The importance of general practitioner information in selection of volunteers for clinical trials

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The safe conduct of phase I volunteer studies requires careful selection and screening of volunteers. We have reviewed the results of the selection procedure in our clinic. The information received from the volunteer's general practitioner revealed clinical problems which had not been disclosed during medical history or examination.

Keywords selection volunteer healthy general practitioner

Introduction

The recruitment and selection of volunteers for phase I clinical trials should aim to prevent rare but potentially serious adverse events suffered by 'healthy' volunteers as a consequence of participation in a trial (The Association of the British Pharmaceutical Industry, 1988; Royal College of Physicians, 1986).

It is normal practice to screen potential participants in phase I trials of new medicines (Joubert & Pannell, 1976). An important part of this screening process is to acquire information on past medical history and, if appropriate, social history from the general practitioners of potential volunteers. We have reviewed our screening procedures including the relevance of information from the general practitioners in our acceptance of subjects who volunteer for clinical trials.

Methods

Volunteers were recruited by local press advertising and by word of mouth. All were aged between 18 and 55 years.

Screening of potential volunteers involved three main stages:

(1) Review of all applications, (2) history, examination and investigation and (3) a request for information from the general practitioner. Stages (1) and (2) are carried out by the medical and nursing staff of Inveresk Clinical Research.

Stage 1

All volunteers completed a questionnaire form giving personal, social and medical details. All applications were reviewed and those persons with significant past or present medical history or current drug therapy were excluded as well as those who were unable to participate for social reasons.

Stage 2

A full medical history and physical examination (including ECG) with clinical chemistry and haematology investigations and serology for Hepatitis B and HIV were carried out. A counselling service is provided before and after screening for HIV. In addition urine was examined for protein, glucose, blood and bilirubin as well as for drugs of abuse. Previously undetected abnormalities, e.g. hypertension, abnormal liver function tests, or drug therapy resulted in exclusion of the volunteer from the study.

Stage 3

Finally in subjects who had not been excluded and with the volunteer's written consent, information was sought from the general practitioners who were asked to complete a questionnaire after reading the relevant lay summary for the proposed study (Figure 1). Information was provided on past medical history and relevant social history which might contraindicate the volunteer's participation in the trial. They were asked also to state whether they had any objection to their patient's participation. A written response was obtained from almost all general practitioners, for which a standard report fee was paid. If no written reply was received, the general practitioner was contacted by telephone.

We reviewed 831 volunteer applications for a clinical study during a continuous 15 month period. We recorded specifically the number of rejections, the reasons for rejection and the stage of screening at which rejections were made.

Results

A total of 831 applications were received: 773 from males, 58 from females. Of these 831 potential volunteers, 237 (28.5%) were not accepted (Table 1).

Patient's Name: _____

Date of Birth: _____

General Practitioner: _____

MEDICAL HISTORY

Yes   No
(Tick as appropriate)

Disorders of the central nervous system: ☐ ☐Disorders of the cardiovascular system: ☐ ☐Disorders of the respiratory system: ☐ ☐Diseases and disorders of the alimentary system: ☐ ☐Disorders of the genito-urinary system: ☐ ☐Psychiatric disorders: ☐ ☐Alcohol/drug abuse: ☐ ☐Other (eg diabetes mellitus, thyroid disorder, allergic): ☐ ☐Recent prescribed drug treatment: ☐ ☐Any evidence of adverse drug reaction: ☐ ☐Do you have any objections to your patient participating in this trial? ☐ ☐If Yes, please specify: ☐ ☐

Has your patient participated in a trial of an unlicensed drug in the last 6 months?

ANSWER: YES/NO/DON'T KNOW How long do your records cover the medical history of this patient? yearsSigned: _____ Date: _____
General Practitioner

Authorisation Stamp: _____

Please note: This statement does not imply your consent.
Responsibility for a subject entering a study is between the volunteer and ICR.

Figure 1 General practitioner questionnaire.**Table 1** Number of volunteers rejected at various stages of screening

Rejected at stage 1	117 (14.1%)*
Rejected at stage 2	45 (5.4%)
Rejected at stage 3	44 (5.3%)
Rejected after stage 3 for non-medical reasons	31 (3.7%)
Total	237 (28.5%)

*Percentage of total number of applications.

One hundred and seventeen (14.1%) were excluded before attending for screening examination (28 for medical reasons and 89 for non-medical reasons). Forty-five (5.4%) were rejected as a result of the screening examination and blood tests (44 for medical reasons).

Forty-four (5.3%) were rejected on the basis of information supplied by the general practitioner. Thirty-one (3.7%) were rejected for non-compliance with the study or clinic guidelines.

In virtually all cases we received an answer to the questionnaire (Figure 1) from the general practitioner before the start of the study. This was sometimes given verbally. On very rare occasions, where no GP could be contacted or notes were unavailable, a decision to proceed was made by senior medical staff.

In all, 116 volunteers (49% of all rejections) were excluded on medical grounds, 44 of these on the basis of information supplied by their general practitioners. The medical reasons for rejection are shown in Table 2.

Many of the disorders which lead to rejection from study participation were detected at the screening stage, e.g. electrocardiographic abnormalities (Wolf-Parkinson-

Table 2 Medical reasons for rejection of potential volunteers

	<i>Total number of cases</i>	<i>% of all medical reasons for rejection</i>	<i>Number as result of GP information</i>
Cardiovascular disease	16	12.8	6
Respiratory disease	10	8.0	2
Liver dysfunction	16	12.8	
Gastrointestinal disease	4	3.2	2
Psychiatric disorder	15	12.0	9
Alcohol problem	24	19.2	18
Drug dependency	4	3.2	4
Neurological disorder	11	8.8	6
Rheumatological disorder	2	1.6	2
Ophthalmological disorder	2	1.6	
Urological disorder	2	1.6	1
Endocrine disorder	1	0.8	
Miscellaneous	18	14.4	2
Total	125*	100	52†

*A total of 116 volunteers were rejected on medical grounds. Nine of these each had two distinct pathologies.

†Includes eight subjects with two distinct pathologies.

White Syndrome or 1st degree heart block), hypertension or retinitis pigmentosa. Many medical reasons for rejection fell into the categories of drug or alcohol dependency and psychiatric illness. On the basis of information from general practitioners, depressive illness (4 subjects), alcohol dependency (18 subjects) and drug dependency (4 subjects) were revealed.

A total of 11 volunteers were excluded because of neurological disorder, six on the basis of information from the general practitioner (including one case of epilepsy and four of recent severe head injuries. Of those with recent head injury, two had been prescribed prophylactic anticonvulsant drugs).

Discussion

Of a total of 831 volunteer applicants during a 15 month period, 237 (28.5%), were rejected. Of these rejections, 49% were for medical reasons including 18.6% as a

result of information supplied by general practitioners.

The previously undisclosed medical conditions brought to our attention by general practitioners were of a significant nature. It is not always possible to detect these problems in a relatively short interview and, in particular, drug or alcohol dependency and psychiatric illness may be difficult to uncover. Subjects with certain neurological disorders may be difficult to detect at medical interview and examination. In particular, volunteers with epilepsy who have discontinued treatment may go unnoticed unless relevant information is obtained from the general practitioner.

Information from general practitioners helped to exclude unsuitable volunteers from phase I clinical trials. Of the 'healthy' subjects who passed stages 1 and 2 of selection, a further 6.6% were rejected on the basis of information supplied by their general practitioner.

Application to the general practitioner for medical information on potential volunteers is an important step in the screening of volunteer subjects for clinical research.

References

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