Research Paper Anatomy

Effect of Lithium Carbonate on Cerebrum of Albino Rats

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ABSTRACT

BACKGROUND: Lithium carbonate is a commonly used drug in the treatment of bipolar disorder and has its adverse effects on many organs including nervous tissues AIM:Thus the Present study was conducted in the Department of Anatomy, Government Medical College Srinagar after approval from animal ethical committee, government medical college Srinagar. METHODOLOGY:Fifty albino rats weighing on average 100 gms were used for the experimental studies. The animals were divided into two groups of 25 rats each group. Group A of 25 rats served as control group while group B served as the experimental group. The process of drug administration continued for twelve weeks .Five rats from each group were sacrificed at 4, 6, 8 and 12 weeks .RESULTS:No gross change was observed in the cerebrum of control or drug treated animals at any interval .However neuronal swelling with decreased density of neurons in cerebral grey matter was noticed during 4-8th weeks of lithium administration in group B animals .These changes were more pronounced during 8-12th weeks of drug administration with changes of chromatolysis.CONCLUSION Though adverse effects of lithium carbonate are common in different organs like heart, liver, thyroid etc but the present study suggests that the drug also affects the cerebrum at microscopic levels thereby suggesting monitoring of patients receiving lithium carbonate for cognitive, behavioural, motor and sensory deteriorations.

KEYWORDS lithium, cerebrum,chromatolysis

INTRODUCTION

Lithium carbonate a commonly used drug in the treatment of bipolar disorder (1). It was discovered by Arfwedson in (2) .The word lithium has been derived from Greek word litho for stone as it was initially used to treat urinary calculi and gout but with little success. Its bromide salt was used as an anti epileptic agent because of its calming effects .Latter it was used to treat mania because of its calming effects. FDA approved it for use in manic depressive illness in 1970. Lithium belongs to alkali group of metals with atomic number 3 (3). It is water soluble and is distributed in all body fluids (4) and is found to cross placenta .It is administered orally and is readily absorbed and its peak level is reached in blood within 2-4 hours. Absorption is complete within 8 hours.95% is excreted in urine, 1% in faeces and 4-5% in sweat (5). Long term use of lithium carbonate causes cyst formation and cellular degeneration in liver (6). Its prolonged use causes chronic interstitial nephropathy (7). It is well tolerable but marginally higher doses cause certain side effects like nausea ,vomiting ,diarrhoea, mild diuresis and polydipsia and fine resting tremor of hands .However severe intoxication causes worsening of tremor and confusion with restlessness, increasing muscular irritability, stupor, coma, sometimes generalised seizures and death. Choreoathetosis occurs also occurs in severe intoxication and in rare cases irreversible damage to cerebellum and basal ganglia has also been reported (5). Close medical supervision is required due to its narrow therapeutic index. Lithium is known to cause wide range of neurological disturbances like dysarthia, ataxia, nystagmus, chorea and parkinsonian manifestations. In animal brain tissue lithium at concentration of 1-10meq/litre inhibits the depolarization provoked and calcium dependent release of nor epinephrine from nerve terminals and may also enhance release of serotonin especially in hippocampus (8).

MATERIALS AND METHODS

The present study was conducted in the Department of Anatomy Government Medical College Srinagar India. The study was aimed to determine effects of lithium carbonate on cerebrum of albino rats. 50 albino rats weighing on an average 100gms were taken after approval from animal ethical Committee of the college. The animals were divided into two groups; Group A and B. Group A (control group) comprised of 25 rats, were fed with normal food and tap water. Group B(the drug treated group)also comprised of 25 rat .Besides

food and tap water, the Group B animals were fed with lithium carbonate mixed with floor and water in the form of pellets in addition to the routine diet. The dose of the drug calculated from human therapeutic dose which is 40 to 50 mg / kg body weight. Thus the daily dose of the drug for albino rats was calculated was 4mg/100gm. The animals were kept under uniform laboratory conditions. 5 rats from each group were sacrificed at intervals of 4, 6, 8 and 12 weeks. The animals were anesthetised with chloroform. An incision was given in the scalp from a point just posterior to nasal bones backward to the occiput. The cerebrum was identified, dissected out and put in dishes containing formalin. The tissues were processed by standard histological techniques, sections of 5 to 7 microns cut , stained with eosin and haematoxylin and mounted. The slides were observed for microscopic changes and the observations were recorded.

OBSERVATIONS

Long term use of lithium carbonate affects many organs including nervous system. In our present study we observed neuronal swelling with decreased density of neurons in the cerebral grey matter of group B animals during 4th to 8th weeks of lithium administration (fig 1). During 8th to 12th weeks of drug administration neurons of cerebral cortex showed more prominent cellular swelling .At some places changes of chromatolysis and pyknosis was also found (fig 2). Some neuronal cells also showed vacoulation (fig 3).

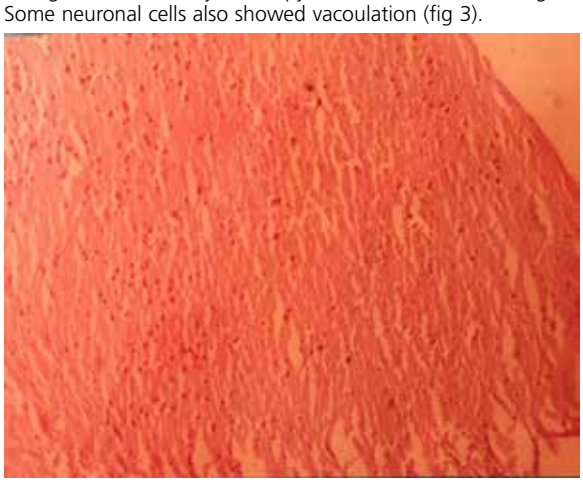

Fig1: Microphotograph of cerebrum of group B animals at 8 weeks showing decreased neuronal density.

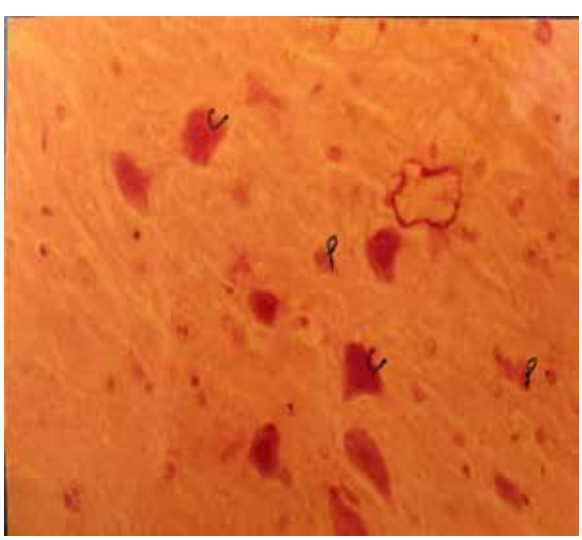

Fig 2: Microphotograph of cerebrum of group B animals at 12 weeks showing neuronal swelling with chromatolysis (C) and pyknosis (P).

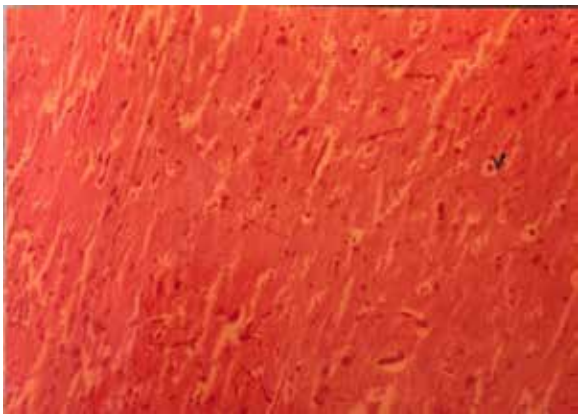

Fig 3: Microphotograph of cerebrum of group B animals at 12 weeks showing vacoulation (V).

DISCUSSION

Lithium carbonate is the drug of choice for the treatment of manic depressive illness. It shortens the duration of individual manic attack as compared with past manic attacks (9). Many organs liver, heart, kidneys and thyroid gland including nervous system are affected by prolonged use of lithium carbonate. The effects on CNS range from commonly observed mild symptoms to life threatening irreversible brain damage in rare instances of severe toxicity (10).Some workers like (Roger Amphlet et al)(11) stated that lithium intoxication causes mild degree of cerebral atrophy. In addition to CNS it also affects the peripheral nervous system in the form of peripheral neuropathy. Histopathological examination of sural nerve revealed moderate loss of myelinated fibres .In our present study we noticed neuronal swelling and decreased density of neurons of the cerebral grey matter which coincide with the findings of these earlier workers. Dixit and smithberg(12) observed loss of cerebellar and cerebral cell mass via the induction of apoptosis with prolonged exposure to lithium. In our present study we observed decreased density of neurons in the cerebral grey matter of group B animals during 4th to 8th week of lithium administration similar to the findings of these earlier workers. Some workers (13) noted Cruezfeldt Jacob like syndrome due to lithium toxicity characterized by spongiform degeneration causing fusion of neuronal processes. The observations made in our present study also show neuronal degeneration in the form of chromatlolysis and pyknosis during 8thto 12thweek of drug administration. The findings in our present study don't match the observations made by SV Tindal et al(14) who observed that prolonged lithium exposure led to the calcification of basal ganglia. During 8th to 12th week of drug administration neurons of cerebral cortex showed prominent cellular swellings. At some places chromatolysis and pyknosis was also found. some neuronal cells also showed vacoulations. These findings are similar to the findings of earlier workers (15) who observed permanent degeneration of cerebellum due to lithium toxicity among rats. Punita Bhala, Dhawan etal (June 2009)(16) while working on effect of aluminium on the cerebrum observed that aluminium results in disorganization of cerebral layers however lithium supplementation resulted in appreciable improvement in the histoarchitecture of the region since we observed cellular loss and subsequent decrease in cerebral density therefore the observations made by Punita and Dhawan are not similar to our findings. This means there is still scope for investigating the role of lithium salts on cerebrum. Some earlier workers (17) while comparing the effects of lithium pylocarpine and high dose pylocarpine on the brain of rats observed that the effects of lithium pylocarpine were more severe than high dose of pylocarpine alone. The effects were in the form of severe brain damage. From the observations made by these workers it is concluded that lithium salts augment the adverse effects of pylocarpine on cerebrum. These findings though not exactly similar to our observations in the present study reveal that lithium carbonate has some role in causing cerebral damage either alone or in combination with other drugs. With advanc-

es in the field of psychiatry and neurology we encounter more and more cases of patients with affective disorders and lithium carbonate remains the drug of choice for the management of these patients. This treatment is continued for long duration and patients are prone to the adverse effects of this drug. In our present study we observed that prolonged administration of lithium carbonate effects cerebrum at microscopic level thus opening a door for further research in neurosciences. Further it is recommended that patients on long term treatment with lithium carbonate must be screened for symptoms related to nervous system. Thus there is need for proper and judicious use of this drug and the patients be screened for any damage to the nervous system either at microscopic or macroscopic levels.

SUMMARY AND CONCLUSION

Like many other organs, lithium also affects nervous system and these effects are observed clinically and by radiological investigations implying computerized tomography and magnetic resonance imaging. These effects are in the form of neuronal degeneration, basal ganglia calcification, etc .Not much work has been done on the effects of lithium carbonate on the histology of cerebrum of experimental animals but in our present study we observed changes like neuronal degeneration, Swelling and decreased density of neurons in the cerebral grey matter of these animals during 4^{th} to 8^{th} week of drug administration. The changes became more prominent with prolonged drug administration. During 8 to 12 weeks of drug administration we observed changes like chromatolysis and pyknosis and some neuronal cells also showed vacoulations. We did not find any changes like calcification of basal ganglia. The changes observed by us were more pronounced in cerebral cortex but the basal ganglia did not show such changes. Further it is recommended that patients on long term treatment with lithium carbonate must be screened for symptoms related to nervous system.

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