EFFICACY OF DIVIDED AND SINGLE DOSE SCHEDULES IN INSULIN COMA THERAPY

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While many technics for the administration of insulin in insulin coma therapy have been advocated(3), recent reports(4) have assessed multiple divided doses as more effective and safer than other methods. Previous studies indicated that the production of coma was directly related to the level of hypoglycemia and its duration (1) and that deep coma for sustained periods was essential to the treatment result in insulin therapy(2, 3). It seemed reasonable to test the suggestion of increased efficacy for a modified insulin administration by comparing the length and depth of coma and the blood sugar levels in patients treated both by single and divided insulin dose methods. If the divided dose schedule were more effective, it would be expected that the induced coma would be equal or greater in depth and duration; that the time for onset would be equal or shorter; and the blood sugar levels lower for divided dosage than single administration.

METHOD

Consecutive patients referred for insulin coma therapy were given daily increasing amounts of insulin in 3 divided doses until a coma level was achieved. The same total dosage was then given in one injection. Six patients were studied in this manner. Each patient was started on the following insulin dose schedule: first day—10 units; second day—10 units and 2 doses of 5 units each at intervals of one half hour; third day—3 doses of 10 units at half hour intervals; and fourth day—20 units followed by 2 doses of 10 units. On each successive day the dose was increased in 10 unit increments. At the time when coma was produced, a single dose equivalent to the 3 doses was given on the succeeding day.

For each treatment, coma depth and the time of onset was determined. Coma was defined as the loss of consciousness (failure to respond meaningfully to verbal signals), associated with the appearance of the Babinski reflex, and the loss of the lid reflex. An adequate coma treatment was defined as the persistence of this depth of coma, or deeper (loss of pupillary or corneal reflexes) for at least one hour.

At half-hour intervals true blood sugar levels were serially determined by the Somogyi method. The resulting blood sugar curves and their level at the time of onset of coma, were compared for each subject with the blood sugar curve and coma data obtained on a single administration of an equivalent dose.

OBSERVATIONS

The blood sugar levels at various intervals after the administration of divided doses of insulin compared with a single dose of insulin in one patient is presented in Figure 1. This pattern has been reproduced in each of the patients studied. For each, the blood sugar curve drops rapidly in the first hour without respect to the initial dose, and flattens at progressively lower levels as the total dosage of insulin increases. Coma characteristically is reported in subjects in whom the blood sugar curve is below 21 mg.% for an extended period of time(1).

The time of onset of coma and the blood sugar level at coma in each of the patients is presented in Table 1. In five of the 6

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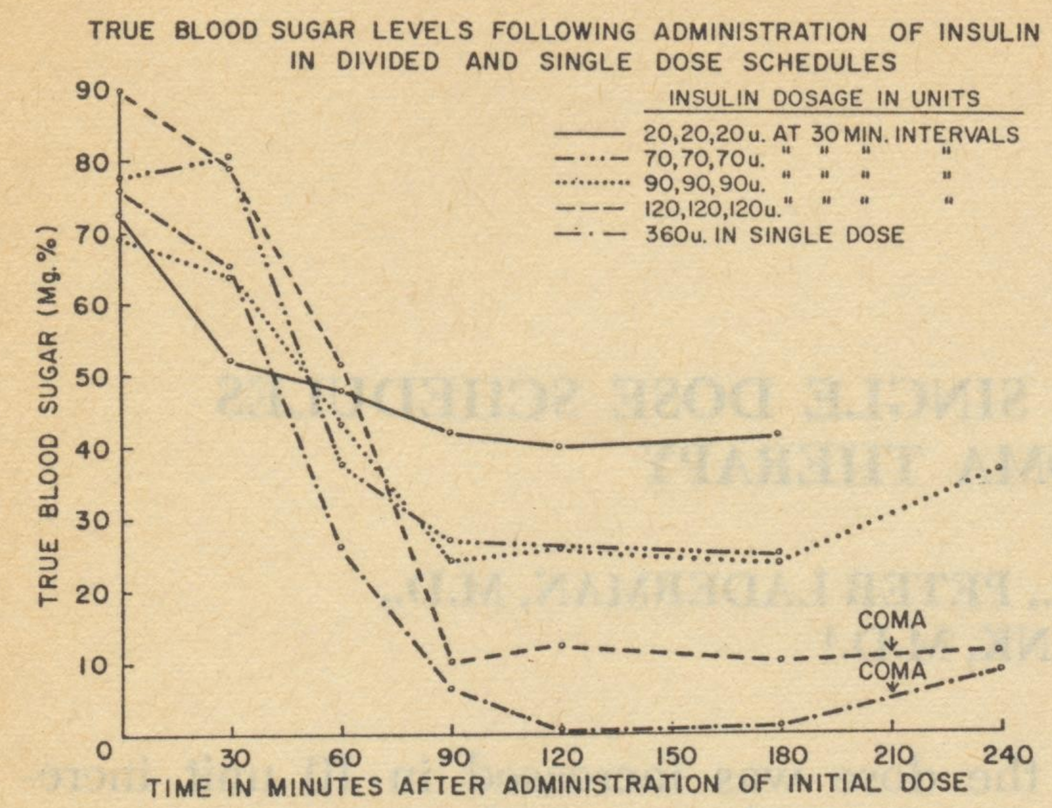

cases, there was no difference in the time required to induce coma by either the single or the divided dose methods. In one subject (Sc) coma was observed in 1½ hours with a single dose as compared with 3 hours with divided doses.

TABLE 1

ONSET OF COMA AND BLOOD SUGAR WITH DIVIDED AND SINGLE DOSAGE SCHEDULES

		Time for Coma (minutes)		*Blood Sugar Value (mg. %)*	
PT	*Insulin Units*	*Divided Dose*	*Single Dose*	*Divided Dose*	*Single Dose*
D	330	210	190	4	0
G	360	210	210	14	4
H	270	210	210	15	15
Sc	390	180	90	12	7
So	360	210	210	12	8
V	210	135	150	8	20

The average blood sugar at the time of coma was lower with the single doses than with divided doses in 4 of the 6 cases. It was identical in one and lower with the divided dose in one.

As there was no evidence in these studies that the divided dose method was more effective in the production of insulin coma than the single dose method, the divided dose technic was discontinued.

CONCLUSIONS

The coma produced with the divided insulin doses did not occur earlier and was not deeper than that produced by the single dose. The increased effort in divided dose schedules is justified neither by increased safety nor by increased depth or duration of the induced hypoglycemia.

There was no evidence that the initial dose of insulin sensitized the subject so that subsequent doses produced a greater hypoglycemic effect. The total hypoglycemic effect of divided doses appears to be less, if anything, than the effect of a single dose.

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