The Clinical Applications of Lithium Orotate. A Two Years Study

by

H. A. Nieper

Silbersee Clinic, Hannover-Langenhagen

THE CLINICAL APPLICATIONS OF LITHIUM OROTATE. A TWO YEARS STUDY

H. A. Nieper

Agressologie 1973, 14, 6 : 407-411

Sixty-four patients were treated with lithium orotate and observed for time periods ranging from four months to two and one half years. Lithium orotate is of truly unparalleled efficiency in the treatment of constitutional migraine, constant headache and hemiplegia. Also in the treatment of depression, alcoholism and epilepsy, lithium orotate has proven very useful without any problems in the application. Lithium orotate is effective at uncommonly low dosages and causes no negative side effects. Lithium citrate and lithium carbonate are far less effective than lithium orotate.

The specific principle is considered to be a directed intracellular transport of lithium by means of the orotic carrier molecule, which has a high affinity for tissue dependent on the pentose pathway, e.g. glia and the blood brain barrier. The directed carrier principle of the lithium orotate therapy makes a determination of the lithium level in blood serum unnecessary. The effectiveness of lithium therapy as such is based on a membranal and cellular displacement of sodium.

In the autumn of 1969, Hamilton reported on the dessication of malignant pleura effusions with the help of lithium succinate, given orally in capsules in daily doses of 600 mg. Lithium carbonate and lithium acetate did not possess this therapeutic capacity. We personally followed the progress of one of Hamilton's patients and can confirm his observations. We used lithium succinate from the Verdon Company in Montreal for this purpose.

The succinates have an especially great affinity for lipid structures, which may explain the superiority of lithium succinate over lithium carbonate and lithium acetate. The dessication of malignant pleura effusions can only be explained as the result of a displacement of sodium by lithium in the cells or membranes. The displacement of sodium by lithium is also the working principle behind the lithium therapy in neurology and psychiatry and is due to the progressive scaling of the atomic radii of these substances.

In the past few years, the use of lithium to control depression, constitutional migraine, constant headaches, hemiplegia, alcoholism and hyperthyroidism (Gerdes 1972) has played an increasingly important role. This led us to examine the applicability of the principle of directed mineral or electrolyte transport to the lithium therapy. Our observations on tissue cultures have established that the orotates such as calcium orotate and magnesium orotate pass through the cell membrane in undisassociated form and release their respective ions only at the site of membranes of cytoplasmic structures. It is assumed that this is also true for lithium orotate (Nieper, 1969, 1970), (fig. 1).

In addition to this phenomenon, the orotates show a special affinity for tissues in which the metabolism involves the pentose pathway, e.g. the glia, vascular walls and especially the blood brain barrier (Nieper, 1973).
Continuous use of drinking water rich in lithium (El Paso) has been correlated with a low of psychoses (Dawson, Mc Ganity and Moore, 1972); the protective effect of hard water with respect to arteriosclerosis is presumed to be due to the high lithium content. Based on our present knowledge of the course of arteriosclerotic damage, it is probable that the lithium is stabilizing the lysosomal membranes and thus preventing lysosomal damage to the vascular walls, perhaps even to the cardiac muscle itself (Voors, 1971. Platt, 1972). An exactly opposite situation is observed when the level of intracellular sodium is high. The lithium ion of lithium orotate is specifically released in the immediate vicinity of the lysosomes.

We have had lithium orotate in clinical use for two and one half years, treating mainly ambulatory patients. The therapeutic effectiveness has been so spectacular that an extensive report on our work is now in order.

We used stomach acid resistant gelatine capsules filled with 150 mg lithium orotate each. During the long-term therapy, an extremely exact Bausch and Lamb spectrometer was used to perform numerous mineral analyses of the patients’ whole blood and blood serum. Therapy with lithium orotate does not cause the approximate level of 0.02 ppm lithium in normal whole blood or serum to be exceeded by more than 30 %. It is significant that a completely effective lithium therapy can be achieved without raising the level of lithium in the blood excessively. This also supports the assumption that the lithium orotate molecules transport lithium ions directly into the cell. The removal of reservations related to the toxicity simplifies the lithium therapy in general, especially in the treatment of migraine. At normal doses, a continuous control of the level of lithium in the blood is no longer necessary.

In only three cases did we observe mild symptoms of muscular adynamy, lack of appetite and general listlessness after six to eight weeks of continuous treatment with lithium orotate. These symptoms disappeared when sodium glutamate (bouillon preparation) was given.

The therapy was continued for a minimum of eight weeks with all patients and was reinstated at the reoccurrence of complaints, generally at the lower doses previously achieved. We observed a complete absence of negative side effects with the use of lithium orotate, especially with respect to cardiac and hepatic symptoms. According to capillarygraphic criteria, the elder patients even showed an increase in blood vessel elasticity during this therapy.

The onset of treatment is usually accompanied by a rapid excretion of water from the body. Myopic and hyperopic patients experience a change in vision due to a slight dehydration of the eyes. On the other hand, flicker scotome and other sensations which usually accompany attacks of migraine disappear.

The identity of lithium concentrations in whole blood and blood serum indicates that this substance is normally not the object of a directed transport across membranes. This is why it is especially important to provide lithium with a suitable carrier mechanism. The widely used acetate, carbonate and citrate compounds hardly fulfill this requirement, the succinate and asparagine do so partially, but the orotate is by far the most effective lithium carrier molecule for the reasons previously discussed in this paper.

We have treated a total of 64 patients with lithium orotate, observing all but 3 of them for more
than four months. The 3 patients who discontinued the therapy prematurely were all alcoholics.

Among the patients were 44 who could be grouped together according to their symptoms of constant headache, migraine and hemicrania. The youngest was fifteen, the oldest seventy-four years old. There were 31 females and 13 males in this group. All of them were dissatisfied with the results achieved by previous treatment. Some complained that the previous therapy had merely lessened the severity of the attacks without preventing them altogether, others claimed that the various treatments were totally ineffective, some were opposed to the use of suppositories and some had experienced unpleasant side effects.

Our analysis of the case histories led us to the discovery that the use of ergotamine preparations, with and without caffeine, yield especially unsatisfactory results. Compounds containing Vitamin B 15 are considered to be helpful in some cases. The most effective compound used to treat constitutional migraine before the introduction of lithium orotate for this purpose is undoubtedly benzoic acid sulfinate (saccharin), which most probably achieves a displacement of sodium similar to the lithium orotate. This compound is, however, virtually unknown in Germany and is no longer applicable.

16 of the 44 patients had previously used analgesic compounds containing lithium citrate (13 patients) or lithium carbonate (3 patients) without therapeutic effect.

Therapy with lithium orotate was started at doses of five to six 150 mg capsules per week. Of the 44 patients, 39 reported the therapy to be thoroughly effective and their use of additional analgesic compounds was drastically limited. The supplementary intake of caffeine was frequently of value. There was virtually no improvement in the conditions of 5 patients, all most probably suffering from occipital pain of cervical or neuradicular origin.

I cannot recall any medication which was able to achieve such remarkable results in so short a time as does lithium orotate. I have reason to believe that a number of the patients, skeptical of the low dosage, were taking lithium orotate capsules more frequently than necessary. This is, however, completely harmless in every respect.

12 patients were given lithium orotate to control depressive moods or larval endogenic depressions, generally a maximum of five 150 mg capsules per week. 9 patients in all reported an improved condition, of which 3, who also showed an accompanying hyperthyroesosis and tendency towards migraine, noted an exceptional betterment.

Of the 8 alcoholics treated with lithium orotate, 3 discontinued the therapy of their own accord after a short time. 2 of them have remained without relapse for more than fifteen months now, especially remarkable since they had each undergone two previous hospitalized withdrawal treatments without success. One had suffered from migraine and both of them suffered from depressions. A comparable case has been under observation for only seven months thus far, but appears to be following the same favorable course. The wives of the remaining 2 patients report that the situation has improved vastly; their husbands are far less explosive and no longer resort to violence, and they are in general more reasonable than before.

We realize that the number of cases presented here is small, but believe that it is sufficient to compare favorably with the excellent results of Klune’s double-blind study (1973), as reported by the U.S. Veterans Administration. Klune achieved a reasonable curative effect in more than half of over 70 sporadic alcoholics with the use of conventional lithium salts. The therapy with lithium orotate appears to be entirely as effective, with the advantage that it is significantly less problematical.

Six patients having manifestations of epileptic disease were also treated with lithium orotate. Four of them, 3 males and 1 female between fourteen and twenty-one years of age, had had an average of one or two convulsive episodes per month. Lithium orotate, given over a period of five to seven months, entirely eliminated the tendency towards convulsions and also lessened the psychic retardation of the patients considerably. These patients had received no medication other than lithium orotate, with the exception of one who also drank an effervescent preparation of magnesium aspartate. Two patients, 1 male and 1 female of thirty-two and forty-five years of age respectively, who were also being treated Mylissin (primidone), also showed a marked improvement on the lithium orotate therapy. All 6 patients received 150 mg lithium orotate four times per week. We know from our earlier experiments performed with whole blood analysis that epilepsy is also connected with a sodium retention in neural tissue. I feel that it would be very worthwhile to expose lithium orotate to an extensive clinical trial in the treatment of epilepsy.
BIBLIOGRAPHY


Résumé

Utilisation clinique d’orotate de lithium. Étude sur deux années

H.-A. NIEPER

Agressologie 1973, 14, 6 : 407-411

Soixante-quatre malades ont été traités à l’orotate de lithium et surveillés pendant des périodes de quatre mois à deux ans et demi. L’orotate de lithium révèle une efficacité incomparable dans le traitement des migraines constitutionnelles, des céphalées permanentes et des hémorragies. Il s’est montré très utile aussi dans le traitement des dépressions, de l’alcoolisme et de l’épilepsie sans difficultés d’utilisation. L’orotate de lithium est efficace à des doses inhabituellement basses de lithium et ne présente pas d’effets secondaires génants. Le citrate et le carbonate de lithium sont néanmoins moins efficaces que l’orotate.

L’apport intracellulaire direct du lithium par le transporteur orotate à affinité élevée pour les tissus à voie des pentoses dominante (glie et barrière hémato-encéphalique) est considéré comme le principe spécifique de cette activité. Ce principe d’apport intracellulaire dirigé rend la détermination du niveau sanguin de lithium inutile. L’efficacité de ce traitement par l’orotate de lithium dépend d’un déplacement du sodium membranaire et cellulaire.

Zusammenfassung

Die klinische Anwendung von Lithium-Oratat, eine zweijährige Untersuchung

H.-A. NIEPER

Agressologie 1973, 14, 6 : 407-411


Disclaimer

The A. KEITH BREWER INTERNATIONAL SCIENCE LIBRARY acts as a clearing house for and a disseminator of information not otherwise readily available. It does not advocate, promote or verify the contents of such information.
RÉSUMEN

LA APLICACION CLINICA DEL OROTATO DE LITIO : UN ESTUDIO DE DOS AÑOS

H.-A. NIEPER

Agressologie 1973, 14, 6 : 407-411

Sesenta y cuatro pacientes fueron tratados con orotato de litio y observados durante períodos de tiempo comprendidos entre cuatro meses y dos años y medio. El orotato de litio es de una eficacia sin precedentes en el tratamiento de la jaqueca constitucional, cefalea constante y hemicrania. Asimismo, el orotato de litio ha resultado de mucha utilidad y sin problemas de aplicación en el tratamiento de la depresión, el alcoholismo y la epilepsia. El orotato de litio es eficaz a dosis sorprendentemente bajas y no produce efectos secundarios negativos. El citrato de litio y el carbonato de litio resultan de una eficacia considerablemente menor que el orotato de litio.

El principio específico parece ser el transporte celular directo de litio por un portador orgánico.

КИНЕФИЧЕСКОЕ ПРИМЕНЕНИЕ ОРОТАТА ЛИТИЯ В ТЕЧЕНИЕ ДВУХ ЛЕТ

АГРЕССОЛОГИЯ, 1973, 14, 6 : 407-411

66 пациентов были лечены оротатом лития в период от 4 месяцев до двух с половиной лет. Оротат лития обладает выраженной активностью при лечении конституциональной мигрени и умеренной головной боли, особенно при болях головной головной боли. При лечении алкоголизма, депрессии и эпилепсии этот препарат обладает выраженной действием без побочных явлений и в очень малых дозах. Оротат лития обладает более выраженной активностью, чем лимоннокислый и углекислый литий.

Авторы предполагают, что действие этого препарата связано, с внутриклеточными транспортами, в которых играет роль восстан.