

The Effects of Thalidomide on Leprosy Reaction

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Reaction complications of lepromatous leprosy—erythema nodosum, neuritis, iridocyclitis, orchitis, arthralgia in the fingers—are painful and recurrent. Of the numerous therapies in use, only one, corticotherapy, produces spectacular results, but too often it gives rise to complications (such as ab lactation in nursing mothers). In the light of the rapid positive results achieved by Sheskin (13-18) using thalidomide, we decided, therefore, to use this drug in the treatment of our reaction patients.

It will be recalled that thalidomide (N-thalimidoglutaramide) was responsible for numerous cases of phocomelia in the children of parturient women who had taken it, and its use as a tranquilizer was forbidden in most countries. In 1963 Manad successfully used thalidomide as a sedative in 35 cases of advanced cancer. In 1964, in the Rothshild Hadassah University Hospital in Jerusalem, Sheskin (13) used it as a sedative on six lepromatous patients suffering from a reaction, and was surprised to note its spectacular effect on the various symptoms of the reaction within 24 to 48 hours, with an oral dose of 100 mgm. three times a day. Sheskin (17) treated an additional 13 lepromatous patients suffering from erythema nodosum (ENL) with 400 mgm. of thalidomide orally per day; the general, cutaneous and local symptoms disappeared in less than 48 hours. For some of the patients who suffered a relapse after the treatment was stopped, he prescribed thalidomide for a period of more than six months; a few toxic effects which appeared with this dose (dryness of mucous membranes in mouth and nose, erythema, bul- lous eruption, eczema-type rash) did not seem serious enough to warrant stopping the treatment, especially as there was no disturbance of the main biologic functions, particularly of the liver, kidneys and blood.

In 1969 Sheskin and Convit (16) under-

took a double blind study to determine the influence of thalidomide on leprosy reaction. The study covered 173 treatments on 54 patients, 85 with thalidomide and 88 with a placebo. Of those patients who received the thalidomide, 91.8 per cent showed great improvement, whereas of those who had been given the placebo, 27 per cent were improved, 50 per cent stationary and 23 per cent worse.

In September 1968, during the Ninth International Leprosy Congress in London, Sheskin and Sagher (18) organized a round table on the effects of thalidomide on leprosy reaction. In addition to the results of their earlier experiments, these authors also reported on the beneficial effects of thalidomide on neuritis reaction, which they had established by measuring the speed of motor conduction of the nerve before, during and after the administration of thalidomide. They reported also that a trial of thalidomide as a specific treatment carried out on 24 patients had produced 11 aggravated cases, 8 stationary cases and 5 improvements from the cutaneous point of view. *Thalidomide therefore cannot be considered as a specific treatment for leprosy.*

Other authors have followed Sheskin in using thalidomide. Terencio de las Aguas and Felix Contreras (20) successfully treated 67 cases of leprosy reaction and 15 cases of reaction neuritis using daily doses of 100 to 500 mgm. Belda, Manzoli, and Jordy (1) noted positive results in the treatment of neuritic pain. Cazort and Ye Kim Song (4) obtained the same positive results with 24 reaction patients in Thailand and suggested that the drug might have an immunosuppressive effect. Opromolla (10) treated 43 reaction patients with a weak oral dose of 100 mgm. daily and obtained some improvements, followed by relapses. Degos, Lortat-Jacob, Civatte and Daniel (5) reported rapid results produced by thalidomide in three cases of leprosy reaction. Saúl (12), Trimi- gliozzi (21), Tarabini (19), and Jonquière (6) reported similar results.

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PERSONAL EXPERIMENTS

Our personal experiments were carried out on 71 lepromatous patients suffering from either an erythema nodosum type of reaction (65 cases) or a reaction equivalent: neuritis of the cubital nerve (4 cases), adenitis (1 case), orchitis (1 case).

Effect of thalidomide on leprosy erythema nodosum (65 cases). For seven days, each patient received 400 mgm. of thalidomide orally per day in four doses of 100 mgm. If certain symptoms persisted until the seventh day, a second course was prescribed, or more if necessary. In 59 cases (90%) a course of seven days was sufficient to check the reaction. We noted how quickly the temperature was affected, being brought back to normal within 24 to 72 hours. General symptoms (asthenia, headaches, insomnia), myalgia, spontaneous pains in the nerves (upper orbital, median, peroneal), and arthralgia in the fingers, generally disappeared in one to four days. Within a few hours of the beginning of the treatment, the nodes became less tense, less painful and less erythematous, and then disappeared in two to four days, leaving a fine scaly layer.

The C-reactive protein (CRP), which we prefer as a test to sedimentation, the latter being too easily disturbed in the African and always highly positive at the beginning of the reaction, was negative on the seventh day. In four cases, two courses of seven days each were necessary to eliminate the nodes and make the CRP negative.

In the case of two cortisone-dependent patients, we tried to replace corticotherapy by thalidomide. We gave 400 mgm. of thalidomide per day, together with Cortancyl for 10 days, then progressively reduced the amount of Cortancyl over 10 days, and finally eliminated it. The change-over was tolerated completely in only one case. In 12 cases there was a relapse to reaction (between the fifth and 12th days after the patient's discharge), but one or two courses of thalidomide were sufficient to check it.

Effect of thalidomide on reaction equivalents. Four cases of reaction neuritis of the ulnar nerve were helped by a course of thalidomide: 400 mgm. per day for seven

days, 200 mgm. per day for four days and 100 mgm. per day for four days. The pain disappeared in two to five days, but the thalidomide had no effect on the body of the nerve or on the paresis which prevented lateral movements of the fingers. We therefore continue to believe that neurolysis followed by transposition of the ulnar nerve is preferable. On the other hand, a case of reaction adenitis and another of reaction orchitis responded favorably to a 15 day course of thalidomide.

SUMMARY

From the publications of Sheskin and others, and in the light of our own personal experience (71 cases), thalidomide appears to have spectacular effects on leprosy erythema nodosum and certain of its reaction equivalents (adenitis, orchitis, iridocyclitis, arthralgia). The optimum dose appears to be 6 mgm. per kgm. of body weight orally per day. The length of the treatment depends on the intensity of the reaction, but in general a course of seven days is sufficient to control it.

Thalidomide can replace cortisone therapy, but the optimum dose must be used before starting to reduce the steroid very gradually. Thalidomide does not appear to have sufficient effect on reaction neuritis to be able to replace neurolysis. Thalidomide was always completely tolerated at the prescribed levels, but its teratogenic effects must not be forgotten, and therefore pregnant women must in no case be treated with this drug.

Finally, thalidomide has no antibacterial effect and cannot be used as a specific treatment for leprosy.

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