

The Use of Flufenamic Acid in Acute Complications of Leprosy, and the Associated Lowering of Raised Serum Transaminase Levels¹

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Flufenamic acid (N-(*a,a,a*-trifluoro-methyl) anthranilic acid; Arlef, Parke, Davis & Co.) is a nonsteroid, anti-inflammatory compound that has been reported to be 16 times as effective as aspirin and 1.6 times as effective as phenylbutazone in reducing the inflammation produced by ultraviolet light in guinea-pig skin (²⁴). Winder and his colleagues (²⁴) have also shown that flufenamic acid (FFA) has an antipyretic action in yeast induced pyrexia in guinea-pigs, and partially depresses the development of inflammatory granulation tissue following implantation of cotton pellets subcutaneously in rats. Edema of the rat paw induced by carrageenin is relieved by FFA and other nonsteroid anti-inflammatory drugs (²⁵). The absence of serious toxicity in man following administration of FFA has been shown by studies in healthy volunteers (¹²) and in long-term treatment of patients with rheumatoid arthritis (¹⁹).

In the therapy of the more severe complications of leprosy recourse is frequently made to corticosteroid treatment, and the dosage required may rise to 75 mgm. prednisolone a day (¹¹). The serious, life-threatening side effects of long-term steroid treatment are well known (¹⁵). The ideal drug for the treatment of erythema nodosum leprosum (ENL) reaction, and other inflammatory complications in leprosy would be one that is effective, free from serious toxicity, specific, effective orally, and preferably relatively cheap. On cessa-

tion of the drug there should be no rebound effect with recrudescence of the reaction. Even with gradual reduction of corticosteroid therapy, there is frequently a serious rebound effect. When acute neuritis occurs in patients with plantar ulcers, the use of corticosteroids is hazardous and a drug that relieves the neuritis but does not exacerbate the intercurrent infection is preferable.

In rheumatoid arthritis FFA has been found to be effective in a dose of 600 mgm. daily (^{2, 6, 7}). Oral doses up to 1,400 mgm. daily for seven weeks have been well tolerated (¹²), dyspepsia, diarrhea and dysuria being the commonest side effects. FFA has been reported to cause an occasional rise in serum transaminase levels (^{1, 19}). This study in leprosy patients included serial estimations of these enzymes both to detect any possible toxic effect of short courses of high dosage FFA, and also to observe any effect of FFA on originally raised levels of serum transaminases. The levels of these enzymes which are found in untreated Ethiopian lepromatous leprosy patients is also reported.

The antipyretic effect of FFA in 22 lepromatous patients with acute ENL reaction has been reported (⁹), one patient receiving the highest dose of 28 mgm./kgm. evincing a temporary neutropenia. The present, extended study has allowed more observations to be made of any toxic effect of high doses of FFA on the blood leucocytes.

MATERIALS AND METHODS

The patients in the study were inpatients of the Princess Zenebework Hospital, Addis Ababa, and the following categories of patients were treated with FFA:

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1. Lepromatous leprosy patients with a history of acute reaction treated with steroids, and at the time of the study exhibiting high fevers and ENL. One of these patients also had steroid-withdrawal edema.

2. Lepromatous leprosy patients with ENL, with or without pyrexia, and untreated with steroids.

3. Lepromatous, borderline, and tuberculoid patients with acute neuritis, diagnosed by the presence of large, tender peripheral nerves, usually the ulnar and median nerves, and muscle weakness without complete paralysis.

4. Patients with exacerbation (acute reaction) of tuberculoid and borderline leprosy lesions.

5. Eight lepromatous leprosy patients with acute iridocyclitis.

The duration of this study was from March 1968 to May 1969, and included some lepromatous patients whose response has been partially described (⁹). A total of 60 patients were studied, 40 males and 20 females. The age range of the males was 14 to 49 years, with an average of 23.9 years, and the females were aged 12 to 40 years with an average of 23.5 years. Forty-nine lepromatous patients were in the trial, 34 of these exhibiting acute reaction with pyrexia and 23 suffering from acute neuritis. Of the five borderline leprosy patients treated, two had acute reaction and four had acute neuritis; of the six tuberculoid leprosy patients three had acute reaction and the other three acute neuritis alone. Forty-two episodes of pyrexia associated with acute lepromatous reaction were studied.

Courses of FFA were monitored by several serum transaminase estimations and, in addition, these enzymes were studied in 16 lepromatous leprosy patients untreated with antileprosy drugs, and in nine patients with leprosy complications untreated with FFA.

All patients in the trial were weighed and the dose in mgm./kgm. of flufenamic acid was calculated. Axillary temperatures were recorded in the morning and evening. In patients with acute reaction, therapy with FFA was started initially with a dose of 200 mgm. thrice daily (10 to 18 mgm./kgm. daily). If this failed to control the fever of ENL the dosage was increased

to 300 mgm. three times a day (16 to 23 mgm./kgm. daily) and occasionally to 400 mgm. thrice daily (20 to 25 mgm./kgm. daily), care being taken to give the drug with food to reduce the incidence of dyspepsia. Four patients, three of them very light weight, were given FFA at a dosage of 28 mgm./kgm. To assess the minimum effective dose of FFA and to lessen the cost of a course, the drug was given for short periods in reducing dosages; for example, after 300 mgm. thrice daily for two days, 200 mgm. was given thrice daily for four days, followed by 200 mgm. twice daily for four days, and then the drug was stopped as soon as possible. In the treatment of acute neuritis the effect of a month's treatment with FFA was assessed. The dosage schedule given to most patients with neuritis was 200 mgm. thrice daily for seven days, followed by 200 mgm. twice daily for 10 days, and 100 mgm. twice daily for 14 days. However, when cost need not be considered so closely, a dose of FFA of 900 mgm. daily might be given initially or a long course of 600 mgm. daily.

The incidence of side effects was carefully noted by questioning the patients, taking serial blood leucocyte counts, serial estimations of the serum glutamic-oxaloacetic (SGOT) and serum glutamic-pyruvic (SGPT) transaminases, and urine analysis. Laboratory tests also included blood sampling for malaria parasites and *Borrelia recurrentis*, the hemoglobin concentration, and the erythrocyte sedimentation rate (ESR) by Westergren's method.

RESULTS

Acute reaction of lepromatous leprosy.

Among 34 patients with acute reaction of lepromatous leprosy there were 42 episodes of pyrexia, with the axillary temperature ranging from 37°C (98.6°F) to 40.3°C (104.7°F) with an average of 38.7°C (101.8°F). After FFA therapy the temperature fell in 24 or 48 hours to an average of 36.5°C (97.7°F) with a range of 36°C (96.8°F) to 38°C (100.4°F).

To illustrate this specific effect of FFA a few details of two patients are given.

Patient No. 35. This female, aged 25, with a BI of 1.3, was admitted on 25 June

1968, with acute reaction of lepromatous leprosy, widespread ENL and a pyrexia of 40°C (104.2°F). Tests were performed to exclude other causes for her pyrexia, such as malaria and relapsing fever, and she was treated with acetyl salicylic acid and chlorpromazine for 48 hours. Her temperature remained at 40°C for the 48 hours, and on 27 June she was given 300 mgm. of FFA thrice daily (20 mgm./kgm.) for three days. Her temperature dropped to 37°C (98.6°F) by the evening of 27 June. Because of a clerical error the 8 a.m. dose of FFA was omitted on 28 June, and by 11 a.m. her temperature had risen to 40°C. FFA was begun again at this time and by 4 p.m. her temperature had fallen to 37°C. On 30 June the dose of FFA was reduced to 200 mgm. twice daily for four days. Her ENL subsided, the malaise associated with the acute reaction disappeared, and she remained afebrile.

Patient No. 8. This male, aged 43, with a BI of 4.0, had experienced in the months immediately preceding this trial recurrent prolonged high pyrexias due to acute lepromatous reaction. He had experienced eight such episodes with a pyrexia of 39°C to 40°C lasting from six to 10 days, and eventually responding to corticotrophin and intramuscular antimony. On four occasions in April, May and June 1968, when he had ENL and a pyrexia of 39°C or 40°C, he was given 12 mgm./kgm. of FFA and his temperature fell in 24 hours to 36°C or 37°C, and remained thereat.

The average dose of FFA required to produce a satisfactory fall in temperature was 16 mgm./kgm. with a range of 4 to 28 mgm./kgm. In 16 episodes a dose of 11 to 17 mgm./kgm. FFA was effective, but in 20 episodes a dose of 18 to 28 mgm./kgm. was required. In three lepromatous patients the ENL lesions were markedly edematous during the acute reaction and the edema was relieved by 13, 17 and 20 mgm./kgm. of FFA respectively. In the one patient with marked edema following cessation of steroid therapy a dose of 28 mgm./kgm. for three days produced a dramatic reduction of the edema.

Effect of FFA therapy on the ESR. Paired ESR observations produced a range

of results, in most patients a fall being observed, but in some patients little or no fall was seen.

Acute reactions in borderline and tuberculoid leprosy. During the course of this trial only two patients with borderline (intermediate) leprosy reaction were treated with FFA and they were not significantly improved. Of three tuberculoid patients with acute reaction two were improved, although one required 21 mgm./kgm. of FFA, and the other patient was slightly improved with FFA but dramatically improved after treatment with prednisolone.

Lepromatous iridocyclitis. In nine episodes in eight lepromatous patients, the scleral injection and eye pain was reduced when FFA was given in addition to topical atropine and cortisone, after these latter two drugs alone had failed to alleviate the signs and symptoms, and including one patient in whom oral prednisolone did not alleviate the iritis. A high dose range of FFA was required, 11 to 25 mgm./kgm., with an average of 16.8 mgm./kgm.

Leprous neuritis. In tuberculoid and borderline neuritis FFA did not have as beneficial an effect as a high-dose tapered course of corticosteroid, such as prednisolone, but in seven out of nine patients who received a high dose of FFA (15 to 20 mgm./kgm. daily in divided doses) marked improvement was observed. This was more evident than that usually observed in association with splinting of the affected limbs alone, which was done in all cases. Inflamed nerves became less tender and the strength of the muscles supplied by those nerves improved. Three of these patients had intercurrent infection and these infections did not appear to be adversely affected by FFA. Of 23 lepromatous patients who had active neuritis, 19 were markedly improved, their nerves becoming less tender and muscle strength increasing. In the remaining four patients, although their nerves were less tender, the strength of their muscles did not markedly increase.

Serum transaminase. 1. Levels of SGOT and SGPT in untreated patients. In 16 lepromatous patients untreated with anti-leprosy drugs the average SGOT was 15 IU/ml. (IU = international unit) with a

TABLE 1. Serial estimations of serum transaminases during treatment with flufenamic acid.

Patient No.	Sex	Age (yrs.)	Days after treatment								Dose FFA mgm./ kgm.
			SGOT				SGPT				
			0	2	8	15	0	2	8	15	
31	M	26	36	35	27	41	50	19	46	59	25
38	M	30	15	12	13	13	11	7	10	14	12
48	M	30	22	20	16	26	10	7	8	15	18
49	F	35	24	12	17	7	30	21	7	10	19
52	M	35	55	33	9	16	26	12	16	10	15
57	M	36	22	16	25	16	12	11	16	20	18
58	M	35	27	18	25	23	5	7	4	8	17
H untreated	F	30	28	20	37	22	18	12	23	18	—

range of 8 to 24 IU/ml. (The range in normal people, as determined by the Schweizerhall test kit for SGOT, is up to 20 IU/ml. and for SGPT is up to 16 IU/ml.) In 18 untreated lepromatous patients the average SGPT was 8 IU/ml. with a range of five to 19 IU/ml.

2. *Transaminase levels in patients with mild leprosy complications.* In four apyrexial patients with ENL, untreated with specific antireaction therapy, the SGOT level averaged 11 IU/ml., and the average SGPT was 14 IU/ml. In four lepromatous patients with subacute neuritis, the average SGOT was 14 IU/ml., and the average SGPT was 12 IU/ml.

3. *The effect of FFA on serum transaminase levels.* A possible toxic effect of high doses of FFA, as indicated by a rise in serum transaminases, was first studied in a series of eight apyrexial inpatients with acute leprosy neuritis. The SGOT and SGPT levels were estimated before treatment with FFA and after 48 hours, 5 days, 8, 12 and 15 days treatment. (Table 1). An active lepromatous patient untreated with FFA (patient H) was sampled on each occasion. The patients (6 males and 1 female, aged between 26 and 35 years with weights ranging from 47 to 60 kgm.), were treated for four days with FFA 300 mgm. thrice daily (15-20 mgm./kgm.) followed by 200 mgm. thrice daily (10-13 mgm./kgm.) for

seven days, and then 200 mgm. twice daily for four days. The initial SGOT was above normal in six patients and the initial SGPT in three patients. These levels might have been due to acute neuritis, or to preceding acute reaction in these patients. Patient No. 38 was the only one with tuberculoid leprosy and his normal transaminase levels remained unaffected by FFA. In the other patients, who had lepromatous leprosy, the immediate effect of FFA was to lower the SGOT and SGPT. The percentage drop, on average, of the SGOT level after 48 hours was 33 per cent, after one week 15 per cent, and after two weeks 29 per cent. On the fourteenth day of treatment, patient No. 31 refused all oral medicines and had a recrudescence of general malaise and acute neuritis with some ENL. These facts may account for the rise in his SGOT and SGPT on the fifteenth day, but with the reintroduction of FFA therapy his symptoms were relieved. From this initial study there was no evidence that high dosage, short, tapered courses of FFA cause a rise in the SGOT or SGPT, but rather the reverse.

Subsequently 24 other courses of FFA therapy were monitored with transaminase estimations. These included 10 patients whose SGOT and SGPT levels were obtained after therapy alone, and in all these cases the levels were normal. In 14 patients

TABLE 2. The effect of flufenamic acid on the levels of SGOT and SGPT.

Patient No.	Sex	Age (yrs.)	SGOT			SGPT			Dose FFA mgm./kgm.	Leprosy complications
			Before FFA	After FFA	% Fall	Before FFA	After FFA	% Fall		
31a	M	24	23	4	83	25	8	52	25	Neuritis
31b	M	24	38	4	90	59	15	75	18	Neuritis
37	F	40	39	21	46	25	15	40	20	Neuritis
40	F	40	52	25	52	10	10	—	22	ENL
41	M	16	24	15	37	18	5	72	28	ENL
43	M	22	80	28	65	70	41	41	16	ENL
45a	M	20	20	5	75	0	5	—	24	ENL
45b	M	20	22	12	45	5	4	—	18	Neuritis
54	F	16	38	20	47	14	10	29	20	ENL
57	M	36	25	15	40	5	5	—	18	Neuritis
60	F	20	24	15	37	9	0	—	25	Iritis
64	F	40	150	17	89	200	9	96	17	Neuritis
65	M	35	34	19	44	36	15	58	14	Iritis
66	M	35	12	14	—	0	6	—	16	Iritis
Average		27.7	41.4	15.3	57.7	34	10.6	58	20	

paired estimations were obtained before and after therapy (Table 2). On average the SGOT fell by 57.7 per cent and the SGPT fell by 58 per cent.

When Student's *t*-test is applied to the 18 initially raised SGOT levels in Table 1 (excluding patient No. 31) and Table 2, it is found that this fall after FFA therapy is statistically significant, $p < 0.01$ ($t = 3.19$). There were only nine patients with initially raised SGPT levels, with an average of 54.3 IU/ml. falling to 14.2 IU/ml. This fall is not quite statistically significant, $0.1 > p < 0.05$ ($t = 2.07$).

Toxicity. Gastrointestinal disturbances. Epigastric pain was experienced by seven out of the 60 patients while receiving FFA. One man tolerated 18 mgm./kgm. for three days, and only after a further three days on 12 mgm./kgm. did he complain of epigastric pain. In a female receiving 16 mgm./kgm. the pain was relieved by antacids, and she was then given 25 mgm./kgm. without any side effects. One boy of 18 had epigastric pain relieved by stopping FFA and he later tolerated 9 mgm./kgm. Three patients experienced vomiting, including a boy of 14 on 16 mgm./kgm., but after stopping FFA for three days he tolerated 6 mgm./kgm. Two patients receiving 20 mgm./kgm. vomited, but both later tolerated FFA, 14 and 16 mgm./kgm. respectively. No gastrointestinal disturbances were experienced after short courses of 17 to 28 mgm./kgm. in 29 patients, nor in an additional 30 patients who received 11 to 16 mgm./kgm.

Neutropenia. Blood leucocyte counts in all patients before, during and after therapy with FFA, revealed no evidence of leucopenia, except in one patient, who received the highest dose of 28 mgm./kgm. for three days, in whom the leucocyte count dropped to 2,500/cmm., neutrophils 850/cmm. FFA was immediately stopped, and nine days later his leucocyte count was 7,900/cmm., neutrophils 5,000/cmm., and subsequent counts were normal (⁹).

Rebound phenomenon. In this study there did not appear to be any marked rebound effect after FFA withdrawal. Three patients had experienced repeated ENL and acute reaction for many months

before the study and continued to have a few such episodes during 1968, but these episodes did not reoccur immediately after FFA withdrawal. No other patients experienced recurrence of acute reaction after the end of FFA therapy.

Analgesic activity. A few patients continued to complain of pain in the limbs while on FFA therapy, although when acute neuritis was relieved by high dosage FFA therapy the symptoms associated with these inflamed nerves were also relieved.

DISCUSSION

Faced with an acute complication in a lepromatous leprosy patient, the clinician may choose to employ one of several drugs to control the episode (⁸). Some clinicians are loath to use corticosteroids to treat acute lepromatous reaction or slowly progressive neuritis in highly bacilliferous patients. The administration of steroids may allow, at least theoretically, a spread of the bacterial infection, and patients may become steroid-dependent (³). During long-term steroid therapy serious toxic effects are encountered, including severe osteoporosis, iatrogenic Cushing's syndrome, hypertension, peptic ulcer, and a spread of intercurrent infections.

Pride of place when steroids are not used is usually given to parenteral antimony compounds (¹³), but because of cardiac and hepatic toxicity, courses of treatment cannot be repeated at intervals of less than two weeks, and some patients are very sensitive to this substance.

Corticotrophin is effective in the treatment of acute phases in leprosy (¹⁴), but in developing countries its relatively high cost and need to be refrigerated, limit its widespread use. Antimalarial compounds such as chloroquin are not very effective in acute reaction (¹³), and phenylbutazone varies considerably in its effects in different patients. Indomethacin is an effective anti-inflammatory agent, but can cause severe gastric ulceration and hemorrhage (²⁰). Thalidomide has been reported to be highly effective in suppressing acute leprosy reaction, and patients previously dependent on corticosteroids could be weaned off them when treated with thalidomide (⁵).

However, the teratogenic activity of this drug limits its widespread use, and in most countries it is not generally available to the medical profession. Other substances, such as antihistamines, are useful weapons in the clinician's armamentarium, but it must be conceded that the ideal drug for acute reaction in leprosy has not yet been found.

With the advent of clofazimine (B.663, Lampren, Geigy), patients suffering from recurrent acute reaction and ENL can receive therapeutically effective antileprosy therapy and at the same time be free from acute reaction and ENL (¹¹). However, red pigmentation of the skin associated with clofazimine therapy is unwelcome to light skinned people such as Chinese (¹⁶), and this may restrict its use to a minority of patients.

This study has confirmed the finding (⁹) that FFA exhibits a significant antipyretic action in acute ENL reaction in leprosy. Some patients responded to a dose as low as 5 mgm./kgm. but in many instances a dose of 15 to 20 or 25 mgm./kgm. was required, although only for two or three days.

FFA relieved ENL and the malaise associated with acute reaction and this was frequently associated with a fall in the ESR. In borderline and tuberculoid leprosy patients with acute reaction or neuritis, but with plantar ulcers or other intercurrent infections, prednisolone is contraindicated and FFA may be the treatment of choice. In bacilliferous patients with acute neuritis, treatment with FFA may not only relieve the neuritis but may also allow continuation of antileprosy therapy.

In lepromatous iridocyclitis FFA appeared to have a beneficial effect, especially in the higher dose range. Inasmuch as secondary glaucoma is a constant hazard in this condition the fact that FFA can relieve edema (²³) may account for its superiority over prednisolone which can cause a rise in intraocular tension (¹⁷). One patient in this series was more relieved by FFA than prednisolone.

This study has confirmed the observation that short-term, high-dosage, FFA therapy is remarkably well tolerated (⁹). One patient in this series appeared hypersensitive

to a relatively low dose of FFA, 10 mgm./kgm. with regard to gastrointestinal symptoms, but the dyspepsia of other patients was rapidly relieved by temporary reduction of dosage of antacids and antispasmodics. In very short courses of FFA with doses up to 20 mgm./kgm. it would appear unnecessary to perform serial leucocyte counts, but for higher doses and longer courses this is probably necessary.

Serial serum transaminase estimations revealed no rise during or after FFA therapy. Little has been published about the normal levels of SGOT and SGPT that obtain in leprosy patients. In one study eight lepromatous patients with normal liver histology had normal SGOT and SGPT levels, while liver changes were associated with an appreciably raised level of SGPT, and a slight rise in SGOT (¹⁹). At Carville leprosarium it has been observed that an occasional patient with ENL, especially when the lesions are deep, has had raised levels of SGOT and SGPT (¹⁰). In Ethiopian lepromatous leprosy patients, the SGOT and SGPT levels are usually within the normal range, and mild leprosy complications do not appear to result in rises in the levels of these enzymes. However, 19 patients with severe complications had markedly raised levels, the SGOT levels usually being higher than the SGPT levels. Further studies in lepromatous patients with severe iridocyclitis, neuritis and ENL may be indicated.

It would appear to be an original observation that the relief of acute leprosy complications with FFA therapy was found to be associated with a significant fall in serum transaminase levels. This may be additional evidence of the anti-inflammatory activity of FFA. In patient No. 31 treatment with prednisolone was associated with a rise in serum transaminases.

Laboratory models indicate that the anti-inflammatory action of fenamates is different from that of steroids, and the action of the former is not exerted by an effect on the adrenals, as fenamates are equally potent in adrenalectomized rats (²³). Fenamates and salicylates suppress erythema induced by ultraviolet light (²⁴) and bronchoconstriction induced by bradykinin in the guinea-pig, whereas steroids are ineffective (⁴). Although FFA slightly in-

creases the plasma cortisol level, the clinical effects of FFA appear to be largely independent of the increased cortisol secretion (⁷). In contrast to salicylates, fenamates cause very little gastrointestinal blood loss (²¹). Thus fenamates appear to have advantages similar to other nonsteroid anti-inflammatory drugs, in not causing adrenal suppression or steroid toxicity, and on the other hand fenamates do not cause as much intestinal blood loss as aspirin or such serious toxicity as phenylbutazone or indomethacin. Flufenamic acid appears much more effective in acute leprosy reaction than the latter two drugs. Meclofenamic acid has been found to have an antipyretic and antigranuloma potency five times that of flufenamic acid (²³), but meclofenamic acid is not yet generally available.

The features characterizing the ideal drug for the treatment of acute inflammatory complications in leprosy have been mentioned earlier, and flufenamic acid has been shown by the present study to possess nearly all these features. It does not have a marked analgesic effect but this may be an advantage in outpatient clinics where a powerful analgesic might be misused by health workers for nonleprosy complaints.

A consideration of the cost of any new treatment is of importance, especially in developing countries. At the present time the wholesale price of 50 capsules of FFA is U.S. \$1.82; while eight injections of 20 units of corticotrophin cost U.S. \$4.80, and a full course of parenteral antimony costs U.S. \$1.02. Prednisolone tablets are much cheaper. Thus FFA treatment is a practical possibility in developing countries, but a cheap tablet would allow it to be used much more widely.

This pilot study suggests that FFA is a useful drug for the treatment of acute leprosy complications, and is relatively non-toxic. It is conceded that the study does not meet the requirements of a controlled trial, as suggested by Waters *et al.* (²²). A lengthy double-blind, controlled trial of FFA is to start soon, and should contribute to the sparse literature of the natural quiescence or otherwise of acute ENL reaction and pyrexia. In this trial, for example

in patient No. 35 whose case history is given, it was apparent that bedrest and treatment with aspirin and chlorpromazine did not alleviate the acute reaction and ENL, and her pyrexia remained at 40°C. Treatment, with FFA, however, specifically reduced the fever and alleviated the reaction and ENL.

SUMMARY

Sixty leprosy patients received short, high-dosage, tapered courses of the non-steroid flufenamic acid. The drug appeared to be effective in relieving acute lepromatous leprosy reaction with pyrexia, and acute neuritis and iridocyclitis. Borderline and tuberculoid reaction were not so well relieved. These high doses were well tolerated, gastrointestinal disturbances being the commonest side effect. Temporary neutropenia occurred in one of the four patients who received 28 mgm./kgm., but his leucocyte count returned to normal 10 days after stopping flufenamic acid.

In patients with raised levels of serum glutamic-oxaloacetic and glutamic-pyruvic transaminase, treatment with flufenamic acid was associated with a significant fall in the levels of these enzymes. Untreated lepromatous leprosy patients, without severe complications, appeared to have normal levels of these enzymes. Flufenamic acid is active orally, and the only limitation to its widespread use in developing countries is its cost.

RESUMEN

Sesenta pacientes con lepra recibieron ácido flufenamínico no esterooidal durante períodos cortos, a altas dosis progresivamente decrecientes. La droga pareció ser efectiva para aliviar reacciones agudas en lepra lepromatosa, con fiebre, neuritis aguda e iridociclitis. Las reacciones en dimorfos y tuberculoideas no respondieron tan favorablemente. Las dosis altas fueron bien toleradas, los efectos secundarios más comunes fueron molestias gastrointestinales. Uno de los cuatro pacientes que recibieron 28mg/kg. presentó una neutropenia temporal, pero su recuento leucocitario volvió a lo normal 10 días después de interrumpir el tratamiento con ácido flufenamínico.

En los pacientes que presentaban niveles elevados de transaminasa sérica glutámico-

oxaloacética y glutámico-pirúvica, el tratamiento con ácido flufenamínico se asoció con una baja significativa de los niveles de estas enzimas. Los pacientes con lepra lepromatosa no tratados, sin complicaciones severas, parecían tener niveles normales de estas enzimas. El ácido flufenamínico es activo en forma oral y la única limitación para su amplio uso en países en desarrollo es su costo.

RÉSUMÉ

L'acide flufénamique, un composé non-stéroïde, a été administré, de manière brève et à dosage élevé, à 60 malades souffrant de lèpre. Le médicament s'est révélé efficace pour soulager la réaction lépromateuse aiguë accompagnée de pyrexie, de névrite aiguë et d'iridocyclite. La réaction tuberculoïde, de même que la réaction borderline, n'étaient pas soulagées de la même manière. Ces doses élevées étaient bien tolérées, des troubles gastro-intestinaux constituant l'effet secondaire le plus habituel. Une neutropénie temporaire est survenue chez un des quatre malades qui avait reçu 28 mg/kg; toutefois, chez ce malade, la numération leucocytaire était revenue à la normale 10 jours après l'interruption du traitement par l'acide flufénamique.

Chez des malades présentant des taux élevés de SGOT (transaminase glutamo-oxaloacétique du sérum) et de SGPT (transaminase glutamopyruvique du sérum) le traitement par l'acide flufénamique était associé avec une chute significative des taux de ces enzymes. Les malades souffrant de lèpre lépromateuse et non traités, ne présentant pas de complications graves, se sont révélés avoir des taux normaux de ces enzymes. L'acide flufénamique était actif par voie buccale. La seule limitation à son utilisation sur une grande échelle dans les pays en voie de développement, provient de son coût élevé.

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