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The *Bulletin on Narcotics* seeks to cover all aspects of national and international drugs control; the work of the international bodies responsible in this field; and developments concerning the research, assessment and prevention of drug abuse and the treatment, rehabilitation and social reintegration of persons dependent on drugs. Particular attention is paid to articles presenting national experience in drug abuse control which may be of interest and value to other countries.

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The treatment with L-aspartic acid of persons addicted to opiates

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ABSTRACT

Two clients addicted to codeine, two to heroin and four to opium tincture were orally administered 2 g L-aspartic acid four times daily for up to five days on an out-patient basis. The clients were withdrawn from the drugs on which they were physically dependent by gradually decreasing the amount of the drug abused. Some mild abstinence signs and symptoms were observed during the treatment, while the clients showed a marked improvement in social contacts and behaviour. At the end of the treatment period, and during the subsequent two weeks, not one of the treated persons showed any sign of the abstinence syndrome or expressed a feeling of need for the compulsive intake of the drug which had been abused.

Introduction

Many attempts have been made to determine the mechanism underlying the development of physical dependence on and tolerance to opiates. In the early 1970s it was thought that free amino acids played a role in the action mechanism of morphine and the problem was approached on the basis of physical dependence. At that time, information on the action of free amino acids and peptides on the central nervous system (CNS) was scarce. The levels of free amino acids in the brains of rats physically dependent on morphine were significantly higher than normal [1, 2] and a further increase occurred after abrupt withdrawal from morphine [2, 3] as well as after administration of a morphine antagonist [3]. The results strongly suggested that free amino acids in the CNS played an important role in the action mechanism of morphine. On these grounds an attempt was made to antagonize the effects of morphine by using L-aspartic acid. This showed that it antagonized the effects of acute and chronic administration of morphine in rats [1, 3–11].

Encouraged by the results obtained from the experiments performed on animals, it was decided to use L-aspartic acid for the treatment of persons addicted to opiates and in this paper the author reports on the therapeutic success.

Method

Eight males addicted to opiates were treated with L-aspartic acid. Of these, two were addicted to codeine, two to heroin and four to opium tincture. Detailed information is summarized in the table below.

Opiate-addicted males treated with L-aspartic acid

Case number	*Age*	*Drug of addiction*	*Duration of addiction (years)*	*Daily drug intake (grams)*	*Number of previous treatments in hospital*	*Use of other drug(s) in combination*
1	52	Codeine	12	0.50 – 0.70	–	–
2	44	Codeine	7	0.40 – 0.50	–	–
3	27	Heroin	9	0.50 – 0.60	2	Cannabis
4	34	Heroin	11	0.50 – 1.00	2	Cannabis, LSD
5	26	Tincture opii	11	20 – 30	2	Cannabis
6	28	Tincture opii	7	20 – 30	1	–
7	29	Tincture opii	8	30 – 40	2	–
8	23	Tincture opii	5	15 – 20	–	–

The addicts used codeine and heroin orally, while opium tincture was injected; this involved heating a pharmaceutical product "Gastro gouttes" containing 10 g tincture opii and 10 g tincture belladonnae to obtain a condensated content. The addicts, especially those abusing heroin and opium tincture were in miserable social and moral conditions. Their attempts to discontinue drug-taking as well as medical treatment were unsuccessful.

A total of 2 g L-aspartic acid (Sigma, St. Louis, United States of America) was dissolved in a glass of water together with 2 g sodium bicarbonate to form easily hydro-soluble monosodium aspartate. This solution was given to the subjects addicted to codeine four times daily, an hour after each meal and an hour before bed for four consecutive days and for five consecutive days to the other subjects. They came to the Department and were observed continually for six to eight hours each day for possible signs and symptoms of the abstinence syndrome during the period of administration and during the following two weeks.

Results

The two subjects treated for addiction to codeine were allowed to take reduced doses of codeine on the first two days of treatment. The reduced doses ranged from 0.70 g to 0.10 g. The codeine was administered to prevent the abstinence syndrome (mild hypersalivation and the feeling of oppression

in the chest). On the third day the clients showed no signs or symptoms of abstinence or any wish to take the drug. The scheduled administration of L-aspartic acid was applied for a further two days under strict observation. No abstinence signs or symptoms were present, and the administration of L-aspartic acid was discontinued at the end of the fourth day.

The reduction in the daily average dose of heroin for the two heroin-addicted clients also began on the first day, while complete voluntary discontinuation of the use of the drug occurred on the morning of the fourth day of treatment. These clients continued to take L-aspartic acid on the fourth and fifth days. During the last two days neither of the clients possessed any heroin and were free of abstinence signs and symptoms. On the first, second and third days of treatment, the abstinence syndrome was fairly accentuated compared with that of the codeine addicts. In addition to hypersalivation and the feeling of oppression in the chest, the two heroin addicts had hypermotility with diarrhoea, nausea, tremors, flushing and agitation.

Two of the four subjects addicted to opium tincture (cases 5 and 7) seemed to be more resistant to treatment with L-aspartic acid compared with the other two (cases 6 and 8). Although they began to decrease their daily compulsory intake of the drug on the first day of treatment, the complete discontinuance occurred somewhat later. Cases 5 and 7 took the drug in decreasing amounts for five consecutive days, whereas cases 6 and 8 no longer showed any need to take the drug on the fourth day.

All the subjects treated with L-aspartic acid improved in their communications with parents, relatives and others and showed increased politeness, tidiness, care of hair, and cleanliness of body and dress. At the end of the treatment period, all expressed a strong desire to return to their ordinary activities (e. g. education, work, hobbies etc.).

Discussion

The use of different drugs which attenuate the abstinence syndrome or reduce the compulsory intake of morphine or other opiates in addicted persons has not been successful enough to solve the problem of opiate addiction. The author's results in experiments on animals lead him to believe that the development of physical dependence on opiates, and the abstinence syndrome upon withdrawal, may be related to a disequilibrium caused by the inhibitory effect of opiates on the activity of L-asparaginase and asparagine synthetase. These two enzymes regulate the biosynthesis of oligopeptides and polypeptides containing aspartic acid and asparagine. These processes are extremely important for the formation of glycopeptides and glycoproteins, as well as for the adaptation of the organism to the consequent biochemical and behavioural alterations resulting from the

disequilibrium. It is likely, however, that other enzymes such as glutaminase and glutamine synthetase might, to a lesser extent, take part in these processes.

The therapeutic action of L-aspartic acid has been attributed to its direct and indirect effects, first, on L-asparaginase and then on asparagine synthetase. L-aspartic acid, being an end product of the activity of L-asparaginase, inhibits the activity of L-asparaginase *in vitro* (unpublished observation) which may result in a reduction in the use of narcotics among addicted people since a sufficient inhibition of L-asparaginase, to which the organism has been adapted, is necessary. If the inhibition of L-asparaginase by L-aspartic acid is not equivalent to that of the opiate consumed, then a supplementary intake of the opiate will normally be needed. This was noted at the commencement of the treatment. After the initial inhibitory effect of L-aspartic acid, it is assumed that L-aspartic acid is converted into asparagine via the activity of asparagine synthetase which seems to be found in relatively higher quantities in opiate-dependent subjects because of the inhibition of L-asparaginase. Once L-aspartic acid is converted into asparagine, asparagine as an end product of asparagine synthetase begins to inhibit the enzyme. At the end of treatment with L-aspartic acid the equilibrium altered by the chronic intake of the opiate between L-asparaginase and asparagine synthetase and the suppressed activity L-asparaginase are thought to be restored and normalized. Such restoration and normalization of the functions of these two enzymes eliminates the need to continue the use of the drug.

As abrupt withdrawal is known as a frightening experience, it is often rejected by many addicted persons who nevertheless wish to curb their addiction. Treatment with L-aspartic acid in a community setting without unpleasant interventions, would therefore be more acceptable to addicted persons. It may, however, be too early to say that the treatment of opiate addicts with L-aspartic acid is well-established. It needs to be confirmed by further clinical trials.

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