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Research Article

Pre-enrolment screening reporting in randomized controlled trials from five pharmacology journals

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ABSTRACT

Background: Randomized controlled trials (RCTs) when appropriately conducted and reported represent the gold standard in evidence based medicine. Various guidelines including the consolidated standards of reporting trials (CONSORT 2010) recommend the reporting of the number of participants screened for potential recruitment. The aim of this study was to assess the reporting of pre-enrolment screening figure in randomized controlled trials from five pharmacology journals.
Methods: RCTs from the five pharmacology journals with descending order of impact factor i.e. The journal of clinical pharmacology (JCP), British journal of clinical pharmacology (BJCP), European journal of clinical pharmacology (EJCP), Journal of pharmacology and pharmacotherapeutics (JPP) and Indian journal of pharmacology (IJP) published between January 2013 to December 2014 were reviewed using standardized criteria.
Results: 37 out of 174 (21.27%) did not report the number of participants screened prior to recruitment. From the 137 RCTs that reported this screening figure, 95,494 (46.30%, range: 41-60.60%) of the screened participants (2, 06,243) were subsequently enrolled. About 52.49% of those screened and not enrolled, did not meet inclusion criteria or met exclusion criteria and about 11.89% declined to participate in an RCT.
Conclusions: Thus, there was about 80% reporting of pre-enrolment screening figure in RCTs from five pharmacology journals which need further improvement. The practice of documenting pre-enrolment screening figure and associated exclusion reasons will help to plan appropriate recruitment strategies during protocol development.

Keywords: Clinical trials, CONSORT, Randomized clinical trials, Recruitment, Screening

INTRODUCTION

Reports of randomized controlled trials (RCTs) when appropriately conducted and reported represent the gold standard in evidence based medicine.[1]While reporting these randomized clinical trials, they should give complete, clear and transparent information on its methodology and findings. Unfortunately many authors fail to give this critical information.[2-4] Evidence indicates that reports of low-quality RCTs, compared with reports of higher-quality ones, overestimate the effectiveness of interventions by about 30% across a variety of health care conditions.[5-7] The scientific world worries, of course, that sloppy reporting reflects sloppy methods, and that with sloppy methods come biased results.[8]

A flurry of activity to address the defect and standardize reporting of RCTs culminated in the most prominent guideline, the consolidated standards of reporting trials (CONSORT) in 1996 which has been revised twice, in 2001 and 2010.[6-8] The objective of the CONSORT is to provide a guideline for authors to standardize and

improve the reporting of trials.[9] Preliminary appraisals suggest that the use of CONSORT items is associated with improvements in the quality of reports published.[10] Consort 2010 statement consist of a checklist of items while reporting a RCT, especially the methods and results section and a flow diagram which shows the flow of participants through each stage of a trial. One of the important information required to complete a CONSORT flow diagram includes the number of participants screened for potential enrolment into the trial and the number excluded at this stage either because they did not meet the inclusion criteria or declined to participate or any other reasons.

Also, the information required while reporting RCT has been nearly standardized by organizations such as the International committee of medical journal editors and the World health organization through their trial registration minimum dataset.[11,12] A checklist of recommended items that should be provided in a clinical trial's protocol and affiliated study documents is given by the SPIRIT 2013 statement.[13] The reporting of the investigator's strategies for recruitment and successfully achieving the targeted sample size is an important part of this checklist.

The reporting of the above information including pre-enrolment screening figure can provide the reader and future investigator with the complete detail, especially in resource-limited clinician initiated trials. So, the aim of this study was to assess the reporting of pre-enrolment screening figures in randomized controlled trials (RCTs) from five pharmacology journals.

METHODS

This study was conducted in three months during the period of May 2015 to July 2015.

Data sources

We selected five pharmacology journals in descending order of impact factor as per the Thomas reuters impact factor list as follows: The journal of clinical pharmacology (JCP), British journal of clinical pharmacology (BJCP), European journal of clinical pharmacology (EJCP), Journal of pharmacology and pharmacotherapeutics (JPP) and Indian journal of pharmacology (IJP).

We conducted a MEDLINE/PubMed search to identify all RCTs published between January 2013 and December 2014 with the following search strategy: "Journal of Clinical Pharmacology" [Jour] OR "British Journal of Clinical Pharmacology" [Jour] OR "European Journal of Clinical Pharmacology [Jour] OR "Journal of Pharmacology and Pharmacotherapeutics" [Jour] OR "Indian Journal of Pharmacology" [Jour] AND (Randomized Controlled Trial [ptyp] AND medline[sb] AND ("2013/01/01 [PDAT] : "2014/12/31[PDAT])

Study selection

A review of each journal's archive database of RCTs published between January 2013 and December 2014 was performed. RCTs of preventive and therapeutic interventions were selected. We included reports in which the allocation of participants to interventions was described as random, randomly allocated, randomized or randomization. Other study designs such as observational studies, economic analyses on RCTs, quasi-randomized trials, cluster randomized trials, diagnostic or screening tests, follow-up studies of previously reported RCTs, editorials, reviews, case-reports and letters were excluded.

Data extraction

We evaluated whether the pre-enrolment screening figure was reported either within the methods/results or an illustrated flow diagram figure from RCTs of 5 high impact pharmacology journals. From this given figure, a percentage was calculated for these RCTs to demonstrate what numbers of participants were enrolled from those that had been screened, and what percentage were excluded. Next, reasons for exclusion from enrolment post-screening were identified. These reasons were further broken down into the categories of: "did not meet inclusion criteria," "met exclusion criteria", declined/refused to participate or "other." The reasons for exclusion that were identified as "other" were further reviewed if provided by the article.

Additional variables were also evaluated. We reviewed the different subject areas that were discussed in these RCTs. We also assessed other characteristics like paediatric (≤ 18 years of age) and adult population, pharmaceutical company sponsored or not sponsored and economic status of trial site as developed or developing or combined. The economic status of trial site as developing or developed was based on the classification provided by the World bank.[14]

Data analysis

Data for descriptive statistics were described as frequencies and percentages. The data were analyzed using Microsoft Excel version 2013

RESULTS

174 randomized controlled trials were analysed from 5 high impact pharmacology journals. Among 174 RCTs included for the study, 28.7% (50/174) were published in JCP followed by 23% (40/174) from BJCP, 19.5% (34/174) from EJCP, 17.8% (31/174) from IJP and 10.9% (19/174) from JPP.

37 out of 174 (21.27%) RCTs did not provide a pre-enrolment and randomization recruitment screening figure. 137 out of 174 (78.73%) RCTs reported pre-

enrolment screening figure. The journal-wise distribution is as follows: 72% (36/50) were from JCP, 77.5% (32/40) from BJCP, 79.4% (29/34) from EJCP, 87.09% (28/31) from IJP and 84.21% (16/19) from JPP.

In these 137 RCTs reporting recruitment screening figure, 2, 06,243 (mean: 41,248 and range: 6,889-94,103) participants were screened and 95,494 (mean: 19,098 and range: 2,825-43,288) were subsequently enrolled. So, 46.30% (range: 41-60.60%) participants from screened participants were enrolled.

1, 10,749 (mean: 22,149 and range: 4,064-50,815) i.e. 53.70% participants were screened but not enrolled. Exclusion figures and criteria were further analyzed for those 137 RCTs that reported reasons for screened individuals not being enrolled. Out of this 1,10,749 screened but not enrolled participants 58,141 (52.49%) "did not meet inclusion criteria " or " met exclusion criteria" and 13,178 (11.89%) participants "declined or refused to participate" and rest were excluded because of "other" reasons. The distribution of above parameters across 5 pharmacology journals is given in Table 1.

Table 1: Journal-wise distribution of pre-enrolment screening figure and associated parameters.

Parameters	JCP	BJCP	EJCP	IJP	JPP
No. of RCTs analyzed	50	40	34	31	19
No. of RCTs reporting pre-enrolment figure	36	31	27	27	16
% of RCTs reporting pre-enrolment figure	72	77.5	79.4	87.09	84.21
No. of participants screened	94,103	51,320	41,615	12,316	6,889
No. of participants enrolled	43,288	23,607	18,310	7,464	2,825
No. of participants not enrolled	50,815	27,713	23,305	4,852	4,064
No. of participants not meeting inclusion criteria/ meeting exclusion criteria	28,965	15,519	8,389	2,911	2,357
Declined/ refused to participate	6,098	3,325	3,263	248	244
Others	15,752	8,869	11,653	1,693	1,463

JCP: Journal of clinical pharmacology, BJCP: British journal of clinical pharmacology, EJCP: European journal of clinical pharmacology, JPP: Journal of pharmacology and pharmacotherapeutics, IJP: Indian journal of pharmacology

Table 2: Journal-wise distribution of other variables.

Variables	JCP (n=50)	BJCP (n=40)	EJCP (n=34)	IJP (n=31)	JPP (n=19)
Subject Area discussed					
Endocrinology	14	09	11	08	06
Cardiology	12	11	08	09	05
Infectious Diseases	05	06	05	05	03
Neurology	04	03	03	04	01
Gastro-enterology	03	04	02	02	02
Nephrology	03	03	02	02	02
Others	09	04	03	01	00
Age group					
Adults	38	32	29	28	16
Paediatrics	12	08	05	03	03
Pharmaceutical company sponsored	31	27	24	04	01
Economic status of trial site					
Developed	43	35	22	00	00
Developing	04	02	07	31	19
Combined	03	03	05	00	00

A range of subject areas were discussed throughout these 174 RCTs: 48 (27.58%) endocrinology, 45 (25.86%) cardiology, 24 (13.79%) infectious diseases, 15 (8.62%) neurology, 13 (7.47%) gastroenterology, 12 (6.89%) nephrology and 17 (9.77%) others. Studies whose participant age criteria were adults (>18 years of age) accounted for 143 of 174 (82.18%) and pharmaceutical company sponsored studies accounted for 87 out of 174 i.e. (50%). 100 out of 174 (57.47%) studies were conducted in developed settings. The distribution of above variables across 5 pharmacology journals is given in table 2.

DISCUSSION

Reporting of accurate participant recruitment and retainment figures which include those screened, enrolled and reasons for exclusion are valuable components of clinical research. In this study, we have observed that 78.73% (137/174) RCTs from 5 high impact factor pharmacology journals reported pre-enrolment screening figure. Tiffany M, Brown H, Paterson DL reviewed 35 RCTs from the journals clinical infectious diseases and the lancet infectious diseases to determine the proportion of RCTs in which the number of screened patients was reported.[15] They found that from the 35 RCTs, 9 of 35 (26%) did not report the number of patients screened prior to recruitment. This indicated the similar result in our study compared to the previous study.

We feel the pre-enrolment screening figures with the details of reasons for exclusion should be reported as they predict the infrastructure required for trial from commencement to final analysis. Any steps that will give clear vision and improve clinical research practices are essential to the future of health research. Conducting a pilot study can prove beneficial as it can detect hidden factors related to recruitment strategies during a study's protocol development. These pilot studies can help to modify inclusion criteria, sample size and inclusion of additional sites when a clinical trial faces unexpected recruitment and enrolment issues especially when there are financial constraints, it can decrease the morale of the study staff. The practice of documenting pre-enrolment screening figure and associated exclusion reasons especially when a formal pilot study is not done can help investigators to take collective steps for recruitment strategies.[16]

Before starting clinical trial when feasibility reports are prepared the questions related to the recruitment like how many patients are seen, how many patients actually fit as per inclusion criteria, how many patients do not fit with possible reasons for exclusion are asked to the potential investigators. There is a possibility that these potential investigators can inflate this recruitment data to get the study from the sponsor as there is a growing competition among the investigators to get the clinical trials. But the practice of reporting the actual figures related to the recruitment can give us the clear and transparent data related to the trial. This retrospective data can help to plan appropriate recruitment strategies during protocol development.

To the best of our knowledge, there are no studies analyzing the reporting of pre-enrolment screening figure in RCTs from pharmacology journals. This is the first study which analyzes the reporting of pre-enrolment screening in high impact factor pharmacology journals that have universal acceptance in the pharmacology research community. Also, we have assessed 174 RCTs published over the last one year from five pharmacology journal compared to 35 RCTs from the study done by Tiffany M, Brown H, Paterson DL.[15]

CONCLUSION

Thus, the findings from this study shows that there was around 80% reporting of pre-enrolment screening figure in randomized controlled trials (RCTs) from five pharmacology journals which can be improved further. The reporting of pre-enrolment screening figures with appropriate details as recommended by various guidelines including CONSORT 2010 should be adhered so that future clinical trials are appropriately designed and executed.

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