CHLORPROMAZINE IN THE "PAINFUL" COMPLICATIONS OF LEPROSY

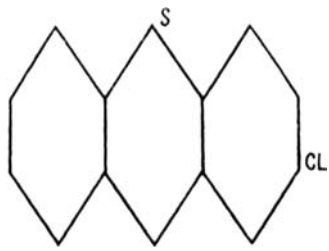
K. RAMANUJAM, M.B., B.S.
The Silver Jubilee Children's Clinic, Saidapet, Madras

Introduction

Consequent on the favourable results obtained with Chlorpromazine in the relief of pain-producing conditions, the clinical trial with "Largactil" brand of Chlorpromazine in the treatment of painful complications of leprosy was initiated at the Government Silver Jubilee Children's Clinic, Saidapet, in April 1955. This being an out-patient clinic, a close watch could not be kept on the condition of the patient. However, except for a few instanecs, the patients were fairly regular in reporting at the clinic as and when instructed to do so. The assessment of the results of treatment was largely based upon what the patient said about his symptoms from day to day, and also, to some extent, on his clinical condition.

Pharmacology

Chlorpromazine is a new synthetic, non-barbiturate, central nervous system depressant. It is derived from the alkylamine derivatives of phenothiazane and has the following formula:



It is a whitish, odourless, slightly granular powder, with a melting point of 180° C. It is freely soluble in water and alcohol, and on exposure to light it tends to change colour.

Although chemically related to antihistaminics like promethazine and diethazine hydrochloride, it has a relatively weak antihistamine action. It has been described as a "young near-relation of the antihistaminic substance."[1] It appears to be a drug with diverse and useful pharmacological action, and has been described as vagolytic, sympathicolytic, spasmolytic, antipyretic, antiemetic and sedative. It also has a potentiating effect on hypnotics, narcotics, anaesthetics and analgesics. At present it is being used in the control of vomiting, management of mental and emotional disturbances, and relief of severe or intractable pain.[2]

It is this last mentioned pharmacological action that forms the theme of the present study.

Chlorpromazine in Leprosy

It was felt worthwhile investigating the use of " Largactil " brand of chlorpromazine in some of the " painful " or pain-producing complications of leprosy, such as acute neuritis, chronic persistent joint pains met with in lepromatous cases, acute painful condition of the eye (for instance, iritis) and general bodily pain of a severe nature seen during and after lepra reaction. It was clearly understood before the initiation of the present investigation that Largactil was not being offered as a treatment for leprosy, but that the drug might be tried by itself or in conjunction with the usual treatment offered for the painful complications of leprosy indicated above.

Dloch,[3] working on three cases of leprosy, a leproma, a tuberculoid and an undifferentiated, administered chlorpromazine either orally or parenterally. In the leproma which was treated with injections of DDS and Largactil orally 25 mgm. per day, remarkable improvement in the lepromatous condition was noticed. He himself expresses the doubt regarding the actual value of Largactil as an anti-leprotic drug. The second case, a tuberculoid with " neural reaction " did well with 12 injections of Largactil, there being complete subsidence of " reaction."

The Present Investigation

1. **The Material:** The painful complications of leprosy in which Largactil was tried were as follows:—

(1) Neuritis, acute and chronic.
(2) Joint pains, acute and chronic.
(3) Generalised bodily pain of lepra reaction along with nerve pain, joint pain and bone pain.

For purposes of this study the bulk of cases were drawn from those suffering from neuritis of varying severity. A few cases with joint pains alone and a small group of cases in lepra reaction with generalised pain were also included. Out of a total of 47 cases taken for investigation, 16 cases dropped out for reasons best known to themselves. The remaining 31 cases were treated for the following painful complications:—

Neuritis	21 cases
Joint pains	3 ,,
Neuritis and joint pain	2 ,,
Generalised bodily pain	5 ,,

2. **The Method:** At this clinic, the routine treatment for the painful complications of leprosy has been the intravenous adminis-

tration of Potassium Antimony Tartrate in doses of 0.02 gm. for three days and 0.04 gm. for the next three days. In addition Mist. Sodi Salicylas 1 oz. t.d.s. is given. The results have been uniformly good in neuritis, joint pains and classical lepra reaction.

When Largactil was offered as a drug that will induce a state of indifference to pain, the investigation was undertaken with a twofold purpose: (a) Whether Largactil could conveniently replace the other forms of pain relieving measures in practice, which are rather messy, needing more attention and care, and (b) whether combined Largactil and the usual pain-relieving measures in practice was more beneficial to the patient in so far as the rapid amelioration of his painful symptoms was concerned.

Largactil was administered orally in doses of 25 mgm. twice or three times a day in addition to the usual Sodi Salicyl Mixture. After some time, a stage was reached when the patients (who, being chronic sufferers, are in the habit of suggesting the line of treatment that should be adopted for the relief of their symptoms) were not quite taken up with the " tablet " treatment but demanded Potassium Antimony Tartrate injections also. Hence in order to satisfy the psychology of the patient and at the same time keeping a watchful eye on the effect of Largactil, " dummy " Potassium Antimony Tartrate injections in the form of Aqua distillata were given, 2 c.c. intravenously every day for six days along with Largactil tablets. In some instances when Largactil alone failed to relieve the distressing symptoms after a reasonable period of time, Potassium Antimony Tartrate injections were given in addition to Largactil therapy.

In other words, the total number of 31 cases can be put in three categories:

(1) A group of 18 cases who were treated with Largactil tablets alone.

(2) A second group of 9 cases who were treated with Largactil tablets plus " dummy " Potassium Antimony Tartrate injections.

(3) A group of 13 cases treated with Largactil and intravenous injections of Potassium Antimony Tartrate (including 5 cases transferred from group (1) and 4 transferred from group (2)).

The Results

Group (1): In the first group comprising of 18 cases treated with Largactil alone, 10 were suffering from neuritis, 2 from neuritis and joint pains, 3 from generalised aches and 3 from joint

pains alone. One out of the 10 cases with neuritis and one of the 3 cases with joint pains were earlier treated with intravenous injections of Potassium Antimony Tartrate, but the painful symptoms persisted unabated.

Under Largactil therapy which was administered orally in doses of 50 to 75 mgm. per day with Phenergan 25 mgm. at bed-time, 7 cases of neuritis (including the one that did not benefit with Potassium Antimony Tartrate), 2 cases of neuritis and joint pains, 3 cases of generalised body ache and one case of joint pains (which was earlier treated with Potassium Antimony Tartrate) obtained complete relief in periods varying from 4 to 16 days. The three cases of neuritis and two cases with joint pains which failed to respond to Largactil were transferred to Group (3).

Group (2): In this second group comprising of 9 cases, 8 suffering from neuritis of a mild to moderate degree and one case of generalised pains and aches, Largactil was administered orally in doses of 50 to 75 mgm. per day. Phenergan 25 mgm. at bed-time along with "dummy" Potassium Antimony Tartrate (viz. 2 c.c. of Pyrogen-free distilled water) intravenously. Out of these 9, 5 cases of neuritis obtained complete relief after a period of 5 to 9 days' treatment. The 3 cases of neuritis and the solitary case of body pains and aches which did not respond favourably but showed exacerbation of symptoms were transferred to Group (3).

Group (3): The third group of 13 cases comprised of 3 cases of neuritis and 2 cases of joint pains transferred from Group (1), 3 cases of neuritis and one case of generalised body pain transferred from Group (2), three fresh cases of neuritis and one new case of generalised body pains and aches. In other words, there were in all 9 cases of neuritis, 2 cases of joint pains and 2 cases of generalised body pains. The 3 fresh cases of neuritis and one new case of generalised bodily pain in this group were straightaway started on combined Potassium Antimony Tartrate and Largactil therapy, because of severe and distressing pain symptoms. All the 13 cases obtained complete relief under combined Largactil and Potassium Antimony Tartrate therapy which lasted for 6 days, the time taken for the course of Potassium Antimony Tartrate injections.

Complications

No untoward effect that could be directly attributed to Largactil therapy was encountered in any of the cases treated.

Discussions

It is obvious from the results obtained in Group (1) Largactil

is quite useful in relieving painful complications of leprosy, provided they are not of severe intensity. Another point that is brought out in Group (1) in favour of Largactil is its usefulness in cases who have had intravenous Antimony therapy, but failed to receive the expected beneficial results.

The Group (2) cases which received Largactil and " dummy " Potassium Antimony Tartrate injections, indicated in some measure the part played by the psychology of the patient with regard to the relief or otherwise of his painful symptoms. Five out of nine cases in this group improved with Largactil. In the remaining four cases, Largactil failed to relieve the symptoms, perhaps due to exacerbation of the existing symptoms. Generally speaking, experience with this group appears to confirm the results obtained in Group (1).

In Group (3), apart from the four cases which were straightaway started on combined Largactil and Potassium Antimony Tartrate therapy (on account of the distressing pain symptoms), the nine cases which had proved resistant to Largactil therapy ultimately received the beneficial result under the combined therapy. It appears likely, the cases which present themselves with agonising painful symptoms, or those who show an exacerbation of mild painful symptoms, are the ones where the combined Largactil and Potassium Antimony Tartrate therapy is strongly indicated.

In the writer's experience, Potassium Antimony Tartrate has proved to be one of the most effective and useful agents that could be employed for the relief of neuritis, joint pains, etc., occurring as the presenting symptoms or as component of the lepra reaction syndrome. Experience in the treatment of painful complications with the combined therapy (Largactil and Potassium Antimony Tartrate) on the one hand and Potassium Antimony Tartrate injections alone on the other, seems to indicate that the former brings about an " easing " of the acute painful state much earlier. Lastly, cases which prove resistant to Largactil therapy alone, obviously due to exacerbation of symptoms, obtained relief with the combined therapy.

Conclusions

1. The pain relieving properties of Largactil in the painful complications of leprosy are confirmed.

2. Largactil, administered alone, seems to obtain the desired results in those cases where the pain is of a mild or moderate severity.

3. Largactil appears to be of value especially in those cases where the usual measures employed for the relief of pain, namely Potassium Antimony Tartrate injections, have failed.

4. Largactil could be used with advantage in outstation clinics, where intravenous injections of Potassium Antimony Tartrate or any other form of therapy necessitating daily attention could not be given.

5. Largactil, given in doses indicated above, appears to be free from toxicity.

6. Combined Largactil and Potassium Tartrate therapy appears to give better and quicker results in cases with agonising pain symptoms, than when either of them is given alone.

Summary

The treatment of 31 cases suffering from one or more of the painful complications of leprosy with Largactil administered orally under various regimen are presented. The results obtained are analysed, discussed and the conclusions drawn from the investigation recorded.

Acknowledgement

Thanks are due to Messrs. May & Baker (India) Private Ltd., for stimulating the interest to undertake this study and for the generous supply of the drug. I wish to place on record my grateful thanks to the patients, without whose co-operation this investigation would not have been possible. Thanks are also due to the Officer-in-Charge, Central Leprosy Teaching and Research Institute, Chingleput, for permitting the publication of this article.

REFERENCES

1. MACGREGOR, M. S.A. Journal of Clinical Science, Vol. **5**, No. 4, Dec. 1954.
2. Symposium on Chlorpromazine in Clinical Medicine. International Record of Medicine and General Practice Clinics, Vol. **168**, No. 5, May 1955.
3. DLOCH, H. Bull. Soc. Path. Exct., Vol. **48**, 402, 1955.