LUMINAL AND PROMINAL IN EPILEPSY A COMPARATIVE STUDY

BY

C. GUY MILLMAN, M.R.C.S., L.R.C.P.

Deputy Medical Superintendent, Cell Barnes Colony

The results recorded in this paper represent an attempt to compare the efficiency of luminal* with that of the more recently introduced barbiturate prominal* in the treatment of epilepsy.

In view of the satisfactory experience with the use of the latter drug reported by Heyde (1932) and other Continental workers, prominal was substituted for luminal in the routine treatment of epilepsy in this colony for mental defectives. The results in the aggregate were so striking as to warrant closer scrutiny and analysis. The comparison is therefore made in retrospect from a survey of routine clinical records, and not according to a pre-determined method. The major and minor fits in all epileptic patients had been recorded on four-hourly charts.

Method of Substitution

The change from luminal to prominal, which was started throughout the colony on the same date, was made gradually by the method recommended by Blum (1932). Thus for the first four days one-third of the total luminal dosage was substituted by one and a half times that amount of prominal, for the second four days two-thirds were similarly substituted, and on the ninth day the whole luminal dose was replaced by a dose of prominal 50 per cent. greater. During and immediately after the change to prominal the majority of patients showed some increase in the number and severity of fits, but in no case did this assume alarming proportions. Subsequently dosage was adjusted to suit individual cases.

Choice of Cases

For the purpose of comparison only those cases known to have been under treatment with a suitably adjusted dose of luminal for some considerable time have been chosen. These cases had thus been observed for varying numbers of weeks immediately before the change to prominal. It should be pointed out that in every case the dose of luminal had been adjusted to a level low enough to avoid hypnotic effects. No case under any other form of treatment has been included.

Although no reference to the subject has been found in the literature, there appears to be some clinical evidence in support of the view that the incidence of epileptic fits and the mood of the patients bear some relation to atmospheric conditions. In order to minimize any error that might have arisen from seasonal variation those cases still available were observed for a similar period of weeks one year later, by which time the effect of prominal had long since become established.

From the records of eighty-two epileptic patients the number available as satisfying the above criteria is thirty-nine. The results in these cases are given in the following table.

Effect on Incidence of Fits

While there is considerable individual variation in results the mean weekly fit rate is reduced as follows: under luminal, 2.621; under prominal, 0.923. Hence the average weekly fit rate per patient on prominal treatment

TABLE I.—Details of Fits Under Luminal and Prominal Treatment Compared (Observation Periods of Equal Duration)

Case Number and Degree of M.D.	Age and Sex	No. of Weeks' Treatment	Luminal Fits				Prominal Fits				Effect on Behaviour of Change to Prominal
			Major	Minor	Total	Average Weekly Rate	Major	Minor	Total	Average Weekly Rate	
1 Id.	23 M.	40	70	7	77	1.93	1	1	2	0.06	+
2 Imb.	36 M.	31	5	5	10	0.32	0	0	0		
3 F.M.	27 M.	40	2	6	8	0.20	0	1	1	0.03	+
4 Imb.	27 F.	30	33	80	113	3.77	9	12	21	0.70	+
5 F.M.	29 F.	31	33	276	309	9.96	15	0	15	0.48	+
6 Imb.	19 M.	35	162	495	657	18.77	88	168	256	7.31	+
7 Imb.	29 M.	41	12	1	13	0.31	6	0	6	0.15	+
8 Imb.	34 F.	31	35	23	58	1.87	22	2	24	0.77	+
9 Imb.	36 F.	32	11	14	25	0.78	15	3	18	0.56	+
10 F.M.	31 M.	36	43	18	61	1.69	19	22	41	1.14	
11 Id.	16 F.	29	9	3	12	0.41	4	1	5	0.17	+
12 F.M.	33 M.	30	30	2	32	1.07	28	0	28	0.93	+
13 Imb.	30 M.	38	35	4	39	1.03	31	2	33	0.87	+
14 Id.	34 M.	13	8	0	8	0.62	0	0	0		
15 Imb.	57 M.	17	3	6	9	0.53	0	1	1	0.06	+
16 Id.	18 F.	11	3	1	4	0.36	0	0	0		
17 Imb.	36 F.	12	18	1	19	1.58	2	0	2	0.17	+
18 Imb.	19 M.	13	20	31	51	3.93	22	0	22	1.69	+
19 Imb.	25 M.	10	30	2	32	3.20	22	2	24	2.40	+
20 Imb.	39 M.	9	51	0	51	5.64	11	0	11	1.22	
21 Id.	34 F.	23	24	18	42	1.82	6	1	7	0.30	O
22 F.M.	27 M.	13	10	14	24	1.85	0	4	4	0.31	+
23 Imb.	26 F.	10	8	1	9	0.90	0	0	0		
24 Imb.	36 F.	12	64	1	65	5.42	9	0	9	0.75	
25 Imb.	27 M.	14	33	2	35	2.50	1	0	1	0.07	
26 Imb.	23 M.	9	2	14	16	1.78	2	2	4	0.44	O
27 Imb.	29 M.	11	28	3	31	2.82	12	0	12	1.09	+
28 Id.	16 M.	13	61	2	63	4.84	38	3	41	3.15	+
29 Id.	8 M.	21	28	23	51	2.43	2	6	8	0.39	
30 Imb.	12 F.	11	47	6	53	4.82	24	2	26	2.36	O
31 Id.	40 F.	10	25	0	25	2.50	4	4	8	0.80	O
32 Imb.	34 F.	10	17	2	19	1.90	2	0	2	0.20	
33 Id.	14 F.	25	5	4	9	0.36	1	4	5	0.20	
34 Id.	17 M.	12	29	4	33	2.75	20	1	21	1.74	+
35 Imb.	38 F.	10	4	3	7	0.70	0	0	0		O
36 Imb.	36 F.	10	7	0	7	0.70	3	0	3	0.30	O
37 Imb.	15 M.	16	61	6	67	4.20	17	5	22	1.37	O
38 Imb.	19 F.	18	8	16	24	1.33	20	13	33	1.83	
39 Imb.	46 F.	11	6	1	7	0.64	20	2	22	2.00	—

M.D. = Mental deficiency; Id. = Idiot; Imb. = Imbecile; F.M. = Feeble minded.

In the last column: + = Improvement; — = Retrogression; O = Condition stationary; a blank signifies no abnormal behaviour attributable to epilepsy.

is 1.698 lower than, or roughly one-third of, the rate on luminal. The question now arises, Could such a difference be due to chance? The necessary statistical test was applied, and it was found that the odds are nearly 300 to 1 against such a result being a mere chance event. The reduction in the total number of fits since the

* The luminal and the prominal used in this study were obtained from Bayer Products Ltd.

change over to prominal is such that to see a patient in a fit in the colony grounds is now a rare occurrence, although a degree of freedom which is perhaps unusual is allowed to the majority of patients.

The individual variations in results are shown in Table II, which is based on the figures set out in Table I. This shows in ascending order of magnitude the number of major and minor fits which might be expected to occur in each patient under prominal treatment if, during an equal period of luminal treatment, he had experienced a hundred fits.

TABLE II.—*Calculated Number of "Prominal Fits," in each Case, per Hundred "Luminal Fits" (Average = 41)*

Case No.	No. of Fits	Case No.	No. of Fits
2	 Nil	37	 32.8
14	 "	27	 38.7
16	 "	6	 38.9
23	 "	8	 41.4
35	 "	11	 41.7
1	 2.6	36	 42.9
25	 2.8	18	 43.1
5	 4.8	7	 46.1
17	 10.5	30	 49.0
32	 10.5	33	 55.5
15	 11.1	34	 63.6
3	 12.5	28	 65.1
24	 13.8	10	 67.2
29	 15.7	9	 72.0
21	 16.7	19	 75.0
22	 16.7	13	 84.6
4	 18.6	12	 87.5
20	 21.6	38	 137.5
26	 25.0	39	 314.3
31	 32.0		

Thus there is a considerable improvement in the majority of cases, while two cases show deterioration and a few show improvement of little or no significance. No common factor has been noted which would lead one to expect a particular type of response.

Effect on Behaviour

It will be seen from the last column of Table I that of twenty-seven cases showing examples of abnormal behaviour considered to be epileptic equivalents, nineteen were improved by prominal, one became worse, and seven showed no change. Again there is no obvious factor underlying a particular response.

Results in Typical Cases

As the effects of prominal on epileptics of relatively normal mentality will be of more general interest feeble-minded cases (rather than idiots or imbeciles) will be described in greater detail. Those nearest the middle and the extremes of the scale as shown in Table II are taken as typical of the varying forms of response.

Case 5.—This patient was a feeble-minded woman aged 29, in good physical condition. On luminal, 2 grains twice daily, her fits averaged nearly ten per week (approximately

one out of every nine being major fits). She lacked initiative and was frequently troublesome; her epilepsy seriously interfered with her work and recreation. On prominal, 3 grains twice daily, she had an average of one fit a fortnight during the period under review. Since then the fit incidence has decreased and she has had no fit for eighteen months. She is now much brighter mentally, and is able to do useful work and to take part in Guiding and other colony activities.

Case 22.—This case was that of a feeble-minded man of 27, simple in manner, in good health apart from some chronic bronchitis. On 1 grain of luminal daily he was often excitable and quarrelsome, and needed much supervision when following his simple occupation. His fits, of which approximately two-fifths were major, averaged nearly two a week. During the corresponding period of prominal, 2 grains twice daily, he had no major fits, and the minor fits averaged one in about three weeks. His conduct was improved and his usefulness increased. Subsequent increase of dosage to 3 grains twice daily has not resulted in any further improvement.

Case 12.—This patient was a feeble-minded man of 33, in good health. He was simple and confused in manner; with a dose of luminal exceeding 1/2 grain daily his confusion increased and his capacity for employment was negligible. On this small dose of luminal his fits, mostly major, averaged about one a week and he became troublesome and resistive at times. He tolerates a prominal dosage of 3 grains three times a day. This produces little effect upon the incidence of fits, but his conduct is greatly improved and he is able and willing to work in the kitchen garden.

Dosage and Tolerance

Many adults in good physical health have received prominal, 3 grains three times a day, for over two years without ill effect. The dose for children has been estimated by the usual formula $\frac{\text{age}}{\text{age} + 12}$, which appears to be entirely satisfactory.

In a few adults of poor physique, particularly when they are constipated, some degree of drowsiness has been observed when the maximum dose of 9 grains daily has been given. In such cases appropriate measures are taken to deal with the constipation, and prominal is withheld for three days, after which the full dose is again established. In view of the well-known intolerance to barbiturates in cases of renal disease, the urine is examined in all cases showing drowsiness, in order to exclude the possibility of incipient uraemia.

While prominal appears to be the drug of choice for the majority of cases, luminal may be used in preference in those cases of low mental grade in which some hypnotic effect is not undesirable and in which the effect of prominal is disappointing.

Summary

A comparison of the efficacy of prominal and luminal in the treatment of epilepsy is made by examining the routine records of all epileptic patients in a colony for mental defectives; each case has been observed during similar periods on the respective drugs.

The principles by which cases were selected are described, and thirty-nine statistically admissible cases are recorded in tabular form.

The results are considered collectively and individually with reference to both incidence of fits and behaviour. The total number of fits under prominal treatment is shown to be approximately one-third of the number during a similar period under luminal therapy, and a beneficial effect on non-convulsive manifestations is found in a large proportion of cases.

Tolerance is discussed, and a dose of 3 grains of prominal three times a day is shown to be satisfactory over long periods in adults.

I am indebted to Dr. Noel H. M. Burke, medical superintendent, Cell Barnes Colony, for permission to publish the results of this investigation. My thanks are also due to Professor Major Greenwood and his staff for kindly looking over the results.

REFERENCES

- Blum, W. E. (1932). *Dtsch. med. Wschr.*, **58**, 696.
Heyde, W. (1932). *Klin. Wschr.*, **11**, 1874.

PROMINAL IN THE TREATMENT OF EPILEPSY

BY

C. J. HENDERSON, M.B.

Medical Superintendent, Royal Albert Institution, Lancaster

The results of the treatment of epilepsy by prominal in mental hospitals recorded in the *British Medical Journal* by Dr. L. G. Millar Page (March 14, 1936, p. 531) and Dr. Leonard Barber (March 28, 1936, p. 666) were so encouraging that it was decided to try the effect of prominal on the mentally defective patients in this institution who had had the greatest number of fits during 1935. The fourteen patients chosen were having various forms of treatment by drugs and diet, etc. Some had had luminal without any marked improvement, but were not receiving it at the time the use of prominal was begun. On April 1, 1936, every other kind of treatment was stopped, and in only one case has anything except prominal been given since then. One of the fourteen cases was discharged to another institution after six months, so that the figures below relate to thirteen only. All the thirteen patients had been having epileptic fits regularly for from three to twenty years, and the number of fits recorded in the preceding twelve months was rather more than in previous years.

The reduction in the number of fits in the first three weeks of treatment with prominal (twenty-eight against 124 in the corresponding period in 1935) was so remarkable that it was decided to keep exact records of these cases for the next twelve months. This has been most carefully done by Mr. D. D. Steadman, surgery attendant.

Case No.	Number of Fits : April 1 to March 31		Decrease in Number of Fits
	(Bromide, etc.) 1935-6	(Prominal) 1936-7	
1	581	107	474
2	327	137	190
3	191	55	136
4	150	112	38
5	122	2	120
6	93	93	—
7	69	67	2
8	72	11	61
9	62	7	55
10	109	45	64
11	51	13	38
12	263	42	221
13	38	5	33
Total	2,128	696	1,432

It will be seen that there was a reduction of just over two-thirds (67.3 per cent.) in the number of fits in twelve months.

To begin with, each patient was given 9 grains of prominal a day—that is, one tablet three times a day—but in nearly every instance this was found to be too much and had to be reduced—in some cases on April 2 and in the rest on April 4. The main symptom of overdosage was drowsiness, and the dose was reduced to 6 grains daily. In Cases 2, 4, 6, 7, and 10 the daily dose was further reduced to 3 grains, but after a few days was restored to 6 grains.

Case No. 1.—For several years this patient was quite useless and under constant observation owing to the frequency and severity of fits. Is now doing housework, and fits are less severe as well as less frequent.

Case No. 9.—Fits reduced from sixty-two to seven. Much brighter mentally.

Case No. 12.—Had been bedridden for six months owing to severity of fits. Is now up and back at school.

Case No. 8.—Has been at work regularly lately (shoemaker).

Cases 2, 3, and 4.—Not much improved mentally.

Cases 5 and 13.—Low-grade imbeciles, but much more lively and cheerful.

Case No. 10.—Physically improved. This patient has had an average of 118 fits a year for the last twenty years. (In 1900 he had craniectomy operation for epilepsy, without any improvement.)

Case No. 11.—Little change. This patient is 67 years old.

Case No. 6.—Has not benefited; 9 grains daily reduces the number of fits, but produces drowsiness to such an extent that he is unable to walk; 6 grains daily has no more effect on the number of fits or their severity than bromides.

Case No. 7.—This is the only patient who has had any other treatment besides prominal. Up to the week ending November 14 he had had nearly 50 per cent. less fits than the previous year. During the week ending November 21 he had forty fits in three days, and was given bromide and chloral hydrate by mouth and by rectum in addition to prominal. Since then he has had only nine fits, against twenty-nine in the corresponding period of 1935. He takes 3 grains of prominal daily.

During the time these patients have been undergoing this treatment there has been no alimentary disturbance. Nothing abnormal has been found in the urine, nor has the blood pressure been found to vary to any great extent. So far there has been no indication that the drug is losing its efficacy. The treatment is being continued, and other cases of epilepsy are receiving prominal. All those treated were suffering from *grand mal* only. Prominal has not been found to have any effect on the few cases of *petit mal* on which it has been tried.

J. J. C. P. A. Roovers (*Nederl. Tijdschr. Geneesk.*, May 22, 1937, p. 2346) records the case of a girl, aged 5 years, who suffered from generalized calcinosis. The Wassermann, Müller, and Kahn reactions in the blood were negative. She was given 3 grammes of sodium citrate a day by mouth and calcium intravenously. In three weeks after the treatment was begun the calcium content of the blood rose from 11.5 mg. to 20 mg. per 100 c.cm. of blood, and the phosphorus content from 4.7 mg. to 10.8 mg. per 100 c.cm. Slow but steady improvement followed. The calcium nodules subsided, the contractures disappeared, as did also the limitation of movements in the joints, and practically complete recovery took place.