

Review Article**THERAPEUTIC APPLICATIONS OF PHENYTOIN**

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ABSTRACT

Phenytoin (Diphenyl Hydantoin or Dilantin) is highly effective and widely prescribed anticonvulsant agent used in the treatment of grand mal and psychomotor epilepsy. Phenytoin has been used to treat thought, mood and Behavior disorders, cardiovascular disorders, Neuro muscular disorders, gastrointestinal disorders, Endocrine disorders.

KEYWORDS Phenytoin ,Diseases , Treatment , Adverse Reactions .

INTRODUCTION

Phenytoin (diphenyl Hydantoin or Dilantin) was first synthesized by Heinrich Biltz in 1902. In 1938, H.Houston Merritt and Tracy Putnam discovered phenytoin usefulness to treat major, absence and Psychic equivalent seizures, without the sedation effects associated with Phenobarbital. Pheyntoin (PHT) is highly effective anticonvulsant. It is widely prescribed anticonvulsant and anti arrhythmic agent in the treatment of grand mal and psychomotor epilepsy. Phenytoin has been investigated as a treatment for more than 100 diseases. Phenytoin has been investigated to treat Thought, mood and Behavior disorders, cardiovascular disorders, Neuro muscular disorders, gastrointestinal disorders, and Endocrine disorders. This review summarizes the uses of phenytoin.

CLINICAL USES OF PHENYTOIN MOOD, THOUGHT AND BEHAVIOR DISORDERS

In Epileptic conditions

The efficiency of phenytoin in controlling seizures in group of patients, noted: Irritability and violent episodes are markedly diminished in frequency and severity ¹. A part from influence on convulsions there are other benefits from the use of PHT. There is marked changes in mental state and personality,

improvement in memory, concentration and sense of composure ². PHT showed an improvement in behavior, well being, cooperation alertness, general attitude, irritability, and temperament ³. PHT is found beneficial for irritability, hyper motility and variability on behavior in epileptic children ⁴. PHT showed a marked reduction in psychotic symptoms⁵.

In non epileptic conditions

The study on the use of PHT in prisoners, improvement was noted in sleep, sense of well being and cooperativeness ⁶. Important behavioral improvement was seen on PHT therapy ⁷. Treatment with PHT resulted in reduced Excitability, less severe and less frequency temper tantrums, reduced hyper activity and distractibility, fewer fears and fewer tendencies to go out of contact ⁸. Treatment with PHT found benefit: like anxiety, depression, agitation, irritability, violence, headache, sleep disturbances, abdominal symptoms, sexual disturbances, hypochondria, visual and auditory phenomena and body image distortion ⁹. PHT corrects excessive bioelectrical activity, causing excessive anger and fear ¹⁰. A therapeutic

response to PHT, ranging from reduction to complete reversal of symptoms like anxiety and tension states, reactive

depressions, certain cognitive disturbances, obsessive-compulsive manifestations, hypochondria, Psychopathy, obesity, and addiction to alcohol and cigarette smoking¹¹. PHT found usefulness in psychic over activity, distractibility, short attention span, irritability, impulsiveness, insomnia and behavioral disorders in children¹². The successful use of PHT in treatment of anxiety, nervousness, nightmares, rage, violent outbursts, confusion, fatigue, abdominal pain, anorexia nervosa, bed wetting, blackouts, dizzy spells, involuntary movements; migraine like headache were reported¹³. Phenytoin was especially useful in emotional liability, poor contact, somatic complaints, anxiety phobia and hypothermia¹⁴.

Violent Behavior

PHT is highly effective in treatment of episodic dyscontrol syndrome¹⁵. Dyscontrol syndrome is the storm of violence¹⁶. PHT is effective in the treatment of violent and aggressive behavior in schizophrenics¹⁷.

Psychoses

PHT has been reported useful in decreasing irritability and improving sense of well being in psychotics. PHT therapy resulted in positive behavioral changes in certain excited patients¹⁸. PHT treatment of prolonged chronic disturbed behavior in psychotic patients unresponsive to other drugs¹⁹. PHT was effective in reducing aggressive behavior in chronic psychotic patients²⁰.

Hypoglycemia

Treatment with PHT of the patients with symptomatic hypoglycemia previously unresponsive to dietary management. Among the symptoms, typical of the hypoglycemic patients, were chronic anxiety, extreme lethargy, frequent nausea, sensory defects and other neurological complaints. These symptoms were disappeared with PHT therapy and clinical

reversal of hypoglycemia was observed in all the cases²¹. PHT inhibited the stimulated insulin release in a patient with an islet cell tumor. PHT is a safe therapeutic adjunct in poorly controlled islet cell tumors²². PHT appears to be a promising agent in the treatment of certain patients with insulinoma²³. PHT was found effective in raising the mean fasting plasma glucose concentration and improved of the immune reactive insulin level during PHT therapy²⁴. PHT is useful in patient of organic hypoglycemia due to insulinoma.²⁵

Cognitive function

PHT was found to be effective in the improvement of concentration²⁶. PHT was found to be significantly effective in delaying the onset of fatigue and accompanying errors²⁷. The poor concentration resulted from forced ruminative thinking or turned on mind can be corrected by PHT. Improvement was seen in ability to maintain attention and concentration with PHT²⁸. Test was carried out with three pilot groups the test result showed significant improvement in performance both in terms of lessened time spent and the increased number of correct response²⁹.

Speech Disorders

The intensity of the stuttering was significantly reduced although the frequency of stuttering was not changed with PHT³⁰. Hydantoin therapy was helpful in a series of patients treated for speech and voice disorders³¹.

Alcoholism and Drug addiction

The treatment with PHT, patients tended to have a much easier and quicker recovery from acute alcoholism and marked improvements in sense of well being, sleep pattern, appetite and motivation were seen³². PHT was effective during withdrawal of patients with various forms of addiction including Heroin. Sleeplessness which is a very

difficult problem with addicts was also modified favorably³³. PHT is most effective in the treatment and prevention of convulsions associated with alcoholic withdrawal^{34, 35}. PHT was found useful for treating the patients had been suffering from flash blacks after the discontinuance of all hallucinogenic drugs³⁵.

Sleep Disorders

The patients with over powering attacks of sleep and other typical symptoms of narcolepsy, improvement was marked by a complete loss of symptoms, appetite improved³⁶. Treatment with PHT the time spent in REM sleep was significantly decreased compared to control. Non REM sleep was increased³⁷. Complete relief with PHT from paroxysmal nightmares, a sequel to a stroke³⁸. With PHT treatment there was an increases in sleep time, decreased in number of stages and disappearance of interrupting awakening were noted³⁹.

Enuresis

Phenytoin treatment to patients with enuresis, significant clinical improvement was observed^{40, 41}.

ANOREXIA, BULIMIA AND BINGE EATING

PHT was found effective in treating the patients who had distinct types of symptoms of compulsive eating. The compulsive eating is usually accompanied by other undesirable symptoms, including depression⁴². The additional eating patients with the syndrome of compulsive eating had abnormal EEG (Electroencephalographs). Treatment with PHT showed no further episodes of compulsive eating. The episodes like guild, vomiting and steeping difficulties⁴³. Subjects with binge eating was markedly reduced during PHT treatment reported butter self control, marked important in self esteem, less preoccupation with eating and more normal eating habits⁴⁴.

Treatment with PHT, disappeared these symptoms of binge eating, difficulty in concentrating, feelings of frustration and guilt in students⁴⁵

CARDIOVASCULAR DISORDERS

Cardiac Arrhythmias

PHT is an effective antiarrhythmic, prompt in its action. PHT may represent a drug with a wide margin of safety that is effective in controlling serious ventricular hyperirritability⁴⁶. PHT was found useful in the treatment and prevention of recurring cardiac arrhythmias in a group of patients⁴⁷. PHT was found benefit in controlling paroxysmal trial and ventricular arrhythmias. PHT appear to be a significant addition to drug therapy of cardiac arrhythmias⁴⁸.

Conduction

PHT was found to decrease P-R interval with the changes highly significant, PHT enhances A-V conduction in addition to suppressing ectopia⁴⁹. PHT enhanced atrioventricular conduction, shortened the P-H interval⁵⁰. PHT eliminated extra systoles and tachycardia of both a trial and ventricular origin. Intravenous PHT was usually promptly effective⁵¹. Depression in intraventricular was noted a lengthening of the H-V interval PHT is effective in arrhythmias accompanied by atrioventricular conduction effect⁵². PHT was found beneficial, not only for the myotonia, but also for cardiac conduction defects⁵³. PHT reduced the relative refractory period of the hispurkinje system or altered the degree of oberrant conduction or both. PHT improved intraventricular conduction in man⁵⁴.

Q-T Interval Syndrome

PHT is probably most effective drug for the management of this syndrome, H suppresses myocardial Irritability as well a reduced Paroxysmal automatic discharge⁵⁵ PHT promptly terminated the tachyarrhythmia.

PHT shortened the QT interval⁵⁶ and ECG returned to normal⁵⁷.

Torsade de points

Torsade de points ventricular tachycardia whose arrhythmias were promptly corrected by intravenous PHT⁵⁸. Patient with complete A-V-block, syncope and torsade de points ventricular tachycardia, the arrhythmia disappeared with PHT⁵⁹. The ventricular ectopy immediately subsided with PHT⁶⁰. A significant decrease in recurrence of torsades de points was noted and aberrant ventricular activity was absent with PHT treatment. PHT decrease ventricular automaticity, especially in purkinje fibres, which results from depression of all phases of repolarization of the transmembrane action potential and increase the atrioventricular conduction velocity and membranes responsiveness without decreasing cardiac output⁶¹.

Cardioversion

PHT is effective in the treatment of post cardio version arrhythmias⁶². PHT is effective in preventing recurrence of fibrillation after cardio version⁶³. The increase risk in cardio version following digitalis administration, cardio version should be preceded by PHT administration⁶⁴.

Myocardial infarction

PHT is used for the control of ventricular hyperirritability complicating to myocardial infarction. PHT was effective in treating ventricular, arrhythmias patients with acute myocardial infarction complicated by atherosclerotic heart diseases⁶⁵. PHT reduced the incidence and severity of ventricular arrhythmias, the preventive use of PHT in acute myocardial infarction⁶⁶. PHT is effective in the treatment of cardiac arrhythmias following

myocardial infarction⁶⁷. PHT abolished the persistent ventricular tachycardia⁶⁸.

Angina pectoris

PHT is effective in the treatment of angina pectoris; there was a marked improvement in the frequency and severity of the attacks, a decrease in the frequency of palpitations and dramatic decrease in need of or nitroglycerin⁶⁹. PHT as a prophylactic significantly reduced the frequency of the attacks and the severity of symptoms in patients with angina pectoris including chest pain, discomfort & tightness radiating to arm, neck or jaw, precipitated by exertion, emotion, cold and accompanied by dyspnea⁷⁰. PHT markedly reduced the incidence of angina attack⁷¹.

Hypertension

PHT decreased or normalized blood pressure in hypertensive patients with Cushing syndrome⁷². PHT is useful in the reduction of both systolic and diastolic blood pressure. PHT provides an alternative antihypertensive agent⁷³ with PHT, Blood pressure, an body temperature were normalized, marked improvement in symptoms such as headache, irritability and feelings of fear, sleep was also improved in patients with hypothalamic syndromes⁷⁴.

Atherosclerosis

The patient treated with PHT had significantly higher serum HDL-C level than the control. Epileptic patients receiving PHT have been impressed by the low incidence of myocardial infarction^{75, 76}. PHT may protect against atherosclerosis⁷⁷. The low serum HDL-C levels can be increased with PHT and this control retards the development of atherosclerotic disorder such as myocardial infarction or stroke⁷⁸. PHT caused increase in HDL-C concentration (average 18% in arterial blood and 15% in venous blood). The ratio of HDL-C to total cholesterol also increased⁷⁹.

The change in the ratio is of particular significances because HDL facilitates the uptake of cholesterol from peripheral tissue and transports it to the liver for breakdown & excretion⁸⁰.

CEREBROVASCULAR INSUFFICIENCIES

PHT increase the mean cerebral blood flow significantly⁸¹. PHT is therapeutically useful in physical illness, frequently cardiac and respiratory disorders resulting in cerebral hypoxia or ischemia⁸². PHT have a reversing effect on post ischemic brain injury⁸³. PHT provides cerebral protection during carotid surgery⁸⁴. PHT greatly increases the levels of intracerebral GABA⁸⁵.

NEUROMUSCULAR DISORDERS

Sydenham's chorea (Chorea Minor)

PHT was found effective in treating involuntary movements in patients with Sydenham's chorea⁸⁶. PHT shorten the duration of the disease, but there was a marked reduction of complications those of cardiac lesions, a frequent and sequel to chorea minor A54. PHT is effective in treating patients with Sydenham's chorea^{87,88}.

Athetosis

Treatment with PHT resulted in prompt and striking improvement in neuromuscular performance⁸⁹. PHT treatment was usually promptly effective in the result of symptoms of paroxysmal choreoathetosis^{90, 91}. PHT was found useful in treating the patients with paroxysmal dystonic choreoathetosis⁹². The cessation of symptoms of familiar kinesigenic dyskinesia treatment with PHT was reported⁹³. The complete elimination of choreoathetoid attacks and marked improvement in step was observed in patients treated with PHT⁹⁴.

Dystrophic and congenita myotonias

PHT was found effective in treatment of the myotonic symptoms. PHT was better tolerated and not increase the preexisting cardiac conductive defects⁹⁵ PHT appears to be the most effective, the safest and best tolerated in treating myotonia⁹⁶ PHT is the treatment of choice in myotonic dystrophy⁹⁷.

Schwartz-Jampel syndrome (myotonic chondrodystrophy)

Schwartz-Jampel syndrome a rare autosomal recessive disease consisting of generalized myotonia and bone abnormalities including dwarfism. PHT improved muscle contractions in those patients. PHT improved muscle contraction in those patients⁹⁸. PHT resulted in improvement in ambulation in patients with marked limitation of joint mobility in adulthood⁹⁹. PHT resulted in improvement in muscle relaxation and motor ability, including gait in Schwartz Jampel syndrome patients¹⁰⁰

Stiff-man syndrome

Treatment with PHT decreased muscular spasms and rigidity in patients. Still man syndrome¹⁰¹ patients with severe leg muscle contractions consistent with stiff man syndrome a combination treatment of PHT and diazepam produced both clinical & electrophysiological improvement¹⁰². Rigidity of lower limbs, notably improved and hypotension lethargy and depression also depression also resolved in treatment with PHT and diazepam¹⁰³.

Parkinson's syndrome

The treatment with PHT in patients with Parkinson's syndrome improvement in involuntary movements was observed and there was a psychic improvement in these patients¹⁰⁴. There was a prompt improvement in isotonic contraction of the muscles resulted,

rigidity disappeared, tremor was moderately improved voluntary motion of the affected extremities was improved significantly in Parkinson's syndrome treated with PHT¹⁰⁵. PHT is useful in treating patient with Parkinson syndrome reported marked in sense of well being, improvement and muscle tone, improvement in general tremor, steadier mobility better expression and improved gait were observed¹⁰⁶.

IN PAIN CONDITIONS

Trigeminal Neuralgia

A Complete cure of essential facial neuralgia in patients treated with PHT is reported¹⁰⁷. In cases of trigeminal neuralgia treated with PHT, reported to completely freed of pain, but pain returned when PHT was withdrawn¹⁰⁸. Treatment with PHT definite relief of pain was obtained and paroxysms of pain were controlled in patients with trigeminal neuralgia and with glosso pharyngeal neuralgia¹⁰⁹.

Glosso pharyngeal neuralgia

PHT is useful in treating patients who has been suffering from glossopharyngeal neuralgia associated with disturbances of cardiac and cerebral function. Treatment with PHT completely relived the pain, the patient remained symptom free^{110, 111}.

Migraine and Other Headaches

PHT is useful to treat migraine¹¹² PHT was far the most useful medication in the treatment of a syndrome in which migraine headaches were related to familial cerebral dysrhythmias¹¹³. PHT is one of the drug of choice in the treatment of headache accompanied by 14-and 6 per second positive spike patterns¹¹⁴. Patients affected with paroxysmal migraine experienced complete relief in treatment with PHT¹¹⁵. PHT is effective in relieving severe recurrent headache associated with other symptoms, including nausea vomiting, dizziness and vertigo in children¹¹⁶. The frequency and severity of the

attack were reduced in cases of basilar artery migraine with PHT¹¹⁷.

Post-stroke or Brain injury

Patients with post stroke hemiplegic and pain in part or all of the body. The patients received a combination of PHT alone responded dramatically with complete resolution of pain¹¹⁸. Patient with thalamic pain experienced good relief with PHT¹¹⁹. PHT is useful in treating facial pain associated with Wallenberg syndromes the symptoms of facial pain were relieved¹²⁰.

PERIODONTAL

In patients with various degrees of periodontal diseases treatment with PHT exhibited less pain and advanced wound healing, PHT increases the rate of wound healing. In other areas of the body and as in burns¹²¹. Treatment with PHT showed rapid regression of gingival bleeding and inflammation, increased healing and decreased dental mobility. PHT is an effective and in the treatment of periodontal diseases¹²². PHT decrease inflammation and increased production of collagen in the healing process. In patients with periodontal diseases¹²³. PHT is formed benefited in particularly on bleeding gum and on pain and histological findings confirmed the fibroblastic action of PHT and the healing with sclerosis which accompanied the decrease in inflammatory infiltration and regeneration of connective tissue¹²⁴.

Ulcers

PHT promoted the healing of chronic leg ulcers¹²⁵. PHT is effective in promoting the complete healing of an antecubital ulcers, diabetic ulcer and peptic ulcers, PHT provided for the regeneration of healthy tissues in the denuded zone¹²⁶. Patients with venous stasis diabetic and other soft tissue ulcers in PHT treated ulcers shoed more rapid infiltration of fibroblastic and greater collagen deposition as well as increased new blood vessel formation¹²⁷. PHT is useful in the treatment of trophic

lower extremity ulcers in leprosy patients, the results consisting of diminished exudates, appearance of healthy granulation tissue, and reduction in water size and suitability for skin grafting¹²⁸.

Burns

PHT is useful in the treatment of second degree burns¹²⁹. PHT decreased burn wound fluid loss induced early separation of slough and promoted rapid burn surface healing. PHT treated patients are more comfortable and had less pain¹³⁰. PHT increased the rate of burn healing and could modulate the activity of the cells at the local level, thereby making cells less prone to bacterial invasion, PHT reduced cell irritability in burns, reduced in seepage of fluid from the burn area¹³¹.

Pruritus Ani

PHT is useful in treatment of pruritus ani as additional oral therapy; a marked symptomatic relief was obtained with PHT treatment^{132, 133}.

Scleroderma

In patients with scleroderma, PHT appeared to prevent progression of sclerosis and also to aid in its resolution¹³⁴. PHT is effective in sclerodermatic patients¹³⁵.

Epidermolysis

In patients with dystrophic epidermolysis bullosa, PHT showed marked improvement in skin fragility. The effect of PHT in blister formation & collagenase activity are consistent with the protective effect is observed^{136, 137}. PHT treatment showed a significant decrease in blistering dystrophic epidermolysis bullosa¹³⁸. There was a decrease in blisters and erosion with PHT¹³⁹.

Pachyonychia

The patient treated with PHT, the hyperkeratotic lesion persisted, mouth, hand, were greatly improved. In patients who have been incapacitated by blisters and erosions of feet, hands and painful lesions in mouth¹⁴⁰.

RESPIRATORY DISORDERS

Asthma

PHT relax the bronchial smooth muscle, to regulate the nervous system and to prevent the effects of hypoxia. PHT was further evidenced by the fact that the patients were able to successfully engage in situations and environments which formerly precipitated attacks to bronchial asthma¹⁴¹. PHT would seem to be a useful antiasthmatic agent improvement in breathing are reported¹⁴². PHT is useful in treating chronic asthma; PHT is used alone or as adjuvant to other antiasthma medications. Significantly reduced frequency and severity of asthma, cough nocturnal awakenings and work absenteeism, improved sense of well being were noted¹⁴³.

GASTRO INTESTINAL DISORDERS

Irritable Bowel syndrome

In patients with irritable bowel syndrome, improvement was observed on treatment with PHT. Abdominal pain, diarrhea, constipation, nausea, vomiting and pyrosis were among the symptoms that responded with PHT treatment resulted in complete remissions of depression, insomnia and anxiety¹⁴⁴.

Ulcerative Colitis

Patients with chronic idiopathic ulcerative colitis, responded to treatment with PHT, remained symptom free returned to normal or near normal bowel habits had a normal mucosal pattern and gained weight¹⁴⁵.

Diabetic neuropathy

PHT is useful to treat painful diabetic peripheral neuropathy, symptomatic relief of pain and paresthesias, results were obtained. PHT was not additive did not procedure sedation¹⁴⁶.

IN OPTIC NERVE PROBLEMS

PHT is useful in the treatment of accommodative esotropia¹⁴⁷. PHT partly protected the optic nerve in vitro when subjected to anoxia, cyanide. PHT might reverse some of the effects of ischemia on the optic nerve in humans. PHT may be able to protect optic nerve function¹⁴⁸.

RABIES

PHT is useful treatment of patient with clinical rabies, recovered completely. PHT has antitoxic effect against a wide variety of substances. PHT is useful in treatment of cat scratch encephalitis¹⁴⁹.

TINNITUS

In the treatment of patients with tinnitus and sensorineural hearing loss, with PHT hearing loss press by cuspis improved. PHT found superior to CB2 for tinnitus¹⁵⁰. PHT decreased the N1 component of the cochlear nerve action potentials. PHT acts predominantly on the upper brain stem and also the cochlear nucleus and nerve to suppress abnormal hyperexcitability¹⁵¹.

MOTION SICKNESS

PHT prevents the symptoms of motion sickness and an increase in the time to development of symptoms was seen¹⁵². PHT and calcium pantothenate combined had a strong anti-motion sickness effect and accelerated attenuation of motion sickness symptoms¹⁵³. PHT is effective against motion sickness, decreased the incidence of subject side effects associated with the rapid administration of PHT¹⁵⁴.

IN INFLAMATED CONDITON

Arthritis

Patients with inflammatory arthritis, rheumatoid arthritis and psoriatic arthropathy on treatment with PHT, There was a reduction in morning stiffness, intensity and frequency of flare-ups, reduction in numbers of painful and

swollen joints¹⁵⁵. PHT may be an alternative safe therapy for rheumatoid arthritics¹⁵⁶. PHT treated patients showed significant improvement in particular index, Erythrocyte sedimentation rate(ESR), Platelets and hemoglobin PHT may be useful in patients with progressive destructive disease with few symptoms¹⁵⁷. In PHT treated patients, early morning stiffness was significantly reduced, pain index, particular index grip strength .showed significant, improvement. There was a significant, reduction in ESR¹⁵⁸.

Discoïd Lupus Erythematosis

PHT treated patients showed a reduction and even total absence of the inflammatory infiltrate in the termis and of the hydropic degeneration of the basal epidermal layer and of the adnexa¹⁵⁹.PHT are useful in the treatment of patients with discoïd lupus Erythematosis (DLE)¹⁶⁰.

ENDOCRINE DISORDERS

Labile Diabetes

PHT is useful in treatment of labile diabetes. PHT stabilized insulin requirements and reduced negative reaction¹⁶¹. PHT therapy resulted in a marked improvement in diabetic control and enabled the individual to lead a relative normal life¹⁶². PHT is effective in the management of labile diabetes associated of with electro cerebral dysfunction¹⁶³. PHT is used as adjuvative therapy in diabetes mellitus when hyper glucagonemia is present¹⁶⁴. Glucose metabolism was faster in subjects treated with PHT.²²

Cushing's syndrome

PHT is useful in treating Cushing's Syndrome, There was an increase in the potassium content in blood the rate of secretion of cortisol decreased, reduction normalization of blood pressure and body weight and in decrease in headache and in weakness were reported^{165, 166}.

Hyperthyroidism

Marked relief of nervousness, characteristic of this disorder, was observed. Patient treated with PHT there was decrease in size of goiter and exophthalmus¹⁶⁷.

Menstrual Disturbances

Patients during ten days before menstrual cycle who had edema on the legs, fingers and puffiness of the face, accompanied by dizzy spells on treatment with PHT. There was a complete free of episode edema and improvement in dizziness was noted¹⁶⁸ with a pattern of recurrent psychotic episodes, which seemed to coincide with the menstrual periods. Episodes were virtually eliminated by treatment with PHT. Patients seemed to be symptom free. PHT is useful for normalization of gonadotrophic functions of the hypophysis¹⁶⁹.

GLYCOGEN STORAGE DISEASES

Patients with glycogen storage diseases like debranching enzyme system deficiency one with phosphorylase deficiency and one with glucose 6. Phosphate deficiency patients treated with PHT, there was a reduction in liver size and hepatic glycogen content and hyperlacticacidemia improved¹⁷⁰.

CONCLUSION

Phenytoin uses have yet to be fully defined. Its mechanism of actions is fully understood in various non epileptic applications yet to be investigated. Its immunological and haematological side effects limit its applications. Its use as an oral medication should be reversed for conditions like epidermolysis is bullosa that lacks other effective therapy. Phenytoin is effective in thought, mood and behavior disorders. Its topical use for the treatment of wounds, ulcers, diabetic foot ulcers seems to be promising effect. The area of research that enhances the therapeutics effects includes a tweaking of its structure. Minimization of side effects would also benefit from molecular engineering. Phenytoin remains a tool to help the patients.

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