

PRELIMINARY REPORT

**The Treatment of Withdrawal Symptoms of
Opium Addicts with Vitamin «E» in Ten Cases***

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The withdrawal of opiates from opium addicts is followed by a train of severe symptoms, especially when the withdrawal is carried out rapidly and completely. This, apart from psychological and social problems, has presented up to now a therapeutic problem. Yawning, lacrimation, rhinorrhea, perspiration, goose-flesh, hot flashes, chills, loss of appetite, mydriasis, tremors, twitching of muscles, insomnia, pain, restlessness and nervousness are present in every case. Anxiety and vomiting and diarrhea may occur in some. In most cases anxiety, insomnia and pain are so severe that the situation becomes unbearable. The severity of symptoms decreases gradually within two weeks, after which no other uncomfortable symptoms remain, except insomnia and pain which may distress the patient for several months.

The usual treatment today is sleep treatment (Brissis 1953) and chlorpromazine (Stahelin 1953). But both methods have their inconveniences, that is to say sleep treatment cannot be used in every case and in any medical centre, as it depends on the physical condition of the patient and the facilities which the treatment centre can provide; and chlorpromazine is known to have disagreeable, if not dangerous, side-effects (Hodges & La Zerte 1955).

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Recently in the United States the treatment of addiction to opiates, as well as to other narcotic drugs, is carried out by substitution of methadon for opiates, followed by reduction of the methadone dose over a period of about ten days. By this method, although methadone will prevent the appearance of signs of abstinence from opiates, and abstinence symptoms from methadone are milder than those from opiates, they may be present for several weeks; Isabelle (1950), Foser & al. (1953), Isabella & al. (1953).

In all these methods most patients need several weeks or months of convalescence before they are restored to a normal state.

A medicament which has given us remarkable results in recovering from the withdrawal symptoms and rendering the withdrawal period bearable is vitamin E. Observations made in the Roozbeh Mental Hospital of Tehran, on 10 cases, who have been treated solely with Ephynal may be summarized as is shown in the table.

Comparing vitamin E therapy with other methods used, such as the replacing of opium by extracts of opium or morphine and gradually reducing the dose; or with Démorphèn* (Biolabo) therapy, the good effect of vitamin E therapy becomes obvious.

The patient treated with Dionine, opium or morphine extracts suffers very much during the treatment period from abstinence symptoms, feels very weak; every movement is painful and he cannot sleep at all except under large doses of hypnotics, which bring him a few hours rest.

The period of treatment with these methods lasts about one month; but after cessation of treatment the patient has weakness, some pain and insomnia for several months. This statement is true also of Démorphène therapy though to a lesser degree; the course of this treatment being from one to three weeks.

Among my patients there had been cases who had previously been treated with one of the above-mentioned methods, and after a few

*) The dose of Démorphène used was 1 ampoule 5cc containing the following solution: olive oil-5 gm, choline distearoglycerophosphate 0.9 gm, castor oil 3 gm, normal saline solution ad 100 gm.

age	Duration of addiction (years)	Habitual daily dose	Use of opium	Dose of Ephynal and period of hospitalisation	Other drugs	Results
31	5	10 gm opium	smoking	200 mg daily for 3 days	None	All the symptoms disappeared on the 2nd day.
38	8	5 gm opium	smoking	300 mg daily for 5 days 400 mg daily for 6 days	None	Withdrawal symptoms were supported easily and on the 9th day of the treatment all the symptoms disappeared.
27	4	20 gm opium	smoking	200 mg daily for 1 day 300 mg < " 2 days 400 mg < " 4 days 600 mg < " 4 days	None	The treatment was carried very comfortably and from the 9th day on the patient had no symptoms.
28	4	7 gm shireh *	smoking	400 mg daily for 1 day 600 mg < " 15 days	None	The symptoms disappeared gradually within 9 days, after which no symptoms remained.
37	18	5gm opium for 7 years & 10 gm shireh for 11 years	smoking	1 mg daily for 2 days 600 mg < " 10 days	None	During the first 3 days of treatment the patient had depression and much pain but slept well. From the 9th day onward no symptoms.
45	7	15 gm shireh	smoking	400 mg daily for 2 days 600 mg < " 8 days 400 mg < " 4 days	None	The severity of symptoms lasted for the first 5 days, but it was bearable. On the 9th day the patient was reasonably comfortable. Sleep became normal from the 11th day onward. On the 14th day no symptoms.
36	11	5 gm opium	orally **	400 mg daily for 1 day 600 mg < " 13 days 400 mg < " 2 days	None	The restlessness was bearable. From the 7th day on sleep became normal, from the 9th day all symptoms decreased considerably; and on the 12th day no symptom.
18	14	40 gm shireh	smoking	1 gm daily for 20 days	20 drops of tincture of opium daily on the first 4 days	The first 4 days the patient was restless, had anxiety, pain and insomnia. From the 8th day the symptoms and the pain decreased. He was discharged from the hospital on the 20th day, still suffering from disturbed sleep.
5	8	8 gm opium	smoking	1 gm daily for 10 days	None	This patient had no severe restlessness and from the 5th day no symptoms at all. From the first day slept well.
3	8	20 gm shireh	smoking & orally	1 gm daily for 19 days	20 drops of opium for 3 days	On the first two days the patient suffered from withdrawal symptoms but the gradually decreased on the subsequent days. From the 10th day on he had no pain and from the 17th day on sleep became regular.

* Shireh is prepared from the residue of smoked opium which is decocted with an equal amount of opium and in practice is much more toxic than opium.

months or a year took again to addiction, because they could not stand the lasting restlessness. These same patients, however, were much satisfied with the vitamin E therapy.

Taking into consideration the various cases treated with vitamin E, it can be stated that this method shortens the period of treatment to an average of 11 days, makes the abstinence symptoms bearable, regulates sleep and relieves pain very rapidly. Patients show no faintness during the treatment period or after the cessation of treatment, so they do not require a convalescent period.

Some of the patients that we were able to follow-up had no recurrence of withdrawal symptoms. They are in good health and spirits and appear contented.

The recommended dose of vitamin E is 600 mg to 1 gm by mouth daily until complete recovery occurs; and 100 - 200 mg daily for a few weeks after that.

When vitamin E therapy is combined with Dionine, opium or morphine extracts, although there is almost no restlessness, the treatment period increases considerably (about 20 days). When the opium addict who takes 5-10 gm of opium adds to his usual dose of opium 1 gm of Ephynal daily, approximatively a half-dose of his usual dose of opium becomes satisfactory to him. One of the patients (case 3) observed that each tablet of Ephynal (100 mg) brought him a sleep of 2 hours and a pleasant warmth of the body. Another (case 10) described how each tablet gave him the dryness of the mouth and warmth of the body associated with administration of each dose of opium.

Seeking a likely explanation for the effect of vitamin E during the withdrawal period, we considered the following:

The tension of the alveolar carbon dioxide is increased during the administration of morphine, leading to a retention of CO₂ in arterial blood and correspondingly in venous blood and tissues. At the same time the tissue oxygen consumption is decreased (Krueger & al. 1941). Besides morphine has an inhibitory action on oxidation of carbohydrates substrates, influencing D.P.N. cytochrome-c-reductase one of the cytochrome

chain enzymes concerned with the oxidation of carbohydrates (Wang & al. 1953). Considering also the increased sensitivity of these patients to insulin (although there is some rise in blood glucose during this period), and the mild lymphocytosis shown by the blood formula, perhaps we can say that opium addicts continue their life with less oxygen and an inhibited action of subcortical centres and the diencephalo-pituitary system, so that sudden withdrawal of morphine frees the function of the above-mentioned centres and reveals the decreased consumption of tissue oxygen which probably would explain many of the withdrawal symptoms.

On the other hand, the anti-oxidising effect of vitamin E has been recognized as one of its principal properties (Markees & al. 1954) and from experimental vitamin E deficiency which produces a degeneration of the visceral nerve-cells of the brain stem (Einarson 1953), we may perhaps draw a parallel between its point of attack and that produced by opium intoxication. Besides, vitamin E has a favourable effect on autonomic disorders of probably diencephalo-pituitary origin, (Schmid 1950), the symptoms of which resemble more or less the abstinence symptoms. Considering also the comparison of clinical effects of vitamin E and opium described by patients, we would venture the opinion that the administration of vitamin E after a complete withdrawal of opium probably compensates some of the opium's effects on the nervous system, though in a curative way, stimulating the nervous centres and restoring the metabolic disorders of cells, and it may remedy the hypoxia of the tissues, i. e. physiologically it could lead to a better utilisation of the poor oxygen supply and thus decrease the withdrawal symptoms.

SUMMARY

The treatment of addiction to opiates, apart from psychological and social problems, has presented up to now a therapeutic problem.

Various methods are used and each has its disadvantages. Residual symptoms of abstinence from opiates are present in all methods and there is a prolonged period of convalescence which seems to be one of the causes of relapses to addiction.

Vitamin E however, has given remarkable results in aiding recovery from the withdrawal symptoms. With vitamin E the period of treatment is shortened, abstinence symptoms are bearable and the convalescent period is eliminated. Patients treated with vitamin E solely are in good health and spirits and appear contented. This treatment also seems to reduce the number of relapses.

The administration of vitamin E after a complete withdrawal from opium probably compensates some of the opium's effects on the nervous system, and remedies the hypoxia of the tissues, thus restoring the patient to a normal physiological state.

RÉSUMÉ

En plus des difficultés d'ordre psychologique et social qu'elle présente et malgré les méthodes de traitement qui existent, la thérapeutique de l'opiomane reste encore un problème. Les cures de désintoxication ont chacune leurs désavantages. Chacune donne lieu à des symptômes d'abstinence et implique ordinairement une longue période de convalescence qui semble être une des causes de récidives.

La vitamine E cependant a donné de très bons résultats en aidant le patient à mieux supporter les symptômes de la désintoxication. Cette vitamine permet aussi de raccourcir la durée du traitement; les symptômes d'abstinence deviennent supportables et la période de convalescence est presque éliminée. Les opiomanes traités avec la vitamine E restent en bonne santé physique et psychique pendant la cure. De plus, ce traite-

ment les satisfait et semble aussi diminuer notablement le nombre des récidives.

L'administration de la vitamine E après un sévrage d'opium compense probablement quelques-uns des effets de la drogue sur le système nerveux et remédie à l'hypoxémie des tissus.

De ce fait, la vitamine E ramènerait plus rapidement les patients à un état physiologique normal.

REFERENCE

- Brisset, C.: Aspect clinique et traitement des toxicomanies, des Stupéfiants. Cah. Laënnec (France) 13, no. 2, 9 (1953).
- Einarson, L.: Deposits of fluorescent acid-fast products in the nervous system and skeletal muscles of adult rats with chronic vitamin E deficiency. J. Neurol. Neurosurg. psychiat. 16, 98-109 (1953).
- Fraser, H.F. and Grider, J.A. jr.: Treatment of drug addiction. Amer. J. Med. 14, 571-77 (1953).
- Hodges, H.H. and La Zerte, G.D.: Jaundice and agranulocytosis with fatality following chlorpromazine therapy. J. Amer. med. Ass. 158, 114-16 (1955).
- Isbell, H.: Manifestation and treatment of addiction to narcotic drugs and barbiturates. Med. Clin. N. Amer. 34, 425-37 (1950).
- Isbell, H. and White, W.M.: Clinical characteristics of addictions. Amer. J. Med. 14, 558-65 (1953).
- Krueger, H. Eddy, N.B. and Sumwalt, M.: The pharmacology of opium alkaloids. U.S. Public Health Report, Suppl. No. 165, part 1, Respiration, p. 215-33, (1941).
- Markees, S.: Zum Wirkungsmechanismus des Vitamin E. Moderne probleme der pädiatrie, vol. I, 283-92, Karger, Basle (1954).
- Schmid, S.: Vitamin E bei vegetativen Störungen. Klin. Med. (Austria) 5, 549-54 (1950).
- Stachelin, J. E. and Kielholz, p.: Ein neues vegetatives Dämpfungsmittel bei psychischen Störungen. Schweiz. Med. Wschr. 83, 581-86 (1953).
- Wang, R.I.H. and Bain, J.A.: Analgesics and enzymes of the cytochrome chain. J. pharmacol. Exper. Ther. (U.S.A.) 108, 354-61 (1953).