THE CAPE OF GOOD HOPE DIVISION OF THE FACULTY OF GENERAL PRACTICE OF THE COLLEGE OF PHYSICIANS, SURGEONS AND GYNAECOLOGISTS OF SOUTH AFRICA

THE WEIGHT GAIN EFFECT OF PERIACTIN IN ANOREXIC PATIENTS*

M. V. SILBERT, M.B., CH.B., *Author and Convener*

SUMMARY

The objective of this study was to evaluate the weight gain effect of Periactin tablets in anorexic patients. Periactin doses of 2 mg, 4 mg and 8 mg were found to be statistically significantly better than placebo in regard to weight gain. Periactin 4-mg and 8-mg dosage groups showed a statistically significantly higher incidence of total side-effects and drowsiness than placebo, Periactin 2 mg and 4 mg (2 mg in morning, 2 mg in evening). A dosage of 2 mg b.d. was found to be adequate to ensure substantial weight increase while side-effects were virtually absent.

The appetite- and growth-stimulating properties of Periactin (cyproheptadine) were first reported by Lavenstein *et al.*[1] in 1962. During clinical evaluation of cyproheptadine, an antagonist of histamine and serotonin, these investigators noted significant weight gain and height increase and an accelerated linear growth rate in 28 outpatient asthmatic children. In studying the appetite-stimulating properties of cyproheptadine, Bergen[2] also confirmed increase in appetite and weight gain. The mechanism of this phenomenon is unclear; however, it seemed possible that this agent might have a hypoglycaemic action that in turn induces hyperphagia. The weight gain was apparently a reflection of simple exogenous obesity and no evidence of fluid retention could be detected.

In consequence, Periactin has recently been marketed as an appetite stimulant. The research committee of the Cape of Good Hope Faculty of the South African College of General Practitioners undertook a survey to determine the optimum dosage required to ensure adequate appetite stimulation and weight gain without undesirable side-effects.

MATERIALS AND METHODS

The survey comprised a double-blind, non-cross-over study with a placebo. The drugs used were Periactin 2 mg and 4 mg, and a placebo as a control agent. The study included 81 underweight patients of both sexes and of all age-groups whose underweight was due to loss of appetite or anorexia. Loss of appetite may have been due to physiological reasons, psychoneurotic or psychopathological illness; included also were convalescents after illness.

The study was conducted over 3 months, during which time patients received continuous therapy. The degree of appetite stimulation and weight gain was observed during this period and any observed or volunteered side-effects were recorded at each visit. Drowsiness was especially noted when it occurred. Patients were seen at weekly intervals after they were given a randomly allocated study treatment denoted by a serial number. Patients were thus examined at weeks 0 (pre-treatment), 1, 2, 3, 4, 6, 8, 10, 12 and 16. However, only at weeks 2, 4, 8, and 12 were enough patients examined for a statistical analysis to be performed. At each examination date, weight measurements and appetite appraisal were made. The study treatment comprised specially marked and coded bottles containing either 2-mg tablets or 4-mg tablets of Periactin or alternatively identical-looking placebo tablets. Patients took their medication before meals at a dose of 2 tablets per day and in this manner the total daily dosage was 2 mg, 4 mg, 8 mg or placebo.

Appetite scoring was: 0—none; 1—fair; 2—good; 3—very good; and 4—ferocious. Adverse reactions noted were drowsiness, dizziness and dry mouth. These side-effects were mild and usually transient. In only 1 case was medication discontinued because of side-effects and this patient turned out to be psychotic.

RESULTS

The results were divided into 5 categories:

Group I: Patients receiving 2 mg Periactin tablets morning and placebo evening.

Group II: Patients receiving 2 mg Periactin tablets morning and evening.

Group III: Patients receiving placebo.

Group IV: Patients receiving 4 mg Periactin tablets morning and evening.

Group V: Patients receiving 4 mg Periactin tablets morning and placebo evening.

Table I gives a breakdown by age and sex for each treatment group. The groups were not comparable as to age distribution. The median age of group IV was found to be statistically significantly greater than that of groups I and II and the median age of group V was found to be statistically significantly greater than that of group I.

TABLE I. AGE AND SEX OF PATIENTS IN EACH TREATMENT GROUP

	No. of patients	*Sex* — *M*	*F*	*Age range*	*Median age**
Group I	17	9	8	3 - 25	9
Group II	16	5	11	4·5 - 31	12·5
Group III	16	10	6	5 - 24	14
Group IV	16	3	13	12 - 29	18
Group V	16	6	10	4·5 - 43	18

*Determined by rank sum test.[3]

For statistical reasons, a logarithmic transformation was made on the weight-gain data. Table II shows the geometric mean weights and percentage increases in geometric mean weights adjusted by analysis of covariance where appropriate (i.e. significant over-all reduction in variance and parallel regressions). All Periactin doses showed statistically significantly greater percentage increases in weight than the placebo group at weeks 8 and 12. The percentage increase appears to become greater as the dose becomes

*Date received: 4 November 1970.

TABLE II. GEOMETRIC MEAN WEIGHTS (LB)

	No.	*Pre-treatment*	*Post-treatment*	*Adjusted* pre-treatment*	*Adjusted* post-treatment*	*% increase*
2 weeks						
Group I	15	46·28	47·89	68·10	70·01	2·8
Group II	11	58·12	60·70	68·10	70·93	4·2‡
Group III	12	78·13	78·25	68·10	68·37	0·4
Group IV	12	95·75	98·07	68·10	70·15	3·0†
Group V	10	80·62	82·02	68·10	69·48	2·0
4 weeks						
Group I	13	51·26	53·60	—	—	3·6
Group II	13	59·45	63·91	—	—	7·5†
Group III	13	78·08	78·65	—	—	0·7
Group IV	15	95·17	100·58	—	—	5·7
Group V	13	85·63	92·48	—	—	8·0†
8 weeks						
Group I	12	54·29	58·16	74·09	77·82	5·0‡
Group II	10	58·92	64·81	74·09	80·31	8·4‡
Group III	11	69·67	70·03	74·09	74·19	0·1
Group IV	13	96·70	103·63	74·09	80·76	9·0‡
Group V	12	97·10	101·23	74·09	78·58	6·1‡
12 weeks						
Group I	10	56·88	62·52	75·56	81·17	7·4†
Group II	8	59·64	66·47	75·56	82·61	9·3†
Group III	6	69·59	70·90	75·56	76·47	1·2
Group IV	12	96·84	105·55	75·56	84·02	11·2‡
Group V	10	94·61	100·56	75·56	81·78	8·2

*Adjusted by analysis of covariance for differences in pre-treatment values.
†Statistically significantly better than placebo (group III), $P<0{\cdot}05$.
‡Statistically significantly better than placebo (group III), $P<0{\cdot}01$.

TABLE III. GROUP I. PATIENTS RECEIVING PERIACTIN 2 mg MORNING AND PACEBO IN THE EVENING*

Serial No.	*Age*	*Sex*	*Gain 1st month (lb)*	*Gain 2nd month (lb)*	*Weight change in 3 months (lb)*	*Appetite*	*Side-effects*
1	7½	F	+ 0½	—	+ 0½	0	0
6	13	F	+ 2	+ 0½	+ 5½	+	0
11	21	F	+ 6	− 3	+ 5	0	0
16	3	M	+ 1½	+ 0½	+ 2	0	0
22	25	F	+ 3	+ 1½	+ 8	+ +	0
26	14	F	− 2	0	− 2	0	0
39	4	M	+ 3	+ 0½	+ 6	+	0
32	3	M					
41	13	M	+ 4	+ 1	+ 5½	+ +	0
46	6	F	+ 1	+ 2	+ 4	+ +	0
52	3	M	+ 2½	+ 1½	+ 4½	+	1
57	4	F	+ 0½	+ 2	+ 2½	+	0
65	7	M	+ 1½	+ 1½	+ 3	0	0
73	4	M	+ 2	+ 3	+ 5½	+	0
78	16	M	+ 1	− 1	+ 1	0	0
80	9	F	+ 1½	+ 0½	+ 1½	0	0
86	14	M	+ 1	+ 0½	+ 1½	0	0

*17 patients were included in this category, 9 males and 8 females; 16 patients completed the 3-month treatment period.
Average weight gain: 1st month +1·81 lb; 2nd month +0·73; total weight change in 3-month period +3·38; appetite scoring +1; side-effects 1.

larger, which could be related, however, to the lack of comparability of the groups as to age. The results are set out in Tables II - VII.

CONCLUSIONS

The results of this survey indicate that all treatment schedules were superior to placebos. Patients in group IV receiving 4 mg Periactin *b.d.* showed the greatest effect as regards appetite stimulation and weight gain. However, the incidence of transient drowsiness was highest in this group. Patients in group II receiving 2 mg Periactin *b.d.* showed a very marked response with hardly any side-effects. In this latter group no side-effects were recorded in the paediatric age-groups, viz. 12 years and under.

Periactin in the dosage of 2 mg *b.d.* thus ensures marked weight increase with minimal side-effects.

The research committee of the Cape of Good Hope Faculty of General Practitioners wishes to thank Messrs Merck Sharpe & Dohme for providing the drugs used in this trial

TABLE IV. GROUP II: PATIENTS RECEIVING PERIACTIN 2 mg TABLETS MORNING AND EVENING*

Serial No.	Age	Sex	Gain 1st month (lb)	Gain 2nd month (lb)	Weight change in 3 months (lb)	Appetite	Side-effects
3	18	F	+ 3	0	+ 3	+	+ +
8	24	F	+ 4	− 2	+ 4	+	0
13	19	F	+ 4	+ 2	+ 6	+ +	0
19	25	F	+ 7	+ 1	+ 9	+ +	0
24	8	F	+ 3	+ 3	+ 7	+ +	0
29	14	M	+ 12	+ 3	+ 15	+ +	0
36	4½	M	+ 1	0	+ 2	+ +	0
43	7	F	+ 3½	+ 1	+ 5	+ +	0
48	5	F	+ 3	+ 2	+ 5½	+ +	0
51	6	F	+ 4½	+ 1	+ 7½	+ +	0
56	5	F	+ 2	+ 2	+ 4	+	0
63	31	F	+ 8	+ 10	+ 12	+ +	0
70	10	F	+ 5	+ 1	+ 7	+ +	0
75	9	F	+ 3½	−	+ 3½	+	0
85	6	F	+ 1				
90	9	M	+ 5	+ 2	+ 8	+ +	0

*16 patients were included in this group; one failed to complete the 3 months' therapy.
Average weight gain: 1st month +4·34 lb; 2nd month +1·86; total weight change in 3-month period +6·56; appetite scoring +2; side-effects—1 patient complained of drowsiness.

TABLE V. GROUP III: PATIENTS RECEIVING PLACEBO MORNING AND EVENING*

Serial No.	Age	Sex	Gain 1st month (lb)	Gain 2nd month (lb)	Weight change in 3 months (lb)	Appetite	Side-effects
2	22	M	− 3	+ 2	0	0	0
7	19	F	+ 2	0	+ 2	+	0
15	12	M	0	0	+ 1	0	0
18	19	M	− 2	− 4	− 10	0	0
21	5	M	− 0½	+ 0½	+ 0½	0	0
30	24	F	+ 0½	0	+ 3	0	0
34	6	M	+ 1	0	+ 2	0	0
37	9	M	+ 3	− 0½	+ 2½	+	0
53	14	M	+ 1				
60	6	F	0	0	0	0	0
62	13	F	+ 1	0	0	0	0
74	9	M	+ 1	0	+ 1	0	0
81	16	M	− 1				
83	8	F	+ 1½	0	+ 1½	+	0
87	23	F	+ 1½	+ 0½	+ 2	+	0

*15 patients were included in this category; 9 males and 6 females.
Average weight gain: 1st month +0·40 lb; 2nd month −0·12; total weight change in 3-month period +0·42; appetite scoring 0; side-effects 0.

TABLE VI. GROUP IV: PATIENTS RECEIVING PERIACTIN 4 mg TABLETS MORNING AND EVENING*

Serial No.	Age	Sex	Gain 1st month (lb)	Gain 2nd month (lb)	Weight change in 3 months (lb)	Appetite	Side-effects
5	24	M	+ 5	+ 2	+ 8	+ + +	1
12	12	M	+ 1	0	+ 1	0	0
17	22	F	+ 5	+ 2	+ 10	+ +	0
23	18	F	+ 4	+ 6	+ 28	+ + +	0
28	17	F	+ 6	0	+ 11	+ + +	0
35	17	F	− 2	− 1	− 4	+	0
40	14	F	+ 10	+ 3	+ 15	+ + +	1
45	18	F	+ 4	+ 3	+ 7	+ +	0
50	18	F	+ 3	+ 1½	+ 4	+ +	0
55	14	M	+ 3	+ 4	+ 8	+ + +	1
58	29	F	+ 10	0	+ 13	+ +	1
64	18	F					
69	25	F	+ 3	−	+ 3	+	1
71	17	F	+ 6	+ 3	+ 10	+ + +	1
76	19	F	+ 14	+ 2	+ 19	+ + +	0
82	21	F	+ 5	0	+ 8	+	1

*16 patients were included in this category, 3 males and 13 females.
Average weight gain: 1st month +5·13 lb; 2nd month +1·82; total weight change in 3-month period +9·40; appetite scoring +2; side-effects—5 patients complained of transient drowsiness.

TABLE VII. GROUP V: PATIENTS RECEIVING PERIACTIN 4 mg MORNING AND PLACEBO IN THE EVENING*

Serial No.	*Age*	*Sex*	*Gain 1st month (lb)*	*Gain 2nd month (lb)*	*Weight change in 3 months (lb)*	*Appetite*	*Side-effects*
4	21	F	+ 7	− 8	+ 8	0	0
14	21	F	+ 3½	+ 1½	+ 5	++	0
20	18	F	+ 4	+ 2	+ 6	++	1
25	7	M	+ 1½	0	+ 3½	+	1
27	24	F	+ 1	− 1	+ 1	0	0
31	28	M	+ 1	+ 1	+ 1½	++	0
38	17	M	+ 4	− 1	+ 4	+	++
44	44	F	0	0	− 2	+	0
49	4½	F					+
54	31	F	+ 3	+ 2	+ 4	++	0
59	11	F	+ 3	+ 1	+ 4	0	++
61	12½	M	+ 2	+ 4	+ 8	++	++
72	23	M	+ 2	+ 1	+ 4	+	+
77	4	M	+ 3	+ 0½	+ 3½	+	++
84	20	F	+ 11	+ 1	+ 11	++	+
88	12	F	+ 4	+ 2	+ 7	++	1

*16 patients were included in this category, 6 males and 10 females.
Average weight gain: 1st month +3·33 lb; 2nd month +0·40; total weight change in 3-month period +4·57; appetite scoring +2; side-effects—10 patients complained of transient drowsiness.

and for their assistance in the statistical evaluation. The committee also wishes to thank Dr P. Goosen, Medical Director of Merck, Sharpe & Dohme, for his assistance; and Drs F. Dornfest, P. Honeywill and A. W. Spratt for submitting data.

REFERENCES

1. Lavenstein, A. F., Dacaney, E. P., Lasagna, L. and Van Metre, T. E. (1962): J. Amer. Med. Assoc., **180**, 912.
2. Bergen, S. S. (1964): Amer. J. Dis. Child., **108**, 270.
3. Dunn, O. J. (1964): Technometrics, **6**, 241.