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LETTER TO THE EDITOR

AN ASSESSMENT OF CLINICAL TRIALS WITH DRUGS

Sir,

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A clinical trial which is not well planned, is bound to yield meaningless results inspite of, the effort, time spent, money used, and the trouble to the patients or volunteers. Many a times the readers encounter conflicting treatment recommendations in the medical literature and quite often these published recommendations are based on the clinical trials with major deficiences (1-5). The critical appraisal of the clinical trial is therefore required to distinguish the genuine therapeutic advances from the ineffective or possibly hazardous treatment methods (6, 7).

We tried to have a critical look at the clinical trials published in one Indian Journal of repute and one British Journal of repute (Br J), from January 1989 to December 1990, by using a modified Evans and Pollock's check list for analysing the clinical trials (8), although this list was primarily used in a trial on prophylaxis of abdominal surgical wound infections. The method was based on allocating a score for each question asked, and giving full or no score for the point under evaluation.

We asked 15 questions about the 'design and conduct' (maximum score 50), 8 about the 'analysis' (maximum score 30) and 8 about the 'presentation' (maximum score 20) of the clinical trials dealing with drugs (Table I).

The mean score for the 'design and conduct', the 'analysis', the 'presentation' and the total score was less in the clinical trials published in the Indian Journal than in Br J, though no statistical analysis was attempted at this stage (Table II).

TABLE I : Percentage of papers mentioning different criteria used to assess design and conduct, analysis, and presentation of clinical trials in journals.

Criteria	*Maximum score* alloted*	*% of papers*	
		Indian Journal	*Br Journal*
Design and conduct :-			
Is the sample defined?	2	100.00	100.00
Are exclusions specified?	2	53.33	96.97
Are known risk factors recorded?	3	46.67	100.00
Is therapeutic regimen defined?	5	100.00	100.00
Is experimental regimen appropriate?	5	86.67	100.00
Is the control regimen appropriate?	5	73.33	100.00
Were appropriate investigations carried out?	2	100.00	100.00
Are end points defined?	5	73.33	100.00
Are end points appropriate?	5	86.67	100.00
Have number required been calculated?	2	0.00	24.24
Was the patient consent sought?	1	33.33	87.88
Was the randomization done?	3	60.00	87.88
Was the assessment blind?	4	40.00	78.79
Were additional treatments recorded?	4	66.67	100.00
Were side effects recorded?	2	73.33	81.82
Analysis :—			
Withdrawls : are they listed?	3	66.67	90.91
is their fate recorded?	4	53.33	90.91
are these fewer than 10%?	4	66.67	90.91
Is there any comparability table?	3	93.33	100.00
Are risk factors stratified?	3	0.00	100.00
Is the statistical analysis appropriate?	5	53.33	100.00
Is the value of p given?	4	53.33	100.00
Is type II error considered in negative trials?	4	0.00	100.00
Presentation :—			
Is the title accurate?	2	93.33	100.00
Is the abstract accurate and helpful?	3	93.33	100.00
Are the methods reproducible?	3	100.00	100.00
Are the sections clearcut?	2	100.00	100.00
Can the raw data be discerned?	2	86.67	100.00
Are the results credible?	3	93.33	100.00
Do the results justify the conclusions?	3	100.00	100.00
Are the references correct?	2	100.00	100.00

*A lack of mention of the criteria was considered as 0 score.

TABLE II : Score for the 'design and conduct', 'analysis', 'presentation' and total score of the clinical trials published in Indian Journal and Br J. (Data are Mean±SEM).

	Indian Journal (n=15)	*Br J (n=33)*
Design and conduct	36.53±2.19	46.85±0.48
Analysis	15.60±1.77	25.09±0.70
Presentation	19.20±0.46	20.00±0.00
Total score	71.00±3.21	91.94±0.89

(n is the total number of trials published)

In the section on the 'design and conduct', no author reported the calculation of the number of patients required (sample size) before the trial began, for the clinical trials published in Indian Journal, whereas it was mentioned in 24.24% of the clinical trials published in Br J. The informed consent was mentioned in 33% and the assessment was blind in 40% of the clinical trials published in Indian Journal (Table I).

In the section on 'analysis' the most common error was the ignoring of type II error. Type II error is the probability of inability to detect the difference when there exist a difference, thus resulting in the rejection of the active compound. The other error in Indian Journal was, not stratifying the risk factors (Table I).

In the section on the 'presentation' the most common fault in Indian Journal was the difficulty in discerning the raw data, means esoteric jargon and liberal use of unexplained symbols (Table I).

We are aware of the limitations of our method of analysis itself. A number of 15 papers in Indian Journal may not be large enough representative for a comment of general nature of all Indian papers published. In some cases the questions raised may have a limitation, e.g. the trial may not be always blind, the fate of the withdrawls is difficult to know, the withdrawls may be more than 10% for the factors beyond control and still not be materially critical for the quality of work. There may be overlap between questions like recording of risk factors and their stratification. It is quite possible that the number of cases required were not stated, being more than adequate. It is also possible that patient consent was taken (in a fashion approved in India) but not recorded.

Irrespective of this, it is apparent from the data that there is a room in the improvement of the quality and reporting of clinical trials published in Indian Journal. It can be due to the fact that the physicians have sub-optimal knowledge regarding the methodology of clinical trials and they have not evaluated the medical literature (9-12).

The situation can be improved, if the importance of the sound Clinical Pharmacology principles such as sample size determination, ethical consideration, blinding, randomization, stratification and the appropriate statistical tests is impressed on all those who would indulge in a clinical trial.

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