VINPOCETINE: A STEP TOWARDS MEMORY ENHANCEMENT

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ABSTRACT

Vinpocetine is a very effective tool used for memory enhancement. It is best known as cerebral vasodilator and very effective in age related memory impairment. Our memory starts decline after certain age it is basically due to damage of neurons, the drug vinpocetine has neuroprotective effect. So this drug is very effective in memory impairment. Vinpocetine dilates the blood vessels and increase the cerebral blood flow. In this review the pharmacokinetics pharmacodynamics, uses, clinical studies, adverse effects and research summary of vinpocetine are discussed.

Key Words: Vinpocetine, cerebral vasodilator, neuroprotective, memory enhancement.

INTRODUCTION

Vinpocetine is a semi-synthetic derivative of vincamine. Vincamine is an alkaloid extracted from the Periwinkle plant, Vinca minor L. Vinpocetine is an herbal supplement used to treat thinking and memory problems, such as Alzheimer's disease. Vinpocetine, as well as vincamine, are used in Europe, Japan and Mexico as pharmaceutical agents for the treatment of cerebrovascular and cognitive disorders. In the United States, vinpocetine is marketed as a dietary supplement. It is sometimes called a nootropic, meaning cognition enhancer. Other names for Vinpocetine include: Ethyl apovincaminate, Ethyl apovincaminoate, and vinca minor. Experiments with this periwinkle extract indicate that it can dilate blood vessels, enhance circulation in the brain, improve oxygen utilization, make red blood cells more pliable, and inhibit aggregation of platelets. Vinpocetine even has antioxidant properties. Levels peak in the bloodstream within an hour and a half after ingestion. Vinpocetine easily crosses the blood-brain barrier. Vincamine and Vinpocetine have been widely researched and used clinically for over 30 years, in disorders ranging from cerebral arteriosclerosis and senile dementia, to Meniere's disease, tinnitus, and diabetic retinopathy. Vinpocetine may help support brain...
functions such as concentration and memory by activating cerebral metabolism.

**MACHANISM OF ACTION:**

Vinpocetine has been shown to selectively inhibit voltage-sensitive Na⁺ channels, resulting in a dose-dependent decrease in evoked extracellular Ca⁺ ions in striatal nerve endings. The Na⁺ channel inhibiting properties of vinpocetine are thought to contribute to a general neuroprotective effect through blockade of excitotoxicity and attenuation of neuronal damage induced by cerebral ischemia/reperfusion. Several mechanisms have been proposed for the possible actions of vinpocetine. Vinpocetine has been reported to have calcium-channel blocking activity, as well as voltage-gated sodium channel blocking activity. It has also been reported to inhibit the acetylcholine release evoked by excitatory amino acids and to protect neurons against excitotoxicity. In addition, vinpocetine has been shown to inhibit a cyclic GMP phosphodiesterase, and it is speculated that this inhibition enhances cyclic GMP levels in the vascular smooth muscle, leading to reduced resistance of cerebral vessels and increase of cerebral flow. In some studies, vinpocetine has demonstrated antioxidant activity equivalent to that of vitamin E.

**PHARMACOLOGY:**

Vinpocetine indicated five main pharmacological and biochemical actions: (1) selective enhancement of the brain circulation and oxygen utilization without significant alteration in parameters of systemic circulation, (2) increased tolerance of the brain toward hypoxia and ischemia, (3) anticonvulsant activity, (4) inhibitory effect on phosphodiesterase (PDE) enzyme and (5) improvement of rheological properties of the blood and inhibition of aggregation of thrombocytes. Vinpocetine has several possible actions, including increasing cerebral blood flow and metabolism, anticonvulsant, cognition enhancement, neuroprotection and antioxidant. Vincamine, the parent compound of vinpocetine, is believed to be a good cerebral vasodilator.

**PHARMACOKINETICS:**

Vinpocetine is absorbed from the small intestine, from whence it is transported to the liver via the portal circulation. From the liver via the systemic circulation, it is distributed to various tissues in the body, including the brain. Absorption of vinpocetine is significantly higher when given with food and can be up to about 60% of an ingested dose. On an empty stomach, absorption of an ingested dose can be as low as 7%. Peak plasma levels are obtained one to one and a half hours after ingestion. Extensive metabolism to the inactive apovincaminic acid occurs in the liver. Only small amounts of unmetabolized vinpocetine are excreted in the urine, the major route of excretion of apovincaminic acid. Most of a dose is excreted within 24 hours as this metabolite. The elimination half-life of vinpocetine following ingestion is one to two hours.

**USES:**

Vinpocetine is widely used as Antioxidant effects, menopause, acute ischemic stroke, and phosphodiesterase-1 inhibition. It is best known for its neuroprotective effects (cerebral infarction and cerebral haemorrhage) and age-related memory impairment. It is widely marketed as a supplement for vasodilation and as a nootropic. It is mainly used as cerebral enhancer and neuroprotector. It is also very
effective in the treatment of short term memory loss.

According to literature numerous studies and investigations on the pharmacological and biochemical actions of vinpocetine. The various mechanism of actions include: 1) effects on brain circulation and oxygen utilization without changes in systemic circulation; 2) increased tolerance of the brain to vascular hypoxia and ischemia; 3) anticonvulsant activity; 4) phosphodiesterase-1 inhibition; and 5) lowering of blood viscosity and inhibition of aggregation of thrombocytes.

Antioxidant effects In vitro and animal data

Vinpocetine has a scavenger effect similar to that of vitamin E. Its antioxidant activity also was tested in vitro against pentoxifylline and piracetam; vinpocetine had significant (P <0.01) scavenging activity compared with these drugs.

Menopause Clinical data

The therapeutic effect of Cavinton (vinpocetine) on menopausal complaints was assessed in 3 groups of women (control or group 1 [n = 30], group 2 with normolipidemia [n = 32], and group 3 with hyperlipidemia [n = 29]) in early menopause. A comparative investigation involving 40 climacteric postmenopausal women studied the effects of hormone substitution therapy and combined hormone substitution and Cavinton adjuvant therapy. Relief or improvement of climacteric symptoms was measured by the Kupperman index. The results were statistically analyzed, and Cavinton appeared to improve symptoms experienced with estrogen substitution.

Antiulcer activity Animal and in vitro data

The efficacy of vinpocetine against several agents that cause gastric mucosal damage was studied in rats. Oral and intraperitoneal administration of vinpocetine inhibited development of dose-dependent gastric lesions caused by 96% ethanol. Vinpocetine provided the most protection when given intraperitoneally 30 minutes before ethanol. It demonstrated activity against gastric injury induced by phenylbutazone, chronic gastric ulcer induced by acetic acid, and histamine-stimulated gastric acid secretion in pylorus-ligated rats.

Phosphodiesterase-1 inhibition

Vinpocetine inhibits calcium calmodulin-dependent phosphodiesterase (PDE) type 1. This inhibition may lead to increases in cyclic adenosine 3',5'-monophosphate and may be responsible for benefits in cerebral circulation and decreased platelet aggregation.

Animal and in vitro data

Vinpocetine potentiated the effect of sodium nitroprusside and nitroglycerin on the smooth muscle cells in a rat aorta model. Vinpocetine produced a dose-dependent inhibition on Ca2+ conductivity and decreased the smooth muscle contractility of the membrane at a concentration of 2 to 20 microM. PDE activity was inhibited at a concentration of 1 microM.

In an in situ-perfused, rat lung preparation, vinpocetine attenuated acute hypoxic vasoconstriction.

Clinical data

Vinpocetine was investigated in nonresponders to standard pharmacological therapy for urge incontinence and low compliance bladder. In 11 of 19 patients, clinical symptoms were improved. Vinpocetine may also have a
potential role in the treatment of urgency and interstitial cystitis.

**Neuroprotective effects**

**Tinnitus Animal data**

Vinpocetine 2 mg/kg prevented hearing loss induced by the aminoglycoside antibiotic amikacin 450 mg/kg in guinea pigs.

**Clinical data**

Details of the study are limited, but Cavinton prevented neurosensory hypoacusis in 118 tuberculosis patients (17 to 63 years of age) who had normal hearing or hearing problems.

**Antiepileptic activity**

Mechanism of action may involve blockade of presynaptic sodium and calcium channels. Brain gamma-aminobutyric acid and serotonergic mechanisms may be involved.

Animal data – Vinpocetine protected mice against convulsions induced by corazol, strychnine, and thiosemicarbazide. It also antagonized the convulsive reactions produced by systemic administration of penicillin or combined administration of penicillin with a tryptophan metabolite (quinolinic acid) in cats. In guinea pigs, vinpocetine 2 to 10 mg/kg inhibited tonic-clonic convulsions and auditory alterations induced by pentlenetetrazole 100 mg/kg. Vinpocetine 2 mg/kg completely prevented the electroencephalogram (EEG) changes induced by pentlenetetrazol for the ictal and postictal periods when administered prior to pentlenetetrazol.

Vinpocetine inhibited the EEG changes caused by 4-aminopyridine for the ictal and postictal periods and increases in auditory brainstem responses in guinea pigs. The dose used for 4-aminopyridine and vinpocetine was 2 mg/kg.

Clinical data – The effect of Cavinton 15 to 45 mg/day on epilepsy was studied with different anticonvulsants. In 20 of the 31 patients treated with Cavinton, frequency of attacks significantly decreased or complete disappeared; 7 patients showed no improvement and 4 experienced deterioration. Cavinton was most effective in generalized tonic-clonic convulsions.

The effect of Cavinton in preventing neurologic disorders was studied in 61 newborns with hypoxic ischemic encephalopathy caused by intracranial birth trauma. Group 1 included 20 patients receiving conventional therapy; seizures disappeared in 6 patients. Group 2 included 41 patients given Cavinton; seizures disappeared in 27 patients. Twenty-nine children were subsequently followed for 1 year. Convulsive paroxysms recurred in 4 patients in group 1. No convulsive syndrome was recorded for patients in group 2; these same patients also had a decrease in intracranial hypertension and normalization of psychomotor development.

**Psychopharmacological effects Clinical data**

Vinpocetine, at increasing doses (30, 45, and 60 mg/day), was ineffective in improving cognitive deficits in 15 Alzheimer patients participating in a 1-year, double-blind, placebo-controlled, open-labeled pilot trial.

In a randomized, double-blind, crossover study, 12 women receiving either vinpocetine (10, 20, 40 mg) or placebo for 2 days completed a battery of psychological tests (critical flicker fusion, choice reaction time, subjective ratings of drug effects, and a Sternberg Memory Scanning Test) on day 3 of treatment, 1 hour after the morning dose of vinpocetine. Statistically significant changes in memory as assessed by the Sternberg Memory Scanning
Test were observed with vinpocetine 40 mg compared with placebo.

Cavinton, when combined with protiadenum, improved psychopharmacotherapy of depressive disorders in patients with organic psychosyndromes. In a 16-week, placebo-controlled, randomized, double-blind, multicenter trial, 203 patients received vinpocetine 10 or 20 mg (3 times daily) or placebo (3 times daily). Primary outcomes were assessed from the Clinical Global Impression scale, using measurements from cognitive performance and quality of life. Side effects were comparable in treatment and placebo groups. Patients treated with vinpocetine reported statistically significant improvements in all tests.

**Acute Ischemic Stroke Animal data**

Vinpocetine significantly decreased infarct volume (42%; P < 0.05) on permanent middle cerebral artery occlusion in rats compared with control; the neuroprotective potency of vinpocetine is compared with that of flunarizine or nimodipine. Vinpocetine also may reduce the development of atherosclerosis. In a 3-month study in rabbits given cholesterol-rich diets, 3 of 4 groups (4 rabbits in each group) fed vinpocetine supplements displayed decreased calcium content in various organ systems.

**Clinical data**

A reduction in red blood cell deformability is a contributory or risk factor for stroke. Vinpocetine, administered in a single oral dose of 10 mg, increased red blood cell deformability in 5 healthy men. When compared with single oral doses of pentoxifylline 300 mg and nicergoline 20 mg, vinpocetine was more effective in increasing red blood cell deformability.

The effect of a single-dose intravenous infusion of vinpocetine on cerebral blood flow and glucose metabolism was studied in poststroke patients. Results indicated that glucose transport (intracellular uptake and release) was affected in the whole brain, in the contralateral hemisphere, and in the peri-infarction area of the symptomatic hemisphere. Numerous studies document the effect of vinpocetine-modifying utilization of glucose in the brain (in acute ischemic and chronic stroke patients), particularly in the affected hemisphere.

A pilot, single-blind, randomized trial examined the effect of vinpocetine on 30 patients diagnosed with acute ischemic stroke who could be treated within 72 hours of stroke onset. Patients were randomly assigned to receive either low-molecular weight dextran alone (mean age, 57.9 +/- 11.6 years; n = 15) or in combination with vinpocetine (mean age, 60.8 +/- 6.6 years; n = 15). The vinpocetine-treated group scored only marginally better at 3 months follow-up (P = 0.05, ANOVA). Patients did not report any adverse reactions.

The effect of vinpocetine on compromised cerebral blood perfusion and oxygenation in 43 patients with ischemic stroke was examined in a double-blind, randomized, placebo-controlled study. Patients received either a single dose of intravenous vinpocetine 20 mg in saline 500 mL or saline 500 mL alone as placebo. Results from transcranial Doppler and near infrared spectroscopy methods indicated increased cerebral perfusion and parenchymal oxygen extraction frontolaterally on the side of the lesion.

**Chronic Cerebral Vascular Ischemia**

Results from animal and human data postulate that the neuroprotective action of vinpocetine is associated with its effect on calcium- and calmodulin-dependent cyclic guanosine
monophosphate-phosphodiesterase 1, voltage-operated calcium channels, glutamate receptors, and voltage-dependent sodium channels.

Clinical data

Eighty-one patients with chronic forms of cerebral ischemia were treated orally or parenterally with Cavinton. Patients reported reduction in subjective manifestations of the disease such as asthenic disturbances. The therapeutic effect ranged from 40 minutes to 6 hours with intravenous infusion. The authors concluded that Cavinton increased cardiac output and cerebral blood supply, and decreased peripheral resistance of the cerebral vessels. A similar study was completed in 38 patients with cerebral ischemia and atherosclerosis alone (n = 22) or hypertension (n = 16). Results for patients receiving Cavinton demonstrated decreased peripheral vascular resistance and tone of small and median vessels of the brain, increased cardiac output, and improved rheological properties of the blood (lower globular volume, viscosity, and hematocrit). A study involving 171 patients found the drug to be more effective in young to middle-aged patients versus elderly patients, perhaps because of the organic changes in cerebral vessels in the elderly. Vinpocetine effects on the rheological properties of blood have been documented in other studies, particularly with parenteral administration.

In a double-blind clinical trial, 42 patients with chronic vascular senile cerebral dysfunction received vinpocetine 10 mg 3 times daily for 30 days followed by 5 mg 3 times daily for 60 days. Placebo tablets were given to another 42 patients over 90 days. Evaluations of the effectiveness of treatment from the Clinical Global Impression scale, the Sandoz Clinical Assessment-Geriatric scale, and the Mini-Mental Status Questionnaire were consistently higher in patients receiving vinpocetine. No serious side effects were reported.

PRECAUTIONS:

Pregnant women and nursing mothers should avoid vinpocetine supplements. Those with a history of allergic reactions or hypersensitivity reactions during treatment with other vinca alkaloids, such as vinblastine and vincristine, should avoid vinpocetine. Those on warfarin are advised to have their INRs (international normalized ratios) regularly monitored when using vinpocetine supplements (see Interactions). Those with hypotension or orthostatic hypotension should be cautioned that prolonged use of vinpocetine may lead to slight reductions in systolic and diastolic blood pressure.

ADVERSE REACTIONS:

Vinpocetine is reported adverse reactions include nausea, dizziness, insomnia, drowsiness, dry mouth, transient hypotension, transient tachycardia, pressure-type headache and facial flushing. Slight reductions in both systolic and diastolic blood pressure with prolonged use of vinpocetine have been reported, as well as slight reductions in blood glucose.

RESEARCH SUMMARY:

Studies have reported significant vinpocetine-associated protective effects in ischemic stroke. These studies, found only one positive study of a truly randomized, unconfounded clinical trials that compared the effect of vinpocetine to either placebo or another reference treatment for acute stroke where treatment started no later than 14 days after stroke onset. There is currently not enough evidence to determine whether vinpocetine does or does not reduce fatalities and dependence in ischemic stroke.
Further research is needed. Vinpocetine may be useful in some other cerebral maladies. In one multi-center, double-blind, placebo-controlled study lasting 16 weeks, 203 patients described as having mild to moderate psychoses, including primary dementia, were treated with varying doses of vinpocetine or placebo. Significant improvement was achieved in the vinpocetine-treated group as measured by "global improvement" and cognitive performance scales. Three 10-milligram doses daily were as effective or more effective than three 20-milligram doses daily. Similarly good results were found in another double-blind clinical trial testing vinpocetine versus placebo in elderly patients with cerebrovascular and central nervous system degenerative disorders. Studies of Alzheimer's disease, however, have shown no vinpocetine benefit. Some preliminary research suggests that vinpocetine may have some protective effects in both sight and hearing. One study of patients with mild burn trauma in the eyes showed that vinpocetine enhanced healing, most likely as a result of increased blood flow to the damaged tissue. Vinpocetine has also been associated with improvements seen in retinas damaged by hepatitis B virus. Damage from acoustic trauma has similarly been reduced by vinpocetine treatment. Vinpocetine gastroprotective effects have been reported in animal models challenged with noxious agents. There are anecdotal reports that vinpocetine is protective against some of the gastric and neurological toxicity of excessive alcohol consumption. There are some reports that vinpocetine may be an effective motion sickness preventative and some early findings in animals that it may exert some anti-atherosclerotic effects through a reported ability to decalcify cholesterol-induced atherosclerotic lesions.

Clinical Studies:

Both animal experimental and human clinical research have shown Vinpocetine to restore impaired brain carbohydrate/energy metabolism. In 1976 Vamosi and colleagues reported their favorable results comparing Vinpocetine with Xanthinol Nicotinate in treating 143 patients with various cerebrovascular diseases. They measured a large number of blood and cerebrospinal fluid variables before and after treatment, such as glucose, lactate, pyruvate, oxygen, pH, electrolyte levels, etc.

Vamosi's study also demonstrated a superior clinical efficacy of Vinpocetine over Xanthinol Nicotinate. Karpoti and Szpony resulted favorable results of Vinpocetine used to treat anaesthetized dogs. Anesthetics reduce brain aerobic metabolism and ATP production - this is a key aspect of their ability to produce unconsciousness.

These are just a few of the many reports indicating the ability of Vinpocetine to safely and effectively restore failing neuronal energy metabolism, even under hypoxic or ischaemic (poor blood flow) conditions.

STORAGE:

Keep all medicine locked up and away from children. Store medicine away from heat and direct light. Do not store your medicine in the bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause the medicine to break down and not work the way it should work. Throw away medicine that is out of date or that you do not need. Never share your medicine with others.

DISCLAIMER:

This product and its statements have not been evaluated by the FDA. This product is not intended to treat, cure or prevent any disease.
WARNINGS:

Before taking Vinpocetine, tell your doctor if you are pregnant or breastfeeding
Do not take Vinpocetine if you have a low blood pressure
Do not take Vinpocetine if you have constipation (difficulty having a bowel movement)
Do not use Vinpocetine if you have a seizure disorder
Do not use Vinpocetine if you have liver problems

DOSE:

Vinpocetine is available as an individual supplement and in combination products. Typical doses for supplement use are 5 to 10 milligrams daily with food. Some take up to 20 milligrams daily. Higher doses are not advised.

CONCLUSION:

Vinpocetine is a unique product is having so many memory enhancing effects. It is widely used as cerebral vasodilator and has good neuroprotective effect. Vinpocetine has very less side effect and it has good pharmacokinetic and pharmacodynamic property. It is best known for age-related memory impairment. So this review conclude that vinpocetine is a very effective step towards memory enhancement.

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REFERENCES


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