

Recent uses of piracetam in pediatric neurology

Aamir Jalal Al Mosawi

Advisor in Pediatrics and Pediatric Psychiatry Children, Teaching Hospital of Baghdad Medical City Head, Iraq Headquarter of Copernicus Scientists International Panel Baghdad, Iraq

Corresponding Author: Aamir Jalal Al Mosawi, Advisor in Pediatrics and Pediatric Psychiatry Children Teaching Hospital of Baghdad Medical City.**Received date: March 06, 2020; Accepted date: June 12, 2020; published date: June 18, 2020****Citation:** Aamir Jalal A, M., (2020) Recent uses of piracetam in pediatric neurology .International Journal of Clinical Case Reports and Reviews. 2(4); DOI: [10.31579/2690-4861/018](https://doi.org/10.31579/2690-4861/018)**Copyright:**©2020 **Aamir Jalal Al Mosawi**, This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Piracetam (2-oxo-1-pyrrolidine acetamide) is a cyclical derivative of GABA (gamma-aminobutyric acid). It was first synthesized during the 1950s by Corneliu E. Giurgea. There are reports of its use for epilepsy in the 1950s. Piracetam can beneficially influence impaired brain function by improving neuronal and cognitive functions without acting as a sedative or stimulant, increasing blood flow and oxygen consumption in the brain, and improving the function of the neurotransmitters and brain neurotransmission. The modes of action of piracetam has been attributed to differential effects on subtypes of glutamate receptors without GABAergic actions Piracetam has no significant side effect nor has acute toxicity at the doses used in human studies. The LD₅₀ is 5.6 g/kg in rats and 20 g/kg in mice, indicating extremely low acute toxicity [1-4].

Piracetam has been used in the treatment of various neuropsychiatric disorders including senile involution [5], geriatric memory impairment [6], *post-concussional syndrome* [7], spasticity in cerebral palsy [8], acute cerebral ischemia [9,10], organic dementia [11,12,13], anxiety [14,15], dyslexia [16], schizophrenia [17], vertigo [18], epilepsy and seizures including myoclonus epilepsy [19,20], cognition and memory deficit [21], acute and chronic consciousness disturbances caused by clinical syndromes of cerebrovascular disease (strokes, syndromes of dementia) [22], rehabilitative treatment of the middle-aged and elderly with a stroke[23], management of neuroleptic side effects and neuroleptic-induced akathisia [42,25,26,27], and learning disability [28]. Table-1 summarizes piracetam experimental and clinical research findings during the 1970s, and Table-2 summarizes piracetam experimental and clinical research findings during the 1980s.

Recent uses of piracetam in pediatric neurology include brain atrophy,

Piracetam has been recently used as a part of multi-factorial therapies in the treatment of brain atrophy has been recently reported. Multi-factorial therapies including intramuscular piracetam, intramuscular cerebrolysin, citicoline (oral and intramuscular), oral pyritinol, and intramuscular nandrolone decanoate was used with a beneficial effect in a very severe form of spastic cerebral palsy associated with evidence of significant brain atrophy [1].

Piracetam was used in the treatment of a boy with idiopathic mental retardation which is a heterogeneous condition. Treatment included a new combination of interventions consisting of the use of intramuscular piracetam, intramuscular cerebrolysin, intramuscular citicoline, and oral pyritinol. Treatment was successful in advancing the mental function of the boy with moderately severe idiopathic mental retardation who was uneducable, but became perfectly educable after treatment [2].

Piracetam was used in the treatment of cerebral palsy which is a heterogeneous condition associated with a non-progressive lesion, but permanent disorder of movement with limited mobility. Cerebral palsy is generally associated with gross motor developmental delay. In moderate to severe cases motor developmental milestones such as walking may never be achieved [3].

Table-1: Summary of piracetam research findings during the 1970s

A double-blind study compared the effect of piracetam treatment with that of a placebo in post-concussional syndrome suggested that piracetam can be a new drug for the treatment of post-concussional syndrome (Hakkarainen and Hakamies, 1978) [7].

The use of piracetam was useful in controlling spasticity in eight of sixteen patients with cerebral palsy with minimal side-effects (Maritz and colleague, 1978) [8].

*The effect of piracetam on regional cerebral blood flow was studied in 18 patients with acute cerebral ischemia by the intra-arterial ¹³³Xenon clearance method using a 10-detector-equipment. The use of piracetam was associated with a statistically significant (*P* is less than 0.005) increase of cerebral blood flow in grey matter which was attributed to activation of central nervous system metabolism (Herrschaft, 1978) [9].*

An experimental study on rats showed that piracetam has anxiolytic properties (File and Hyde, 1978) [14].

<i>A study showed that in the social interaction test of anxiety, piracetam (100 mg/kg) had an anxiolytic effect very similar to that observed after five days of chlordiazepoxide 5 mg/kg/ day, and piracetam (50-300 mg/kg) had a non-sedative anxiolytic effect (Sandra File and Hyde, 1979) [15].</i>
<i>A double-blind study with a cross-over technique found that piracetam significantly increased verbal learning of dyslexics by 15.0% and volunteer students by 8.6% over and above their placebo increase (Wilsher and colleague, 1979) [16].</i>
<i>A study reported that treatment of chronic schizophrenic patients with piracetam was associated with cognitive improvement but with no improvements in symptom rating, social behavior rating or the disease state (Dimond et al, 1979) [17].</i>
<i>An experimental study showed that piracetam can be useful in the treatment of post-hypoxic edema of the brain by improving the microcirculatory changes and reducing the manifestations of post-hypoxic edema of the brain (Polunin and colleague, 1979) [29].</i>
<i>A study reported that the use of piracetam (10 g i.v./hour) in 26 in normal course of delivery at term was associated with a stabilization of cerebral functions with a resistance against transient hypoxia during the expulsion period and improved Apgar scores (Klink et al ,1979)[30].</i>

Table-2: Summary of piracetam research finding during the 1980s

<i>In an experimental study on the brain of cats, piracetam (100 mg/kg i.v) was associated with an increased local cortical cerebral blood flow in 84% of the experiments on cats without hypoxia and in 40% of the experiments with slight hypoxia (Vlahov and colleague, 1980) [31].</i>
<i>In a double-blind trial, comparing the effects of piracetam and a placebo in 22 patients, the use of piracetam was associated with a significant reduction of symptoms associated with vertigo of central origin. The effect of piracetam was attributed to an enhanced control of the cerebral cortex on the subordinated vestibular centers. (Oosterveld ,1980) [18].</i>
<i>Experimental studies on mice showed that piracetam can significantly improve learning capacity of young mice, and performance in old mice suggesting that it is effective in improving the function of the aging brain (Valzelli and colleague, 1980) [32].</i>
<i>A clinical study showed that piracetam 6 g daily given by drip infusions for 10 days was associated with improvement in the acute and chronic syndrome of consciousness disturbances caused by clinical syndromes of cerebrovascular disease and dementia (Sobczyk , 1980) [22].</i>
<i>An experimental study showed that piracetam had protective effects in various types of hypoxia in mice, cats and rats except hemic hypoxia induced by injection of sodium nitrite (Roshchina and Ostrovskaia, 1981) [33].</i>
<i>A study compared the effects of piracetam with placebo in a double-blind cross-over study of 30 learning disabled boys. Piracetam caused a decrease in the amount of delta activity and an increase in the average EEG frequency. This effect of piracetam was attributed to increased alertness and/or decreased fatigue (Volavka et al, 1981) [28].</i>
<i>An experimental study showed that piracetam/choline combination (100 mg/kg of each) was associated with memory enhancement several times better than rats received piracetam alone (Bartus et al ,1981) [34].</i>
<i>The use of piracetam in the management of neuroleptic side effects has been reported (Sikora and colleague,1981), and a clinical study showed that piracetam in a dose of 40 g given intravenously was effective in reducing the extra-pyramidal side effects induced by neuroleptic drugs Kabes et al (1982) [25].</i>
<i>A double-blind cross-over controlled trial with a placebo showed that piracetam was effective in tardive dyskinesia (Kabes et al, 1983) [26].</i>

In a retrospective observational study, patients with spastic cerebral palsy were treated with individualized treatment plans providing a new combination of interventions including nutritional support, muscle relaxants and the use of oral pyritinol, intramuscular piracetam ,intramuscular cerebrolysin, citicoline (oral and intramuscular), and

intramuscular nandrolone decanoate. Treatment aimed primarily at improving motor development particularly standing and walking. Six patients (3 girls and 3 boys) with spastic cerebral palsy and marked motor disability were treated. The patients' age ranged from 22 months to three years. All patients were unable to stand or walk, and had poor speech

development. Four patients had severe cerebral palsy and were even unable to sit. The other two patients had moderately severe disorder and were unable to stand or walk. All the patients were not saying any word or were saying only few words. After treatment, all the treated patients experienced improvement in motor development without the occurrence of any side effect. Five patients were able to stand with support, and four of them were also able to walk few steps with support. The sixth patient remained unable to stand and the limited benefit of treatment was attributed to some degree of deformity and muscle contracture. In all patients treatment was associated with initiation of speech development or improved speech. It was possible to demonstrate improvement in fine motor skills in three patients. This study suggested that treatment of patients with spastic cerebral palsy (moderate and severe) with this individualized treatment plans was associated with a beneficial effect on motor development particularly standing and walking [3].

Corpus callosum is a large nerve tract consisting of a flat bundle of commissural fibers that runs below the brain cerebral cortex. It connects the left and right cerebral hemispheres. Absence of the corpus callosum because of failure of development is a rare congenital defect called "Agenesis of the corpus callosum" [4]. In a recent study, two Iraqi infants with non-syndromic agenesis of the corpus callosum were observed. One infant had the isolated type and the second infant had agenesis of the corpus callosum associated with colpocephaly. Both infants had the clinical features of the syndrome resulting from the associated failure of neuronal migration including hypotonia with poor head control, no response to voice, not recognizing faces, and they didn't show any eye contact. They have never smiled and had poor spontaneous movements. The patient with colpocephaly was a girl and, she was treated with courses of intramuscular piracetam and cerebrolysin for three months with aim of improving brain functions and accelerating her development. The second patient was a boy and he didn't receive any specific therapy. Treatment was not associated with any side effects, and after three months of treatment, the patient experienced improvements in feeding, muscle tone, alertness and response to voice, and movements. The untreated patient didn't show any obvious improvement despite he didn't have colpocephaly [35].

References

- Al-Mosawi AJ. (2017) A novel therapeutic approach for the treatment of brain atrophy (Ed). LAP Lambert Academic Publishing, Germany.
- Al-Mosawi AJ. (2018) A novel therapeutic approach for idiopathic mental retardation (Ed). LAP Lambert Academic Publishing, Germany.
- Al-Mosawi AJ. (2019) 2578-4838 .New therapies for the treatment of Spastic cerebral palsy. *Med J Clin Trials Case Stud.*3 (2): 000209.
- Al-Mosawi AJ. Agenesis of corpus callosum with colpocephaly: A novel therapy. 1st ed., Saarbrücken; LAP Lambert Academic Publishing.
- Abuzzahab FS Sr Merwin GE, Zimmermann RL, Sherman MC. (2019) A double blind investigation of piracetam (Nootropil) vs. placebo in geriatric memory. *Pharmakopsychiatr Neuropsychopharmakol* 1977 Mar; 10(2):49-56. PMID: 360232.
- Stegink AJ. (1972) The clinical use of piracetam, a new nootropic drug. The treatment of symptoms of senile involution. *Arzneimittelforschung.*22 (6):975-977. PMID: 4559159.
- Hakkarainen H, Hakamies L. (1978) Piracetam in the treatment of post-concussional syndrome. A double-blind study. *European Neurology.*17 (1): 50-55. PMID: 342247.
- Maritz NG, Müller FO, Pompe van Meerdervoort HF. (1978) Piracetam in the management of spasticity in cerebral palsy. *S Afr Med J Jun* 3; 53(22):889-891. PMID: 356288.
- Herrschaft H. (1978) The effect of piracetam on global and regional cerebral blood flow in acute cerebral ischemia of man. *Med Klin.* Feb 10; 73(6):195-202. PMID: 340868.
- De Reuck J, Van Vleymen B. (1999) The clinical safety of high-dose piracetam: Its use in the treatment of acute stroke. *Pharmacopsychiatry.*32 Suppl 1: 33-37. PMID: 10338106.
- Waegemans T, Wilsher CR, Dannaïu A, Ferris SH, Kurz A, Winblad B. (2012) Clinical efficacy of piracetam in cognitive impairment: a meta-analysis. *Dementia and Geriatric Cognitive Disorders.*13 (4):217-224. PMID: 12006732.
- Gustafson L, Risberg J, Johanson M, Fransson M, Maximilian VA. (1978) Effects of piracetam on regional cerebral blood flow and mental functions in patients with organic dementia. *Psychopharmacology (Berl)* Mar 1; 56(2):115-117. PMID: 417361.
- Lloyd-Evans S, Brocklehurst JC, Palmer MK. (1979) Piracetam in chronic brain failure. *Curr Med Res Opin;* 6(5):351-357. PMID: 540525.
- File SE, Hyde JR. Piracetam : (1978) a non-sedative anxiolytic drug? *Br J Pharmacol* Mar;62(3):425P-426P. PMID:25106.
- File SE, Hyde JR. (1979) Evidence that piracetam has an anxiolytic action. *J Affect Disord* Dec;1(4):227-235. PMID:95599.
- Wilsher C, Atkins G, Manfield P.(1979) Piracetam as an aid to learning in dyslexia. Preliminary report. *Psychopharmacology (Berl) Sep;* 65(1):107-109. PMID: 116285.
- Dimond SJ, Scammell RE, Pryce IG, Huws D, Gray C. (1979) Some effects of piracetam (UCB 6215, Nootropyl) on chronic schizophrenia. *Psychopharmacology (Berl) Sep;* 64(3):341-348. PMID: 116278.
- Oosterveld WJ. (1980) The efficacy of piracetam in vertigo. A double-blind study in patients with vertigo of central origin. *Arzneimittelforschung;* 30(11):1947-1949. PMID: 7006617.
- Koskiniemi M, Van Vleymen B, Hakamies L, Lamusuo S, Taalas J. (1998) Piracetam relieves symptoms in progressive myoclonus epilepsy: a multicentre, randomised, double blind, crossover study comparing the efficacy and safety of three dosages of oral piracetam with placebo. *Journal of Neurology, Neurosurgery, and Psychiatr;* 64 (3): 344-348. PMID: 9527146.
- Fedi M, Reutens D, Dubeau F, Andermann E, D'agostino D, Andermann F. (2001) Long-term efficacy and safety of piracetam in the treatment of progressive myoclonus epilepsy. *Archives of Neurology;* 58 (5): 781-786. PMID 11346373.
- Chouinard G, Annable L, Ross-Chouinard A, Olivier M, Fontaine F.(1983) Piracetam in elderly psychiatric patients with mild diffuse cerebral impairment. *Psychopharmacology;* 81 (2): 100-106. PMID: 6415738.
- Sobczyk W. Effectiveness of parenteral administration of piracetam in acute and chronic consciousness disorders in cerebral arteriosclerosis. *Neurol Neurochir Pol* 1980; 14(2):177-182 PMID: 6993975 [Article in Polish].
- Man'kovskii NB, Kostichenko VG, Tereshchenko LA, Tordii GD. Use of piracetam (nootropil) in the rehabilitative treatment of the middle-aged and elderly who have had a stroke. *Vrach Delo* 1980 Sep ;(9):73-77. PMID: 7423958[Article in Russian].
- Sikora J, Kabes J, Pisevc J. Management of neuroleptic side-effects with piracetam. *Cesk Psychiatr* 1981 Apr; 77(2):137-142. PMID: 6114800 [Article in Czech].
- Kabes J, Sikora J, Pisevc J, Hanzlicek L, Skondia V. Effect of piracetam on extrapyramidal side effects induced by

- neuroleptic drugs. *Int Pharmacopsychiatry*. 1982; 17(3):185-192 PMID: 6128331.
26. Kabes J, Sikora J, Starý O, Pisvejc J, Hanzlíček L. Effectiveness of piracetam in tardive dyskinesia-double-blind cross-over controlled trial with a placebo. *Cesk Psychiatr* 1983 Oct; 79(5):339-345. PMID: 6357509 [Article in Czech].
 27. Fleischhacker WW, Roth SD, Kane JM. The pharmacologic treatment of neuroleptic-induced akathisia. *J Clin Psychopharmacol* 1990 Feb; 10(1):12-21.
 28. Volavka J, Simeon J, Simeon S, Cho D, Reker D. Effect of piracetam on EEG spectra of boys with learning disorders. *Psychopharmacology (Berl)* 1981; 72(2):185-188. PMID: 6782609.
 29. Polunin BA, Tumanov VP, Avrutskiĭ Mla. Effect of nootropil and contvykal on the structural changes in the central nervous system in hypoxic brain edema. *Biull Eksp Biol Med*. 1979 Dec; 88(12):726-729. PMID: 316339 [Article in Russian].
 30. Klink F, Grosspietsch R, von Klitzing L, Oberheuser F. The protective effect of piracetam during delivery. *Fortschr Med*. 1979 Dec 6; 97(46):2163-2165.
 31. Vlahov V, Nikolova M, Nikolov R. The effect of piracetam on the local cortical cerebral blood flow in cats. *Arch Int Pharmacodyn Ther* 1980 Jan; 243(1):103-110. PMID: 6770768.
 32. Valzelli L, Bernasconi S, Sala A. Piracetam activity may differ according to the age of the recipient mouse. *Int Pharmacopsychiatry* 1980; 15(3):150-156. PMID: 6165698.
 33. Roshchina LF, Ostrovskaia RU. Effect of piracetam on the body's resistance to hypoxia. *Farmakol Toksikol* 1981 Mar-Apr; 44(2):210-213. PMID: 7274430 [Article in Russian].
 34. Bartus RT, Dean RL 3rd, Sherman KA, Friedman E, Beer B. Profound effects of combining choline and piracetam on memory enhancement and cholinergic function in aged rats. *Neurobiol Aging* 1981 Summer; 2(2):105-111 PMID: 7301036.
 35. Al-Mosawi AJ. The use of piracetam and cerebrolysin in the treatment of agenesis of corpus callosum with colpocephaly. *EC clinical and medical case reports* 2020; 3(1): 01-05.