The Effects of Glucocorticoids on Metabolic Balance of Diabetics[1] (34223)

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Daily glucocorticoid administration in high doses is known to evoke serious negative nitrogen and calcium balances (1–4). Alternating corticoid therapy in nondiabetic subjects is associated with increased nitrogen excretion on the medication day. When glucocorticoids are given as a single high dose on alternating days (5), serious negative nitrogen balances are not encountered although some increase in nitrogen excretion is noted on treatment days. These conclusions (5) were derived from studies on nondiabetic patients. Since it is sometimes necessary to administer glucocorticoids to diabetic patients, the following studies were designed to test the effect of such alternating dosage on the metabolic balance of diabetic subjects.

Methods. The subjects were a group of insulin-dependent diabetics studied on the metabolic ward. Balance periods were of 7-days duration and were initiated after a preliminary period of regulation on diet and insulin. Alternating carmine and brilliant green stool markers were used. Stools, urines, and sample diets were ashed and the content of nitrogen, sodium, potassium, and calcium was determined on the AutoAnalyzer. Balance data were calculated by the methods of Reifenstein *et al.* (6).

After the base-line periods, the subjects were started on a regimen of a single dose of prednisone of 50 or 75 mg every other day. After a period of re-regulation of the diabetes, the balance periods were repeated.

Results. Balance data for nitrogen, sodium, potassium, and calcium are shown in Table I. The only significant difference for each group with treatment was a mean increase in negative nitrogen balance of 8.80 g/week in the group treated with 75 mg of prednisone.

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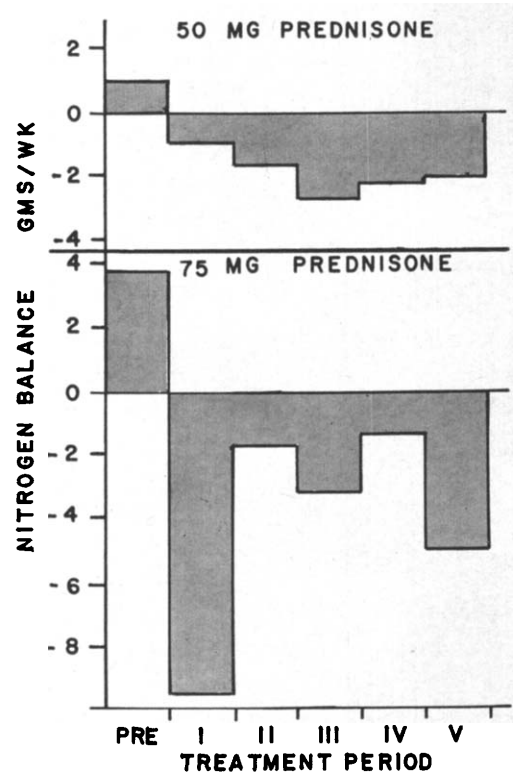

FIG. 1. The nitrogen balance means for various periods before and during treatment are shown for the patients receiving 50 mg of prednisone and for those receiving 75 mg of prednisone every other day. The only significant mean difference was that between the pretreatment and the posttreatment period in the group receiving 75 mg of prednisone.

Twelve of the 20 patients showed a more negative nitrogen balance with treatment; while 8 showed a more positive balance. Only 4 patients converted from a positive to a negative nitrogen balance on treatment. When examined according to periods (Fig. 1), the nitrogen balance reached a nadir at the third treatment period in the 50 mg group and in the first period in the 75 mg

TABLE I. Balance Data.

	Nitrogen (g/week)						Sodium (meq/week)						Potassium (meq/week)						Calcium (meq/week)					
	Before Rx			After Rx			Before Rx			After Rx			Before Rx			After Rx			Before Rx			After Rx		
No.	M	δm	*N*	M	δm	*N*	M	δm	*N*	M	δm	*N*	M	δm	*N*	M	δm	*N*	M	δm	*N*	M	δm	*N*
Prednisone, 50 mg																								
1	−2.60	0.17	2	−0.27	0.39	5	+84	3	2	+148	25	5	−130	5	2	−15	32	5	−42	151	2	−22	32	5
2	+8.87	3.51	3	−2.20	3.14	5	+69	84	3	+2	29	4	+109	113	3	−24	26	4	+120	79	3	+132	55	5
3	+12.55	8.27	3	+15.20	3.58	10	—			—			—			—			—			—		
4	+9.34	0.90	2	+12.00	0.91	5	+126	15	2	+71	27	5	−12	15	2	+15	17	5	+48	62	2	+34	12	5
5	+14.53	1.69	2	+7.07	2.24	5	−370	343	2	−11	26	5	−46	14	2	−57	8	5	−7	151	2	0	32	5
6	+1.66	0	1	−4.16	3.18	6	+250	0	1	+186	48	6	+112	0	1	+50	12	6	+176	0	1	+10	33	6
7	−3.45	0	1	−8.67	2.52	5	+185	0	1	+236	22	5	+64	0	1	+42	17	5	−104	0	1	−7	21	5
8	+11.38	0.04	2	+12.46	2.20	4	+161	67	2	+55	33	4	+68	3	2	+54	23	4	+28	29	2	+38	12	4
9	+6.85	0	1	−9.35	4.10	5	+121	0	1	+57	25	5	−13	0	1	+10	19	5	+28	0	1	−101	23	5
10	+2.79	0	1	−6.09	3.40	5	−8	0	1	+84	17	5	+89	0	1	+22	14	3	−134	0	1	−52	31	5
11	−3.32	1.88	2	+4.88	.9	4	+101	22	2	+152	27	4	+1	19	2	+21	33	4	−72	23	2	−16	29	4
12	−8.81	0	1	−13.55	3.40	5	+150	0	1	+57	38	5	−34	0	1	+1	37	5	−23	0	1	−148	156	5
13	−14.54	0	1	+3.13	4.57	5	+208	0	1	+255	37	5	+85	0	1	+87	42	5	+80	0	1	−269	140	5
14	−15.14	0	1	−14.77	4.43	5	+160	0	1	+212	37	5	+97	0	1	−160	182	5	+22	0	1	+50	34	5
Mean difference			−1.80						+21						+24						−29			
δ D			2.29						34						25						33			
p			>.05						>.05						>.05						>.05			
Prednisone, 75 mg																								
15	+11.80	0	1	+4.53	1.75	5	+73	0	1	+30	29	5	+105	0	1	+38	33	5	+12	0	1	−96	32	5
16	+17.07	0	1	+13.34	6.10	4	—			—			—			—			—			—		
17	−9.09	0	1	−12.72	1.51	5	+287	0	1	+143	41	5	+115	0	1	+69	15	5	+36	0	1	−35	17	5
18	−3.47	0	1	−6.57	3.20	5	+273	0	1	+61	48	5	+193	0	1	+74	34	5	−18	0	1	−48	60	5
19	−14.55	0	1	−29.97	15.70	5	—			—			—			—			—			—		
20	−5.89	0	1	+10.60	8.01	5	+81	0	1	+128	122	5	+29	0	1	+44	14	5	+7	0	1	+13	33	5
Mean difference			−8.80						−88						+54						−48			
δ D			1.18						56						27						26			
p			<.01						>.05						>.05						>.05			

N is the number of 7-day periods sampled either before treatment or during treatment.

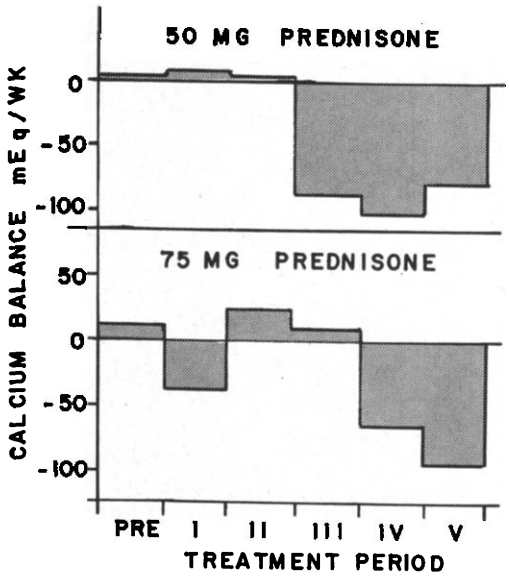

FIG. 2. The calcium balance before and during treatment with prednisone is shown for the group receiving 50–75 mg of the drug. Mean differences are not significant for the group.

group, after which it improved slightly.

Calcium balance followed a similar pattern (Fig. 2) although mean differences were not significant. Four of the patients reverted from a positive to a negative balance.

Great variability in state of balance vitiated the significance of the group differences. This variability was seen to a similar degree in both the pretreatment and treatment periods and appeared to be related more to the labile diabetic state of the patients than to the treatment *per se*.

Discussion. The metabolic balances were quite variable, which appeared related to the lability of the diabetic state. Although in some cases there was a greater negative nitrogen balance on prednisone therapy, in others there was actually a greater positive balance so that the mean changes for the group were not significant. Attention should be given to the occasional patient in whom a persistent negative nitrogen balance results. The lack of serious negative nitrogen balance in most of these patients on alternating prednisone therapy is in contrast to the well-known effect of continuous glucocorticoid therapy in this respect. In a few of the patients an increased nitrogen excretion was noted on prednisone treatment days. Similar findings were noted with the calcium balance. Variable changes were noted in the sodium and potassium balances reflecting intra- and extracellular fluid shifts but these for the entire group were not consistent and did not reflect any mean change of significance. The variability in the metabolic balance of these diabetic patients is in contrast to the stability of nondiabetic patients under similar conditions on this ward (7).

It would appear that prednisone can be given in this fashion to most diabetic patients without any serious worsening of nitrogen and calcium balances; however, such conclusions should be modified for the individual patient where unfavorable effects may appear. In general, but not always, the 75-mg dose of prednisone tends to augment the undesirable effects on diabetic regulation and nitrogen balance while with the 50-mg dose these effects are usually minimal.

Summary. The effects of a single high dose of prednisone on alternate days on the metabolic balance of 20 diabetic subjects was studied. Only four subjects converted from a positive to a negative nitrogen balance. No consistent trend was noted in balances of sodium, potassium, and calcium.

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