Diabetic Control on Once- and Twice-daily Insulin Injections

Dear Sir,

In the June 1980 edition of *Diabetologia*, Tchobroutsky et al. [1] reported a significant inverse correlation between the number of daily insulin injections and the HbA_{1c} concentrations. In a recent study we have failed to find such a relationship.

We measured $HbA_{1(a+b+c)}$ concentrations in a sample of 376 diabetic out-patients, established on once or twice-daily insulin injections, at one of two teaching hospitals (Table 1). No patient whose regimen had been changed within six months was included in the study. HbA_1 was estimated by a rapid column chromatographic method [2]. The within and between assay variability were <3% and <4% respectively. The distributions of the HbA_1 levels in the once and the twice-daily injection groups and comparisons between the means were analysed for each hospital separately and for both together using the Kolmogorov-Smirnoff and Student *t* test methods respectively, after the data had been shown to be normally distributed.

No significant differences were found between patients on once and on twice-daily injections either by comparing the means of HbA_1 levels or by comparing their distribution (Table 1). This applied whether data from the two hospitals was analysed separately or collectively. The numbers studied were sufficient to exclude the possibility of a type II error in analysis for differences at the 5% level or above [3]. Only 18.1% of the once-daily and 21.0% of the twice-daily group had HbA_1 levels within our normal range (i. e. below an HbA_1 of 10.5% or within 1.7 standard deviations of our non-diabetic patient mean). Tchobroutsky et al. give figures (based upon HbA_{1c} values falling within three standard deviations of the normal mean) of 4% for those on once-daily injections, 21% for those on twice-daily injections and 19% for all groups combined. The discrepancy is thus most obvious between the results obtained in the once-daily injection groups and would be accentuated if a range within 2 standard deviations of the normal mean were used in Tchobroutsky's analysis. This could either reflect an unrepresentative sample of 25 patients on once-daily insulin in Tchobroutsky et al's data or suggest that HbA_{1c} is a better discriminant of poor control than $HbA_{1(a+b+c)}$.

While our results are disappointing in failing to support those of Tchobroutsky et al. it is clear that most of our patients on

divided doses of insulin had been started on them because of difficulties in management with once-daily insulin. On clinical grounds, therefore, this group might have been expected to be less well controlled than those on once-daily insulin.

The difference in ages, as Tchobroutsky et al. suggest, may explain the differences they found between the groups. HbA_1 also rises with age and since our twice-daily dose patients were younger than those on single doses they could have been expected to have lower HbA_1 levels, but comparable levels of control may still have been achieved because of the use of divided doses for the more difficult patients. Comparison of regressions of HbA_1 on age in Tchobroutsky's data may clarify this point.

Prospective studies of long-term control will be needed to define the contributions of divided insulin doses to patient care as compared to the many other factors affecting control.

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References

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Table 1. Values of Glycosylated haemoglobin (HbA_1) in patients from two hospitals; on once or on twice daily insulin. Comparison of group means (*t* test) and distribution (*z*) (see text)

Patient	Groups	n	Mean HbA_1 , %	±	Standard error	Significance of <i>t</i> test	% in normal range ($HbA_1 < 10.5\%$)	Significance of <i>z</i> test
L. H. ^a	Total	188	12.87	±	0.19	NS	19.1	NS
S. J. H. ^b	Total	188	12.66	±	0.18		19.6	
L. H. ^a	Once daily	109	12.84	±	0.24	NS	18.3	NS
L. H. ^a	Twice daily	79	12.92	±	0.30		20.2	
S. J. H. ^b	Once daily	115	12.66	±	0.21	NS	18.3	NS
S. J. H. ^b	Twice daily	73	12.65	±	0.31		21.9	
L. H. ^a + S. J. H. ^b	Once daily	224	12.75	±	0.16	NS	18.1	NS
L. H. ^a + S. J. H. ^b	Twice daily	152	12.79	±	0.22		21.0	

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^b St. James Hospital, Leeds