Measuring side-effects of β -adrenoceptor antagonists: a comparison of two methods

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The prevalence of side-effects of β -adrenoceptor antagonists among hypertensive patients was assessed by two methods. Using visual analogue scales, scores for tired legs, cold digits and vivid dreaming were significantly higher in patients taking β -adrenoceptor blockers than in patients not taking β -adrenoceptor blockers. When measured by numerical scales, from 1 to 10, these symptoms showed no relation to β -adrenoceptor blocker treatment. The visual analogue scales were more sensitive than the numerical scales because the scores were distributed more evenly over the analogue scales.

Keywords β -adrenoceptor antagonists visual analogue scales side-effects

Introduction

Patients with mild hypertension usually have no symptoms, and the benefits of therapy to the individual are generally small (Pickering, 1983). Side-effects of antihypertensive drugs are therefore important as these may outweigh the benefits of treatment, particularly if overall quality of life is affected. β -adrenoceptor antagonists are widely used for the treatment of hypertension and are associated with a number of side-effects (Kendall & Beeley, 1983), but it is not known whether these symptoms interfere significantly with life. Much of the uncertainty stems from difficulty in quantifying side-effects and in measuring quality of life.

The quantification of subjective phenomena is difficult because words may not describe the subjective experience accurately. The use of descriptive scales, where the severity of the symptom is graded as slight, moderate, severe etc. has been described (Keele, 1948), but the paucity of terms in common speech limits the amount of information which can be transferred (Aitken, 1969). An important change in the severity of a symptom can occur without causing a category change in such a scale and would not be detected (Sriwatanakul *et al.*, 1982). However, such scales are easily understood by most patients.

Visual analogue scales (VAS) have also been used for the quantification of subjective phenomena. We have shown that VAS can consistently detect some side-effects of β -adrenoceptor antagonists, particularly tired legs and cold digits (Lewis *et al.*, 1984, 1985). However some patients do not understand visual analogue scales (Huskinson, 1974), and we have found that at least 7% of patients could not complete VAS questionnaires despite detailed written instructions (Lewis *et al.*, 1985).

We have tried to combine the ease of comprehension of descriptive questionnaires with the sensitivity of VAS by scoring the severity of symptoms on a numerical scale, from 1 to 10. We have compared the sensitivity of this numerical scoring questionnaire (NSQ) to that of visual analogue scales (Lewis *et al.*, 1984) in detecting side-effects of β -adrenoceptor blockers in hypertensive patients.

Methods

Two study groups, each of 100 patients, were obtained by the same sampling procedure from patients attending the Sheffield hypertension clinic. Possible side-effects of β -adrenoceptor

blockers were examined in one group by visual analogue scales, and in the other by a numerical scoring questionnaire. Apart from the method of instruction (see below) the methods of study, data collection and analysis were identical for the two groups.

Visual analogue scales

Sixteen symptoms were examined by horizontal 10 cm VAS which have been described previously (Lewis *et al.*, 1984). Twelve were putative side-effects of β -adrenoceptor blockers, three were dummy symptoms, and one assessed overall wellbeing. Instruction on completing the VAS was given verbally by one investigator who was unaware of the patient's treatment. The replies were divided according to drug treatment, and the scores for patients taking different treatments were compared by Kruskal Wallis analysis of variance and the Mann Whitney U test. The findings have been described in detail elsewhere (Lewis *et al.*, 1984), but raw scores rather than proportional scores were used for the present comparison.

Numerical scoring questionnaire

The same symptoms were assessed by asking patients to allocate to each a score between 1 and 10. The questionnaire was presented with written instructions, and the subsequent analysis was as described above.

Results

Comparability of groups

The two groups did not differ significantly as regards age (VAS, mean 52, range 27–76 years; NSQ, mean 54, range 16–76 years), sex (VAS, M:F = 0.83; NSQ, M:F = 0.70), or the number and type of antihypertensive drugs taken (see below). One patient in the VAS group was excluded, as stipulated by the protocol, because he was taking five drugs.

Symptom scores

In the VAS study the four treatment groups compared were: no β -adrenoceptor blocker ($n = 23$), β -adrenoceptor blocker alone ($n = 21$), β -adrenoceptor blocker plus diuretic ($n = 32$), and β -adrenoceptor blocker, diuretic, plus a third drug ($n = 23$). These groups differed significantly for three symptoms, namely tired legs, cold digits and vivid dreams. These differences were between patients taking a β -adrenoceptor blocker, alone or in combination, and those taking no β -adrenoceptor blocker (Table 1).

In the NSQ study the numbers in the four treatment groups were: no β -adrenoceptor blocker ($n = 34$), β -adrenoceptor blocker alone ($n = 16$), β -adrenoceptor blocker plus diuretic ($n = 17$), and β -adrenoceptor blocker, diuretic plus a third drug ($n = 33$). These groups did not differ significantly for any symptom, including those which were positive in the VAS study (Table 1).

Distribution of scores

The distributions of scores for tired legs and cold digits by the VAS and NSQ methods are shown in Figure 1. The VAS scores were spread fairly evenly over the 10 cm scale, whereas the NSQ scores were markedly skewed, with a strong preference for a score of one. The difference in distribution of scores by the two methods was significant for tired legs ($P < 0.05$), but not cold digits.

Discussion

The findings for nine of the twelve symptoms thought to be possible side-effects of β -adrenoceptor blockers (Lewis *et al.*, 1984) were negative with both the VAS and NSQ methods of measurement. This may mean that both methods were insensitive for these symptoms, that the sample sizes were too small, or that

Table 1 Comparison of symptom scores for hypertensive patients not taking a β -adrenoceptor blocker and for those whose treatment included a β -adrenoceptor blocker.

Symptom	Visual analogue scales (cm)		Numerical scoring questionnaire	
	No β -adrenoceptor blocker ($n = 23$)	β -adrenoceptor blocker ($n = 76$)	β -adrenoceptor blocker ($n = 34$)	β -adrenoceptor blocker ($n = 66$)
Tired legs	4.0	6.1***	4.0	3.9
Cold digits	3.8	5.4*	3.4	3.9
Vivid dreams	2.2	4.0**	3.4	3.5

Significance of differences from no β -adrenoceptor blocker group; *** $P < 0.005$; ** $P < 0.01$; * $P < 0.05$.

Figure 1 Frequency distribution of scores using numerical scoring questionnaire (NSQ) and visual analogue scales (VAS).

these symptoms are not in fact side-effects of β -adrenoceptor blockers. These possibilities are being examined in a much larger study. The finding of note in the present study is that visual analogue scales could detect three side-effects of β -adrenoceptor blockers, namely tired legs, cold digits and vivid dreaming, whereas the numerical scoring method could not. This suggests that these visual analogue scales were more sensitive than the corresponding

numerical scores, but other explanations for the findings must first be considered.

The differences observed might reflect real differences between the two groups of patients studied and not between the methods of measurement. This is very unlikely, as the two groups were drawn from the same patient population by the same method, and they were similar in age, sex and drug treatment. The two methods of measurement were not compared in the same patients because it was felt that this would introduce bias. The response to a second questionnaire might well be influenced by prior exposure to the first questionnaire. The differences between the two groups are unlikely to have been observed by chance, as the visual analogue scales used have detected tired legs and cold digits consistently, with significant separation of patients taking β -adrenoceptor blockers from those not so treated (Lewis *et al.*, 1984, 1985).

The findings therefore suggest that the visual analogue scales were more sensitive than the numerical scoring method for detecting tired legs, cold digits and vivid dreaming. Inspection of the distributions of scores (Figure 1) reveals one probable reason for this. The numerical scores were markedly skewed with a strong preference for scores of one, whereas the VAS scores were distributed more evenly over the 10 cm scales.

Side-effects of β -adrenoceptor blockers have usually been studied using descriptive questionnaires, and their prevalence may have been underestimated because this method lacks sensitivity. On the other hand visual analogue scales may be oversensitive and detect side-effects which do not really matter. It remains to determine whether side-effects which can be detected and quantitated by visual analogue scales have any impact on general wellbeing.

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