising that TBI is much more frequent in male [18]. People with posttraumatic epilepsy have a higher risk of formation of epilepsy in the future. Moreover, self-reported stress is the most common seizure precipitant. Therefore, acute stress due to traumatic events could trigger an epileptic seizure [19].

Signs and Symptoms Of PTE: -

These complications include headache, vision impairment, tinnitus, difficulty focusing, Imbalance, loss of hand-eye coordination, cognitive Impairment, and affective disorders The impact of TBI on close family members The overall prevalence of PTE symptomatology across the three age groups were 22%[20]Symptoms can include; staring and unresponsiveness, stiffening or shaking of the body, legs, arms or head; strange sound, taste, visual images, feeling or smell; inability to speak or understand, etc. TBI is the most significant cause of symptomatic epilepsy in people from 15 to 24 years of age.[21]

Other symptoms are Dizziness, Twitching of limbs, Repetitive movement, Muscle stiffness

Temporary confusion, etc. A staring spell Stiff muscles ,Uncontrollable movements of the arms and legs, Loss of consciousness or awareness Psychological symptoms such as fear and the anxiety.

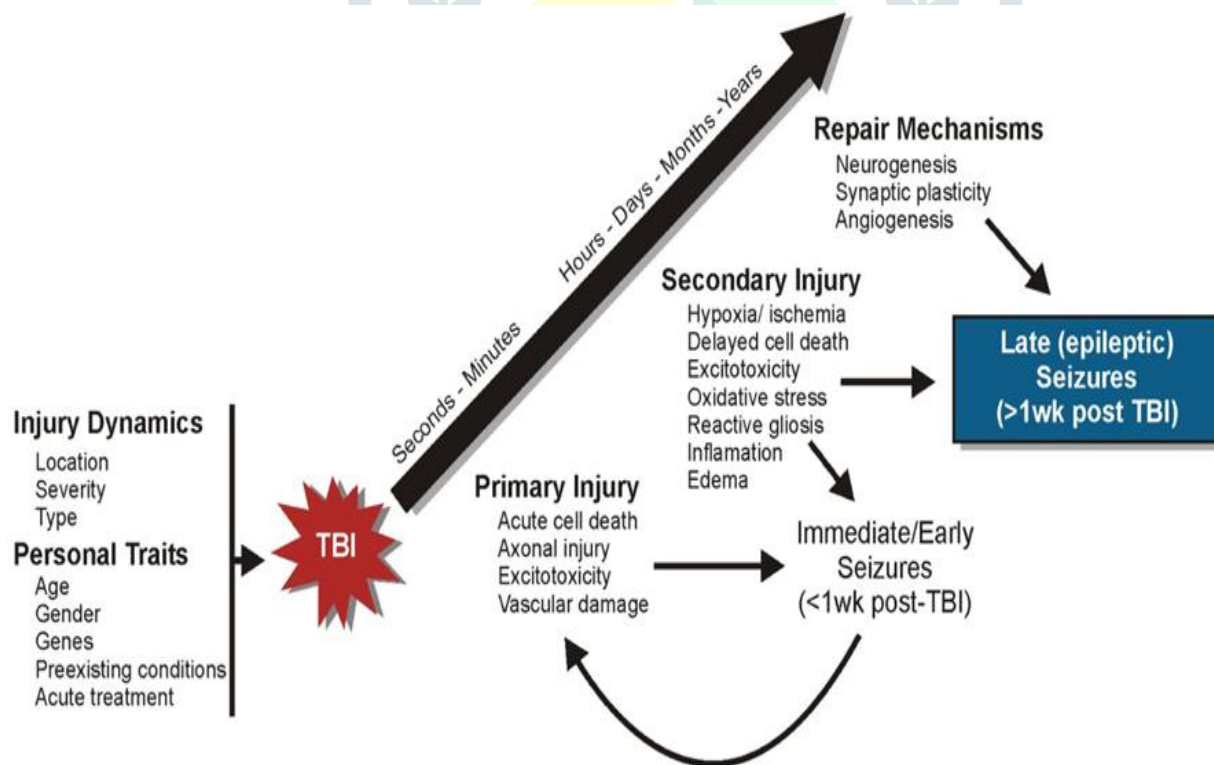


Fig 3- Symptoms basis of epileptogenic following TBI.

Complex and multifaceted events triggered during primary injury contribute to secondary Injury. These number one and secondary events, which take area over months or years, constitute a length of palatogenesis. Changes

which include post-translational Modifications of synaptic proteins, reorganization of neural circuits and manufacturing and activation of neuroinflammatory molecules/pathways bring about PTE. PTE is a Progressive process which is a result of mossy fiber sprouting, hippocampal sclerosis, neuroinflammation, neurodegeneration and SRS. PTE, post-traumatic Epilepsy; SRS, spontaneous recurrent seizures. [22]

Pathophysiology: -

Pathophysiology Traumatic mind damage consequences in probably epileptogenic mind harm via numerous mechanisms, which regularly coexist inside an unmarried patient. Immediate and early seizures are probably to have a special pathogenesis than overdue seizures, and are taken into consideration to be direct reactions to mind harm. Pathophysiology additionally varies in step with the kind of damage, as closed head accidents produce diffuse axonal damage with shearing of axons, diffuse edema, and ischemia main to the discharge of excitatory amino acids, cytokines, bioactive lipids, and different poisonous mediators inflicting secondary cell harm. Penetrating mind damage produces a cicatrix withinside the cortex and is related to an accelerated chance of PTE of about 50%. Following head damage or hemorrhagic cortical infarction, there's deposition of ferrous compounds into neural tissue. This is accompanied via way of means of a Haber–Weiss iron-catalyzed response that consequences in hyperproduction of hydroxyl radicals, triggering next formation of peroxidative agents, peroxidation of phospholipid membranes, and disruption of the mobile wall main to mobile death. The induction of an epileptic attention via way of means of iron deposition is likewise associated with reduced nitric oxide synthase hobby. These feasible pathophysiological mechanisms of PTE had been studied the use of an animal version of PTE, firstly advanced via way of means of Willmore et al. wherein epileptic seizures withinside the rat mind had been prompted via way of means of iron injection]. Iron liberated from hemoglobin, and hemoglobin itself, are related to the era of reactive oxygen species (ROS) and reactive nitrogen species (RNS), each of that have been tested to be concerned withinside the mechanism of seizures prompted via way of means of iron ions withinside the rat mind. Excessive activation of excitatory amino acid neurotransmitter receptors all through seizures is thought to generate NO and ROS, such as O_2^- , H_2O_2 , and OH, pressured following their damage However, EEG can be useful in predicting relapse earlier than anticonvulsant medicinal drug is withdrawn. [23]

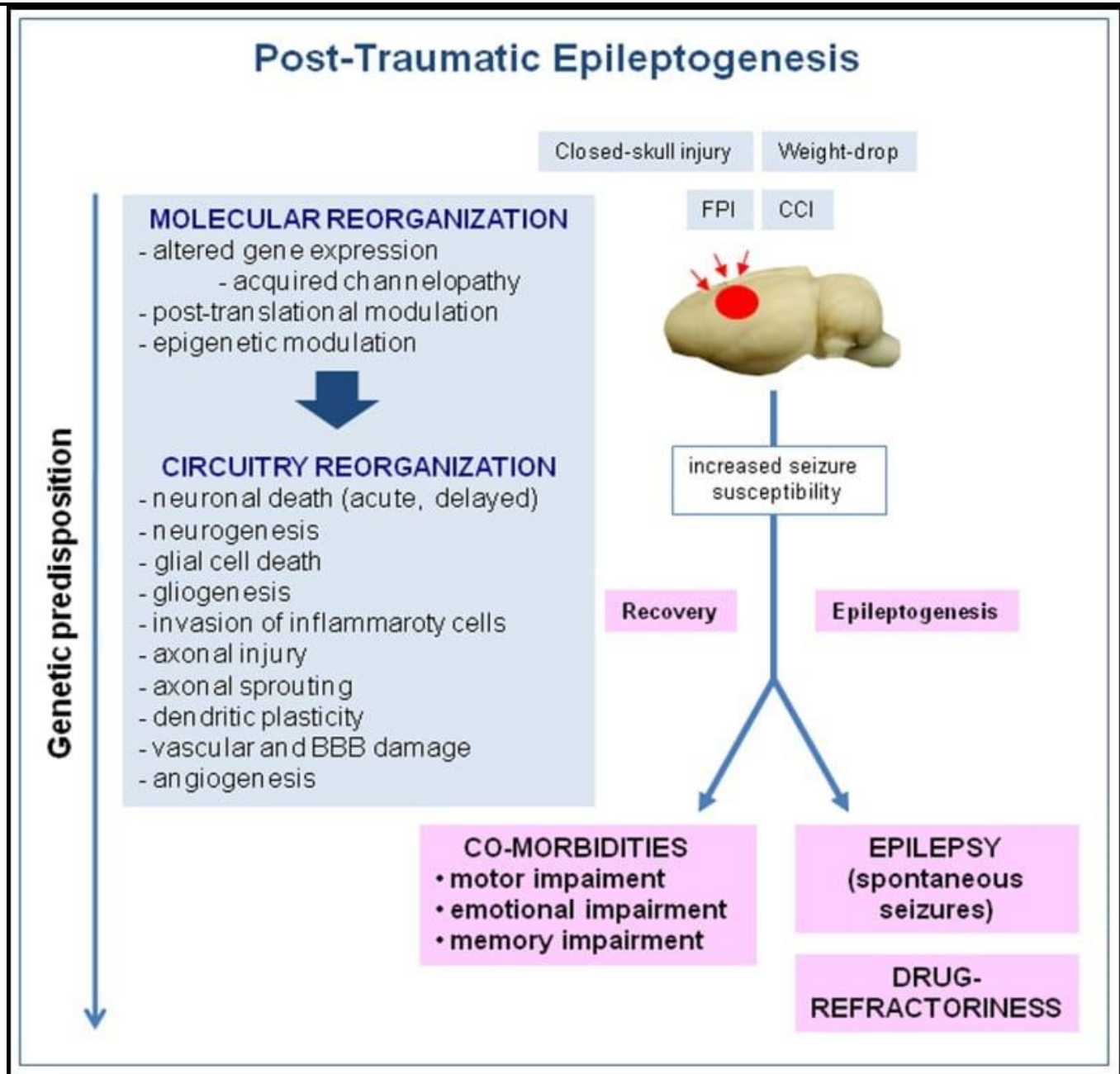


Fig4: - A schematic illustration of post-demanding epileptogenic[24].

Epilepsy is a disease of the mind characterized via way of means of a long-lasting predisposition to generate epileptic seizures. An epileptic seizure is a brief prevalence of symptoms and symptoms and/or due to strange immoderate or synchronous neuronal hobby withinside the mind.⁶ The definition of epilepsy calls for the prevalence of as a minimum one unprovoked epileptic seizure. Post-demanding epilepsy is a recurrent seizure disease secondary to demanding mind damage (TBI).5% of all epilepsy and 20% of structural epilepsy withinside the well-known populace is PTE.PTE is the maximum not unusual place purpose of new-onset epilepsy in younger adults. [25]

Mechanism Of Epilepsy: -

Epileptic seizures typically involve excessive firing and synchronization of neurons. This interrupts the normal working of the parts of the brain involved, leading to the clinical symptoms and semiology of the specific type of epilepsy.[26] A number of different types of Classes of AEs can also additionally arise because

of management of medication. Head-to-head trials are maximum beneficial for assessing dose-associated AEs. These are AEs that arise in few sufferers at decrease doses, while at better doses the bulk of sufferers can also additionally revel in them. Head-to-head trials are much less beneficial for assessing different kinds of AEs including idiosyncratic Aesthete include serious drug reactions such as Stevens Johnson syndrome, hepatic failure, pancreatitis, and aplastic anemia. These events tend to occur very infrequently, and often not a single event will occur among the several hundred patients enrolled in a typical head-to-head comparison trial.[27] The study of epileptogenic focuses on the cellular and molecular alterations caused by pathogen etic events that result in an active epileptic condition.[28]

Epilepsy is the most common neurological condition affecting Individuals of all ages and a cause of substantial morbidity and Mortality The mainstay of epilepsy therapy is the prophylactics use of anti-seizure drugs also Known as anticonvulsant or antiepileptic drugs [AEDs]. Which gives symptoms dependent treatment of recurrent seizures, the major symptom of desired epilepsy. Available ASDs thus target mechanisms associated with seizures generation and propagation in the epileptic brain. This involves modulation of voltage-gated ion channels, enhancement of c-amino butyric acid (GABA)-mediated inhibition, interactions with elements of the synaptic release machinery, or blockade of ionotropic glutamate receptor. However, approximately 30 % of patients with epilepsy are not controlled by current medication and, despite a high prevalence of acquired epilepsy, no preventive treatment exists for patients at risk of developing epilepsy.

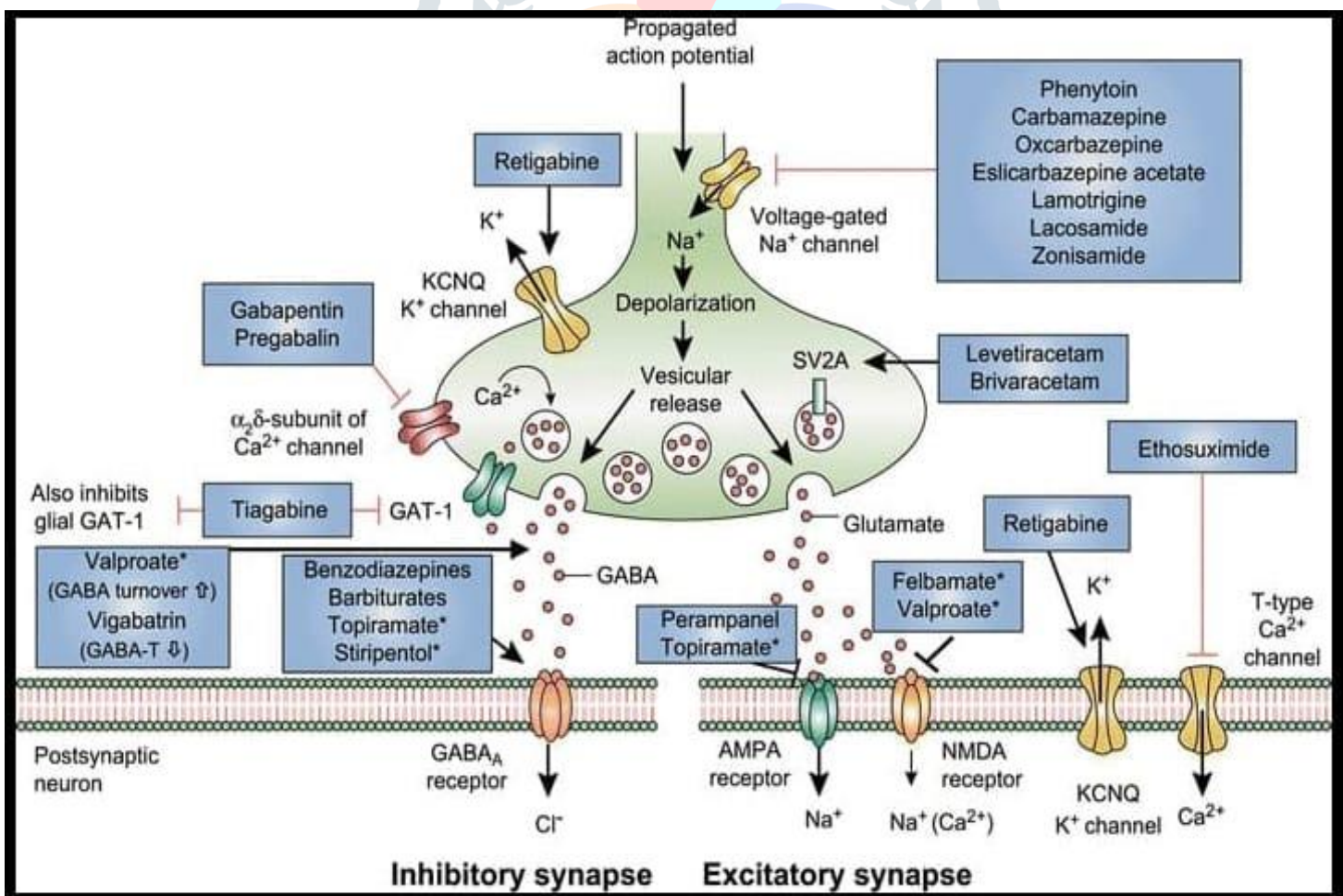


Fig5: Mechanism of clinically approved anti-epileptic drugs.

Updated and modified from Laubscher and Schmidt. Drugs marked with asterisks indicate that these compounds act by multiple mechanism GABA-T GABA aminotransferase, AT GABA transporter, SV2A synaptic vesicle protein 2A, GABA Gamma-aminobutyric acid, NMDA N-methyl-D-aspartate, AMPA an amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid, KCNQ a family of voltage-gated potassium channels. Thus, novel treatments for the pharmacy resistant patient and the prevention of epilepsy are major unmet clinical needs. The approaches underlying epileptogenic (the improvement of epilepsy following mind harm or different predisposing factors) and chemoresistance are complicated and probably mirror multifactorial phenomena, concerning changes in networks alternatively than in single targets.[29]

Risk of Posttraumatic Epilepsy After Traumatic Brain Injury: -

The possibility of PTE extensively correlates with the severity of damage. In general, TBI can be divided into Three businesses in line with the severity of damage: moderate (lack of recognition, posttraumatic amnesia for <30>24 h).[1] In a Population-primarily based totally study, the 5 -12 months cumulative possibility of seizures changed into 0-7 percentage in sufferers with moderate TBI, 1-2 percentage with mild TBI, and 10. zero percentage with Severe TBI [30]. The months cumulative prevalence changed into 16.7 percentage. In a specific study, about two-thirds of sufferers skilled as a minimum one seizure inside 1-12 months and about eighty percentage inside 2 years [31]. The prevalence of PTE is maximum after wartime penetrating Head accidents, possibly due to their severity [32]. [1]

Risk of Posttraumatic Epilepsy in Veterans with Traumatic Brain Injury: -

The charges of PTE in veterans with combat-associated TBI In World War I, World War II, and the Korean struggle fare ranged from 35 to 45% [33]. In the Korean War, no remedy changed into furnished to veterans, at the same time as with inside the Vietnam struggle fare, phenytoin (PHT) changed into given for six months to All veterans with penetrating TBI with none attempt to Monitor compliance. In approximately 50 percentage of sufferers, the primary seizure Occurred inside 12 months of TBI, however approximately 15 percentage of patients advanced PTE extra than five years after TBI. The Risk elements for growing PTE after penetrating fitness Include retained steel fragments, intracranial Hemorrhage, continual neurological deficits, and mind Parenchyma loss [34].

The contemporary meta-evaluation affords quantitative estimates of the Magnitude of affiliation among danger elements and PTE. While there has been sizable heterogeneity among Studies in gender, focal neurologic signs, lack of recognition at initials TBI, cranium fracture, mind contusion, SDH, ICH, SBI, and ASS, those Factors had been additionally strongly related to an elevated danger of PTE .The danger of growing PTE peaked in the first 12 months after cranium fracture, MBI, and SBI, after which progressively reduced and changed into Sustained at an excessive degree for >10 years.[35]

Diagnostic Evaluation

The differential prognosis for post-annoying spells wishes to consist of PTS/PTE, concussive

convulsions, psychogenic nonepileptic seizures (PNSs) (e.g., pseudo seizures), syncope (e.g., concussive syncope), confessional states (i.e., delirium), acute reminiscence disorders (i.e., fugue state), dizziness, and imbalance. Concussive convulsions aren't real PTS and aren't predictive of post-traumatic epilepsy. Features that distinguish PNS from epileptic seizures on VEEG tracking consist of loss of stereotypy in semiology and period of the seizures, loss of scalp EEG correlate to the events, and abnormal evolution of the behaviors, consisting of start-and-prevent phenomena. In sufferers with mild to extreme annoying mind damage cited a Comprehensive Epilepsy Center for assessment of refractory PTE, approximately 30% had been observed to had been misdiagnosed and feature psychogenic attacks. This percent is much like sufferers with epilepsy after nontraumatic etiologies. Therefore, if abnormal functions and seizures hold no matter treatment, the prognosis ought to be proven via way of means of VEEG instead of assuming the affected person has PTE. [36]

To be recognized with PTE, someone need to have a records of head trauma and no records of seizures previous to the damage. Witnessing a seizure is the best manner to diagnose PTE. Electroencephalography (EEG) is a device used to diagnose a seizure disorder, however a massive part of human beings with PTE might not have the abnormal "epileptiform" EEG findings indicative of epilepsy. In one observe, approximately a 5th of folks who had regular EEGs 3 months after a damage later evolved PTE. However, at the same time as EEG isn't always beneficial for predicting who will increase PTE, it may be beneficial to localize the epileptic recognition, to decide severity, and to expect whether or not someone may have extra seizures in the event that they prevent taking antiepileptic medications. Magnetic resonance imaging (MRI) is done in human beings with PTE, and CT scanning may be used to stumble on mind lesions if MRI is unavailable. or a prognosis of PTE, seizures need to know no longer be on account of every other apparent cause. Seizures that arise after head damage aren't always because of epilepsy or maybe to the top trauma [37].

Treatments Of Post Traumatic Epilepsy: -

Due to the regularly suboptimal consequences related to AED use withinside the control of epilepsy, opportunity healing techniques and strategies had been explored at extraordinary lengths. One of these maxima usually mentioned withinside the scientific literature is the implementation of a ketogenic diet. Ketone our bodies had been proven to have anticonvulsant consequences with fasting reducing the quantity of seizures in sufferers with epilepsy in figure. This method became hired via way of means of Schweitzerian and associates in a pre-scientific observe addressing flurothyl-caused seizure susceptibility following lateral fluid-percussion damage. However, nutritional routine had no impact on seizure susceptibility on this observe while thinking about seizure threshold and period. Another non-pharmacological method to stopping seizures post-TBI formerly recommended and evaluated in pre-scientific fashions is hypothermia. Hypothermia has lengthy been diagnosed and evaluated as a capacity neuroprotective approach and in a few instances has been related to protecting behavioral and biochemical consequences, each in pre-scientific and scientific research of neural damage. Atkins and associates evaluated the cap potential of hypothermia to adjust PTZ-caused seizures at continual time factors following TBI. The observe confirmed that hypothermia, while administered beginning 30 min post-damage for a complete of four h, decreased the range of seizures caused via way of means of PTZ

in addition to mossy fiber sprouting however had no impact on seizure severity.

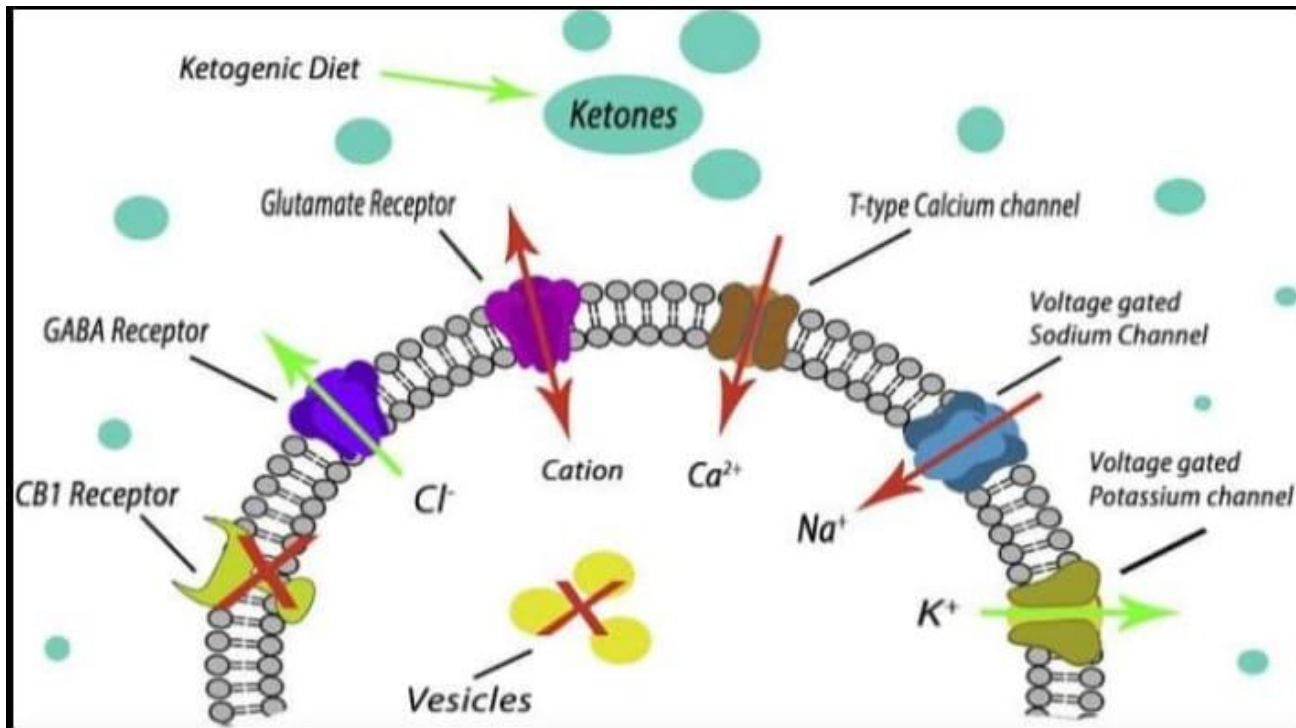


Fig6: -Novel treatment of epilepsy is mainly focused to the law of GABA.

The glutamate ligand gated channels in addition to voltage gated cation channels. Previously Explored remedies consist of: inhibition of cannabinoid receptor CB1, ketogenic diets, and law of vesicle activity. These remedies warrant in addition investigation. Treatment alternatives for drug-resistant PTE.

All scientific research so far has emphasized acute manipulate of Seizures post-damage and feature didn't become aware of any retailers that Successfully modulate seizures chronically. This is an essential attention due to the fact the Relative chance of PTE stays heightened even at a decade post-Injury, in adults and children. In spite of vast AED development (over 15 third-Generation AEDs because the 1980s), 30–40% of sufferers enjoy Unsatisfactory manipulate of seizures. Further studies are being performed to Investigate the protecting homes of dietary supplements consisting of n-Acetyl cysteine and progesterone to deal with PTE, however the consequences are inconclusive. In sufferers failing clinical control, Surgical resection can be an alternative if a seizure recognition may be Identified on imaging and/or electrophysiological research. That aren't deemed surgical applicants for resection, other control alternatives are to be had consisting of placement of a Vagal nerve stimulator [38].

Prevention and Managements of seizures and epilepsy: -

Where patients may be at high risk of developing epilepsy it is tempting to consider medication to prevent seizures. They located that treatment (phenytoin or carbamazepine) may reduce the incidence of early post-traumatic seizures but has no impact on late seizures or on mortality after TBI Valproate and levetiracetam were also compared to phenytoin and no benefit was found. The Brain Trauma Foundation Guideline does now no longer make a recommendation. Prophylaxis for those who have not had seizures cannot be recommended without better classification of risk. However, a definite event, bringing a patient for a medical attention with a

significant post epilepsy risk, it is a relatively unusual situation in clinical epilepsy and presents an archetype to consider the antiepileptogenesis in humans [39].

Surgery was initially employed to avoid or minimize the Meningocerebral scar, considered a highly excitable lesion, by a Series of steps. Meticulous removal of contused and necrotic Brain tissue, leaving adequate vascularization to the surroundings intact gyri and removal of blood clots and reconstruction of the torn dura. Unfortunately, these attempts were unsuccessful Strangely enough, neither retained bone fragments in penetrating Injuries, use of Dural grafts, cranioplasty nor the presence of a Brain abscess or a family history of epilepsy seem to impact on the incidence of PTE.

Due to the frequently suboptimal results associated with AED Use in the management of epilepsy, alternative therapeutic Approaches and techniques have been explored at great lengths.[40].Electroencephalography (EEG), which is usually used as a short (<1 hour) recording but can also be used for continuous video monitoring of seizures in epileptic conditions, Magnetic resonance imaging has the highest sensitivity to detect structural brain changes, and is the imaging modality of choice in people with PTE.

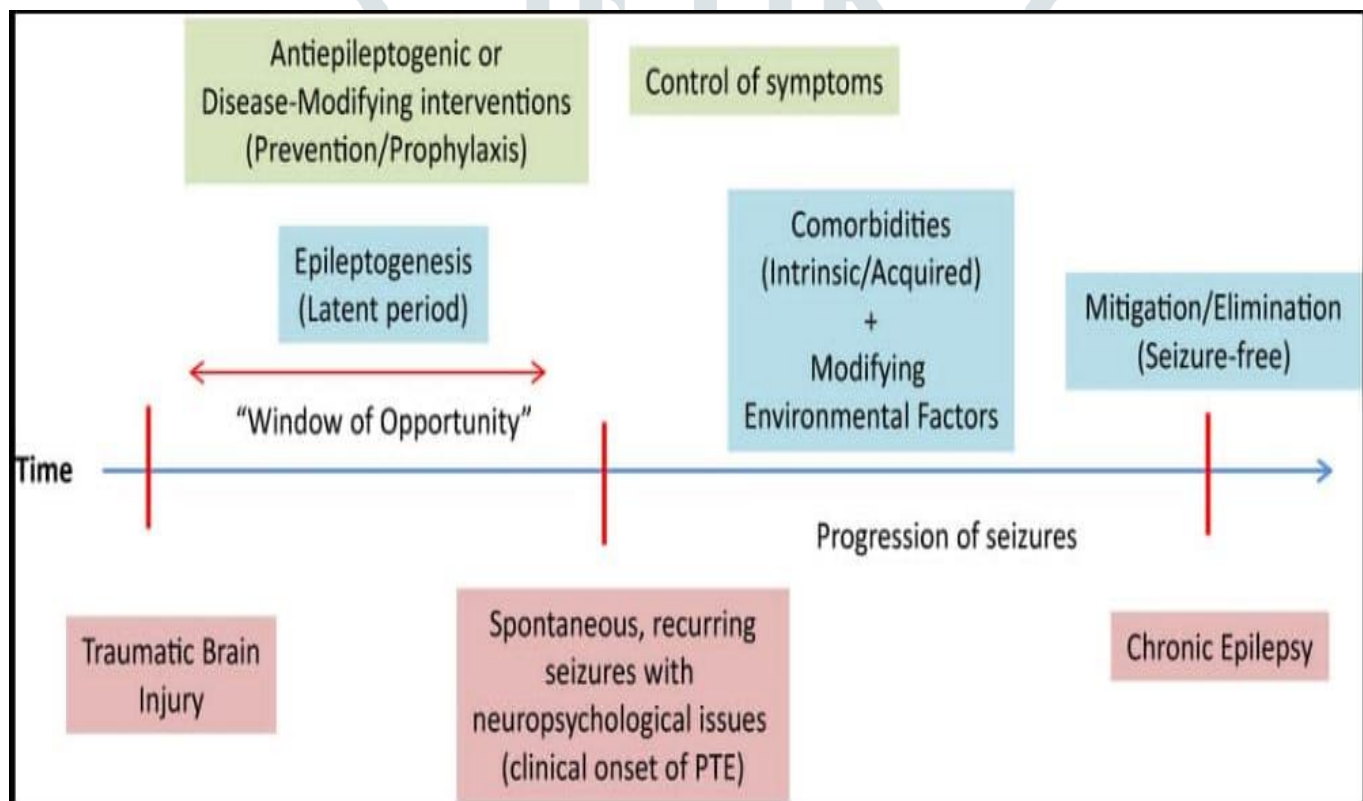


Fig 7: - management of post traumatic epilepsy

Management of brain injury focuses primarily on preventing signs of secondary injury. Currently, no therapies are available for permanently treating TBI-related injuries, although more than 20 drugs are available to treat epilepsy (however one-third of epilepsy patients are refractory to these drugs) Moreover, over 40 failed drugs have been tested in the clinical trials against epilepsy in the past decade, most of which were ion channel targets. The failure of these compounds to treat PTE could perhaps be due to the complexity of PTE and the new unknown mechanisms that regulate epileptogenic after TBI. Therefore, it is important to investigate novel neuronal targets/mechanisms other than ion channels, such as enzymes, glial cells, neurovascular components,

oxidative stress molecules, and nuclear proteins. No existing treatments can prevent the long-lasting neurodegenerative changes in PTE, but targeting free radicals during the acute phase of inflammation might prove to be more effective[35].

Conclusion:

This article we conclude that, Posttraumatic epilepsy is a serious clinical problem in both civilian and military. Clinicians involved in the regular care of patients with epilepsy know that posttraumatic epilepsy is an extremely disabling condition. Post-traumatic epilepsy is a not unusual place etiological thing most of the epilepsies. Severity of TBI and presence of intracranial bleeding are predictors for PTS. Seizures with inside the first week after TBI appear like a provoked response to the pinnacle injury. Preventing those early seizures with AED remedy is possible, however it does not now no longer adjust the susceptibility to past due seizures or the improvement of PT. We defined inflammatory additives of mobile and molecular mechanisms in the CNS that can contribute to the epileptogenic progression following TBI. It is also important to recognize the pathophysiology of PTE are also likely to be playing a role post-post traumatic epileptogenic development, and such variables require in addition investigation.

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