Emergency Medicine: Open Access
ISSN: 2165-7548

Habibollahi et al., Emerg Med (Los Angel) 2016, 6:6
DOI: 10.4172/2165-7548.1000339

Mini Review Open Access

Central Nerve System Symptom of Tri-Cyclic Acids Antidepressants

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Received date: October 26, 2016; **Accepted date:** November 06, 2016; **Published date:** November 14, 2016

Abstract

CNS is the main site of therapeutic action of TCAs and these have direct effects on the CNS. The TCAs antidepressant effect is recognized to be the blockade of monoamine reuptake, at both noradrenergic and serotonergic nerve endings. Tricyclic compounds have anticholinergic effects and predominantly action on myocardium sodium channels then this group has a various symptoms; Since TCA has various presentation; we must ready to find different signs and symptoms of that. We must know all of sign and symptoms to be ready for manage it or them because cannot predict what patients will manifest.

Introduction

Cyclic antidepressants contain pertinent compounds. The older agents include of three-ring tertiary and secondary amines and the newer agents one-, three-, and four-ring structures. Several antidepressant agents such as trazodone and fluoxetine simulate those previously mentioned in structure [1,2]. CAs are absorbed orally and quickly distributed, this are very lipophilic and bind strongly to tissue and plasma proteins and with relatively large volume distributed (10 to 50 L/kg). Metabolism begins oxidation of Hepatic microsomal enzymes by combined with glucuronic acid.

There is significant first-pass metabolism, enterohepatic recycling, and modest excretion into urine and gastric fluid. In overdose combined effects of slow dissolution, poor absorption when ionized by gastric acid, peak plasma concentrations can achieve up to 12 hours [3,4], elimination half-life ranges from 1 to 3 days via inhibition of gastric emptying by anticholinergic actions [5].

Two years after the identification of clinical efficacy of tricyclic the side effects of overdose were reported [6]. Now tricyclics are most frequently ingested substances in self-poisoning along with paracetamol, benzodiazepines, and alcohol [7]. They are commonest in the fatal drug overdose and second only to analgesics [8,9].

Pharmacology

CNS is the main site of therapeutic action of TCAs and these have direct effects on the CNS. The TCAs antidepressant effect is recognized to be the blockade of monoamine reuptake, at both noradrenergic and serotonergic nerve endings. Tricyclic compounds have anticholinergic effects and predominantly action on myocardium sodium channels. These may all be relevant to their CNS effects in overdose [10].

The clinical effects of TCAs succedent overdose case series published from the 1960s and in the 1970s [11,12] effects of TCAs overdose were similar to clinical features associated with the antimuscarinic compounds.

Antimuscarinic effect

Early common effects were myoclonic and chores-athetoid movements (up to 43%) and other effects included dilated pupils, drowsiness and tachy- cardia [11]. One potentially important interferer is the change in the availability of other drugs to co-ingest, in particular, benzodiazepines [12].

Seizure

Grand mal convulsions are the most important CNS effect. Convulsions were an early complication, and occur 12 hours after overdose ingestion [12]. Seizures are usually self-limiting but benzodiazepines are the choice of treatment [13]. Efficacy of phenytoin has never been proven but some introduced the use of it [14]. And the use of phenytoin in a rat model was found to be of no benefit [15]. In the loss of consciousness and respiratory depression in seizure, intubation is required.

Coma

Duration of coma in TCA poisoning tended to be relatively short-lived, noted in 1976 [16].

In this series, one-third of patients presenting in the coma were awake in 2 hours, and two-thirds in 24 hours. Some texts have referred to the ability of TCAs to depress brain-stem reflexes in overdose. So, White reported on three cases, two of which included a tricyclic compound, which had absent brain-stem reflexes [17]. Yang and Dantzker reported a loss of brain-stem reflexes in amitriptyline overdose of 9 g in a 46-year-old patient [18]. More recently, a case was reported of 5 days of coma following ingestion of a combined overdose, which included amitriptyline and venlafaxine associated with loss of brain stem reflexes but no features of cardiovascular toxicity [19].

Gaze

During the course of coma in TCA poisoning external ophthalmoplegia, manifesting clinically as divergent squint. Pulst and

Lom-broso were reported one such case associated with seizures and respiratory arrest [20]. Larger case series do not provide sufficient data to assess an occurrence. Gaze paralysis and Internuclear ophthalmoplegia are other CNS features [21,22].

Hyperpyrexia

Reduced ability to sweat may result of Anti-muscarinic features of TCA poisoning. Disturb thermoregulation by central cholinergic muscarinic antagonism and thus chip into hyperpyrexia [23]. Temperature disturbance may have more than one cause in TCA poisoning because TCA poisoning has been associated with the development of a serotonergic syndrome [24]. Baca and Martinelli reported the therapeutic use of desipramine in a 50-year-old woman who developed features of hyperpyrexia and elevated creatine kinase activity [25].

Delirium

Prolonged delirium in the recovery phase of TCA poisoning. The typical clinical pattern of incoherent mumbling and plucking at the bed clothes in patients who had serious intoxication in our experience accompanied is a relatively common feature. The cause of delirium is unclear, and it does not respond to treatment with physostigmine [26] Therapeutic use of antidepressants created a less severe pattern of behaviour [27,28]. These observations suggest that the excess central monoamine activity, rather than the anti-muscarinic effects cause of delirium.

Neuropathy

Therapeutic use of amitriptyline causes Peripheral neuropathy [29,30], also a small number of cases in association with coma and skin blistering [31]. Blistering is a feature seen in many types of the coma but Peripheral neuropathy not seen (It is unclear). The specific effect of amitriptyline on the neuronal microvasculature as a cause of neuropathy is recommended by the reporter [20].

Hyponatremia

Hence serotonin control of antidiuretic hormone (ADH) secretion, hyponatremia relating to an unsuitable ADH release is a theoretical risk [32].

Ataxia

Beginning of a serotonin syndrome in patient who developed progressive cerebellar atrophy and cerebellar ataxia reported by Fujino et al. [33].

Dystonia

Dystonic reactions and the serotonergic syndrome are CNS effects that have been reported [24].

Conclusion

Most of poisoned patients are young female in developing countries and must focus to prevent in receiving such a drug and educate community [34,35]. Since TCA has various presentations; we must ready to find different signs and symptoms of that. We must know all of sign and symptoms to be ready for manage it or them because cannot predict what patients will manifest.

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