ASSESSMENT OF DRUGS IN GENERAL PRACTICE

M.R. SALKIND

Hackney, London

Assessment in general practice necessarily differs in some respects from assessment in hospital, because general practice is itself different in some fundamental respects.

General practice provides a continuity of care for the patient in all sorts of illness, often through many generations of a patient's family and sometimes through many generations of doctor. Each patient is seen approximately five times a year, while those with emotional disturbances are seen much more frequently. We general practitioners work with the knowledge that if contact with the patient is lost after one episode of illness it is comparatively easy to re-establish communications. This capacity to regain contact alters the quality of the consultation. We know and treat the family as an entity in the same way as we treat individual members, and the patient is seen functioning within his social and economic framework. We are in the community, near the homes, near the shops—indeed, in the homes and in the shops.

We see a different part of the total spectrum of illness when compared with hospital workers who see only patients whom family doctors regard as being ill and as having the status of patienthood. These patients are those whom we have previously put through the sifting process. On the other hand we first see patients when they themselves, or those in their environment, feel that their symptoms have attained the dignity of 'illness'; when the symptoms have slipped over the borders of what may be safely allowed to take its own course. When this happens the patient goes to his family doctor whom he has chosen and with whom he can live and work. We appear to choose, albeit unknowingly, our own patients; we do have a choice; we gather around those who need us, but also those whom we need.

A further distinction is that general practitioners have had even more diversified types, places, duration and amounts of psychiatric training, ranging from those who have virtually no formal training since qualifying and precious little before that, to those who have spent up to 15 years in 'Balint' groups sensitizing themselves to the emotional needs of the consultation. Psychiatric assessment is consequently even further from standardization than it is in the hospital setting.

In discussing general practice assessment I shall deal with the assessment of psychoneurotic disorders, since I suspect that this presents most difficulty. I would like also to distinguish between two aspects of

assessment, the broad evaluative aspect and the aspect of measurement. The broad evaluative procedures involve a sensitive observer who looks for significant cues and then integrates them into a total impression. The significant cues are often intangible feelings, aura emanating from a well known individual and registering with us as change.

We tend to work with significant target symptoms from which we generalize. I believe, for example, that most of us use depressed mood as the major target symptom in assessing neurotic depression rather than using the whole constellation of depression symptomatology. In anxiety/depression it is the level of *depressed* mood rather than *anxious* mood which determines whether a patient is consigned to an anxiety diagnostic group or a depression diagnostic group. We are good at making broad assessments; we know our patients when they are functioning normally, so a departure from normality is recognizable. Should we miss it, however, then the family or neighbours are quick to inform us.

I believe we are highly sensitive assessors in much the same way as a mother is a highly sensitive assessor of a child, and we make these assessments with feedback from the whole practice team.

Measurement is quite different. This implies concern with things, real elements, or traits, which have an implied existence, and is comparable with the physical sciences in which common aspects of dissimilar objects are identified and then described numerically by location on a scale of units. Among other requirements a good measure needs to be highly reliable in the sense of being reproducible (stable over time and situation), and in this sense general practitioners are imperfect measuring instruments, even more so than hospital workers. Multicentre trials across many general practitioners may be invalid unless there is previous standardization of diagnostic and rating procedures. If we measure by using target symptoms we may each be measuring different entities believing them to be the same.

These differences which I have outlined relate only to the different situations and relationships pertaining to general practice, but there are some important clinical differences which partly stem from the different conditions.

The level at which patients regard themselves as being ill—that is, the level at which their neurotic distress symptoms impel them into surgery—is much lower than the level at which we refer patients to

Figure 1 Group 1 patients.

Figure 2 Group 2 patients.

hospital. A very large proportion of our patients presenting initially with or without a somatic presentation do not suffer from depressive illness. They present in the consulting room with a change of mood which is an unpleasant reaction to a situation; the response may be appropriate, but it is nevertheless distressing. Because of the relationship which we have with our patients, which exists also in relationship to the family as a whole, they come to us for relief, and because they are not ill in the sense in which we normally use the term, a large proportion experience spontaneous remission after a comparatively short time.

It is possible to illustrate the importance of this point using the broad variable of morbid anxiety. In my own practice, using the 'morbid anxiety inventory' (Salkind, 1973) it has been possible to establish basal anxiety levels for many individual patients in much the same way as basal blood pressure levels. It appears that at least three distinct strata can be identified.

Group 1 (Figure 1)

In this group, patients with low basal levels have encountered particularly severe stress, but although they may react with quite high response levels they appear to improve within 6 weeks. Either the life event to which they have reacted resolves, or they adjust to the situation.

Group 2 (Figure 2)

This prerepresents the next group with an anxiety level at or near the cut-off point. These patients merge into higher anxiety levels with very much less stress; they are ill, their response may be inappropriate. Their high anxiety levels last much longer, up to 6 months. Removal of the stress improves this group in the same

Figure 3 Group 3 patients.

fashion as in group 1; they respond well to supportive therapy as well as to psychoactive drugs.

Group 3 (Figure 3)

These are the chronically ill patients with basal levels well above the cut-off level. This group corresponds broadly to the group that we refer to hospital. They do not respond to treatment, whatever and wherever given, and sooner or later they find their way back to us.

If we examine all these differences in the light of the usual clinical trial, it becomes very clear why most trials in anxiety/depression produce inconclusive results. I believe it to be a result of these fundamentals being largely overlooked. Examining the protocols of many trials is a depressing exercise because it is

possible to prophesy almost invariably that the active drug will not appear significantly superior to placebo, and that two active drugs will be indistinguishable. It is also possible while proceeding through the usual protocol headings to identify some guidelines to sharpen the discriminating power of a trial.

Setting

General practitioner trials are best carried out in either a small number of selected practices in which the diagnostic criteria have been agreed by personal briefing, or on a multicentre basis using appropriate specific self-assessment methods. Specificity of scale is very important—for example, scales should be chosen to be appropriate to state or trait. I find visual analogue scales (Aitken, 1969) mainly useful as *ad hoc* rating devices, that is, for rating conditions for which no well validated scales exist; but I find that batteries of line scales are very confusing and surprisingly time consuming.

Selection of patients

The appropriate selection of patients is critical to the success of a trial. Too many general practitioner trials are loaded with group 1 patients. The very high rate of spontaneous remissions and the considerable placebo response lead to a diminution in the difference between placebo and treatment groups. Since this is also true of the refractory group 3 patients, it is preferable to isolate and select the group 2 patients who do respond to drugs, and who without treatment tend to have a more prolonged illness before remission occurs. In some trials it may be worthwhile to isolate groups of group 1 or group 3 patients in order to examine specific objectives; for example, in group 1 for examination of speed of response rather than proportion improved or cured.

Dosage

It is important to know the exact dose taken, or even if the drug is taken at all. I am sure that lower doses of psycho-active drugs are required in general practice, but then most of our patients continue to work and being less tolerant to side-effects tend to fix their own dose régime regardless of instructions. They admit to this more readily in general practice than in hospital in my own experience. I find serum levels easier to undertake in general practice since the patients come so willingly to the surgery for the venepuncture. It is possible to do this even during a busy surgery.

One solution to the dosage problem is to count returns of tablets and capsules but one cannot exclude falsification of returns. By taking the guilt out of the situation and allowing patients to fix their own dose within given limits (Hollister, 1970), in fact by making

a virtue out of a necessity, more accurate returns may be obtained. Using this method the daily dose selected by patients in a trial of anxiolytics in neurotic anxiety (Bonn *et al.*, 1971) was oxypertine 28 mg and diazepam 14 mg (two capsules of each daily) but they took over four capsules daily of the placebo, a statistically highly significant difference. I suppose this might be another way of assessing drug/placebo difference, although it may only reflect side-effects.

Side-effects are easy to assess in general practice as patients readily seek advice if they find them too severe; the location of the surgery within the community area facilitates the exchange of information. In any case in my own surgery we use pursuit rota, reaction time and tapping speeds in highly standardized conditions to investigate side-effects. It may surprise many that I find it at least as easy to do this in my practice as in hospital conditions: it is possible to use relatively sophisticated procedures.

Defaulting

The high rate of defaulting ruins many hospital trials but, presumably because patients find it so convenient to attend surgery to ask for advice, defaulting in general practice is often very low. My own defaulting rate runs from 1 to 5%. In some trials of up to 60 patients we have had no defaulters at all. In any case it is easy to chase them up during home visits.

Another aspect of general practice trials that constantly impresses me is the importance of external life events, non-patient-mediated, that happen in the course of a trial. It always strikes me as curiously myopic that in a scientific experiment with the exclusion of as many non-specific variables as possible, one of the most important, if not the most important of these non-specific variables is somehow bypassed.

Table 1 Fortuitous events

1. <i>Family</i>	Health: Physical and psychological Death Finance Other problems
2. <i>Work</i>	Promotion Demotion Redundancy Shutdown, strike
3. <i>Social environment</i>	Housing School Neighbours
4. <i>Isolated events</i>	Victim of crime Automobile accident

Figure 4 Final analysis of morbid anxiety inventory ($n=58$). □, before correction; ■, after correction.

According to Rickels and his co-workers (1967) the life events variable appears to affect drug and placebo outcome in such a way as to diminish drug/placebo difference. It is comparatively easy in general practice using a simple check list (Table 1) to assess the importance of these non-patient-mediated events.

As an example of what may occur, one patient in the trial investigating the efficacy of anxiolytics in neurotic anxiety complained of being burgled twice in 4 weeks during the course of the trial, and while bending over at a foundry a workmate tripped and poured molten metal over his buttocks. How you analyse results in the light of this kind of life event does affect the result. Using a correction based on Rickels's findings the result shown in Figure 4 was obtained, but it must be confessed that using the correction is by no means generally acceptable, since it involves excluding those on active drugs with a negative life event who deteriorate and those on

placebo who improve following a positive life event. Perhaps a better method is to exclude from the analysis all cases experiencing significant life events with the admission that adequate assessment of the drug effect in these patients is scarcely possible.

In most general practice trials 50–60% of patients in a placebo group improve as do approximately 70–80% of those on active drugs. This means that very large groups are required to discriminate between active drugs and placebo, and even larger groups to discriminate between active drugs. It is a consistent failing of trials in general practice that groups are too small for statistically significant results to be possible. This leads to the inevitable conclusion that most trials are foredoomed to an inconclusive result.

We in general practice have learned a great deal from our hospital colleagues; it is possible that much of what we are now learning in general practice may be applied with some profit to hospital trial methods.

References

- AITKEN, R.C.B. (1969). Measurement of feelings using visual analogue scales. *Proc. roy. Soc. Med.*, **62**, 989.
- BONN, J.A., SALKIND, M.R. & LINFORD REES, W. (1971). A technique in the evaluation of psychotropic medication based on a patient-demand schedule: a comparison of the efficacy of oxypertine, diazepam and placebo in anxiety. *Curr. ther. Res.*, **13**, No. 9.
- HOLLISTER, L.E. (1970). Methodological considerations in evaluating anti-anxiety drugs. *J. clin. Pharmac.*, **1**, 12.
- SALKIND, M.R. (1972). Anxiety neurosis in general practice. *Postgrad. med. J. Suppl.* (4), **48**, 41.
- SALKIND, M.R. (1973). Morbid anxiety, PhD thesis, Univ. London.
- RICKELS, J. & DOWNING L. (1967). *Proc. Fifth International Congress Neuropsychopharm.*, 717.