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Meta-Analysing Methodological Quality of Published Research: Importance and Effectiveness

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Abstract. The Inappropriate design of experimental studies in medicine inevitably leads to inaccurate results and biased conclusions. The aim of our study was to compare prevalence of implementing basic principles of experimental design in preclinical experimental studies published in international journals with low and high impact factor. The samples for analysis ware randomly chosen among publications retrieved from PubMed and Web of Science (WoS). Implementation rate of basic experimental research principles (local control, randomization and replication) was established by careful reading of the sampled publications and their checking against predefined criteria. The difference in number of satisfied criteria among the groups was not significant, however, number of citations was significantly higher in the group of studies published in high-impact factor journals (30.5 ±38.5 vs 2.6 ± 4.1, p=0.000). The studies published in low-IF journals less frequently used pseudo replication (30% vs 56%, p=0.000) and more often randomized their units of observation (40% vs 5%, p=0.000). Prevalence of experimental preclinical studies that did not implement completely basic principles of research design was high in both low- and high-impact factor journals. Although much more cited, studies published in high-impact factor journals bore the same risk of incorrectness, bias, and consequent misleading of future researchers.

Keywords. Randomization, control experiments, replication, internal validity

Introduction

An important way of systematically reviewing studies is through meta-analysis (1). Meta-analysis is a statistical and analytical method that combines and synthesizes various mutually independent studies and integrates their results into a single, common result. If well designed and properly implemented, it can be a very powerful tool for proving hypotheses. It is based on strictly established mathematical and statistical principles for critical analysis of medical data (2).

Meta-analysis refers to the analysis of analyzes (3), with the purpose of integrating their results. The meta-analytic approach described by Glass in 1981 requires: finding the studies, evaluating studies for their importance, describing the results on a common scale and using statistical methods to summarize the importance of studies and results (3) (4). Using meta-analysis, a wide range of outcomes can be explored, as long as there is an acceptable number of research articles. The peculiarity of the meta-analysis is that

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it actually combines all the research of a topic into one major work in which many participants take part. However, there is also the danger that, when merging a large set of different studies, the structural definitions may become imprecise and it may become difficult to interpret the results meaningfully. Like any other research method, meta-analysis has its advantages and disadvantages. The advantage is its objectivity, but as with any research, its value depends on the creation of certain qualitative explanations as well as on the understanding of objective data (4). Meta-analysis became indispensable in understanding a large collection of raw data or literature that is sometimes contradictory, inconsistent, and unclear on a topic, and in understanding the true importance of statistical results when addressing a scientific topic, such as efficiency. Readers of a meta-analysis should be able to understand not only the objective of the analysis, but also methods of summarizing results and their interpretation.

An inappropriate design of experimental studies in medicine inevitably leads to inaccurate or false results, which serve as basis for erroneous and biased conclusions (5). Although numerous attempts were made in the past to prevent errors in research design, like establishing guidelines for experimental studies (6) or teaching experimental design at postgraduate studies (6), evidence shows that some of the basic principles of experimental research design are still not implemented in more than half of the studies published in medical journals (5,6). There are three basic principles of proper experimental design: having appropriate negative and positive controls for testing treatment, replicating experiments on independent experimental units a sufficient number of times and randomly assigning a treatment (or factor) that is tested and control treatment (or factor) to experimental units (5, 6). Failure to acknowledge and implement these principles when planning a study usually causes production of false positive results, which are rather a consequence of uncontrolled factors or maturation of experimental units, than of the treatment (or a factor) that is actually tested (6).

The aim of our study was to investigate the prevalence of implementing basic principles of experimental design in preclinical experimental studies, performed either on animals in vivo, or animal/human material in vitro based on meta-analysis of articles published in high- and low-impact factor journals.

1.Methods

The studies in our research were retrieved for analysis from the Web of Science and PubMed database, published in medical journals printed in B&H and worldwide. The following inclusion criteria were used: journal article, original experimental study, animal study, in vitro study and full text availability. The exclusion criteria were: review articles, clinical trials of phase I-IV, cohort studies, case control studies and cross-sectional studies. The size of the study sample preclinical studies (n=86) was calculated on the basis of the following assumptions: rate of inappropriate research design 0.5 (1) and width of the 95% confidence interval ± 0.15. The formula $n = (1.96)^2 \times 4*p*(1-p)/d^2$ was used for the calculation, where „n“ was the sample size, „p“ probability of inappropriate research design and „d“ width of the confidence interval (2). Since the studies retrieved by the abovementioned search strategy were numbered orderly in the PubMed database, the study sample of 86 studies was extracted by simple randomization technique, activating for 86 times random number generator in Excel, using formula RANDBETWEEN (1; 666,342).

The extracted studies were analyzed for internal methodological validity, checking whether basic principles of correct experimental design (replication, control and randomization) were implemented. For the purpose of this analysis, the checklist with 8 questions was prepared, as shown in the Table 1. The results of the analysis were tabulated and described by rates and percentages when categorical, and by means, standard deviations, medians and interquartile ranges, if continuous.

Statistics: After statistical description, normality of the data distribution was checked by Kolmogorov-Smirnov test, and if not achieved, Mann Whitney U test was used for comparison of continuous variables among the groups defined by size of the journals' impact factor (IF). SPSS statistical program, version 18, was used

2. Results

Categorical variables were compared across the study groups by Chi-square test or Fisher's exact test where appropriate. Maximum acceptable probability of null hypothesis was set at 0.05. Total amount of papers which has been taken into analysis of the preclinical studies was 86. The studies from the extracted sample were divided to two groups according to the IFs of the journals where they were published: the group with IF ≥ 1.5 and the group with IF < 1.5. Results of the survey are shown in the Table 1. Our study showed that difference in number of satisfied criteria among the groups was not significant, however, number of citations was significantly higher in the group of studies published in high-impact factor journals (30.5 ± 38.5 vs 2.6 ± 4.1, $p=0.000$).

Table 1. Results of the survey of the preclinical studies (n = 86).

Requirement	Study groups	Satisfied n (%)	Not satisfied n (%)	Unclear n (%)	Not applicable n (%)	p
Sample size reported for the experiment?	IF < 1.5 (n=47)	33 (70%)	14 (30%)	-	-	0.396
	IF ≥ 1.5 (n=39)	24 (62%)	15 (38%)	-	-	
Number of observations reported for the experiment?	IF < 1.5 (n=47)	35 (74%)	12 (26%)	-	-	0.583
	IF ≥ 1.5 (n=39)	31 (79%)	8 (21%)	-	-	
Value of test statistics, exact p value and degrees of freedom reported?	IF < 1.5 (n=47)	7 (15%)	39 (83%)	-	1 (2%)	0.489
	IF ≥ 1.5 (n=39)	4 (10%)	35 (90%)	-	-	
Error bars correspond to the analysis?	IF < 1.5 (n=47)	19 (40%)	7 (15%)	2 (4%)	21 (41%)	0.002*
	IF ≥ 1.5 (n=39)	17 (44%)	4 (10%)	12 (31%)	6 (25%)	
Only independent observations were taken into account for statistical tests?	IF < 1.5 (n=47)	33 (70%)	8 (17%)	6 (13%)	-	0.000*
	IF ≥ 1.5 (n=39)	17 (44%)	2 (5%)	20 (51%)	-	
Is there negative control?	IF < 1.5 (n=47)	33 (70%)	4 (15%)	-	6 (15%)	0.893
	IF ≥ 1.5 (n=39)	30 (77%)	9 (23%)	-	-	
Was positive control necessary, and if so, was it used?	IF < 1.5 (n=47)	32 (68%)	9 (19%)	-	6 (13%)	0.048*
	IF ≥ 1.5 (n=39)	18 (46%)	17 (44%)	-	4 (10%)	
Were treatments randomly allocated to experimental units?	IF < 1.5 (n=47)	19 (40%)	23 (49%)	-	5 (11%)	0.000*
	IF ≥ 1.5 (n=39)	2 (5%)	26 (67%)	2 (5%)	9 (23%)	

Number of citations: mean, standard deviation, median, interquartile range	IF < 1.5 (n=47)	2.6 ± 4.1; 2.0; 3.0	0.000*
	IF ≥ 1.5 (n=39)	30.5 ±38.5; 13.0; 33.0	
Time passed from the publication (years): mean, standard deviation, median, interquartile range	IF < 1.5 (n=47)	6.0 ± 6.6; 5.0; 5.0	0.004*
	IF ≥ 1.5 (n=39)	11.6 ± 10.2; 9.0; 12.0	
Number of satisfied criteria per study: mean, standard deviation, median, interquartile range	IF < 1.5 (n=47)	4.2 ± 1.8; 5.0; 2.0	0.146
	IF ≥ 1.5 (n=39)	3.7 ± 1.9; 4.0; 3.0	
Impact factor of the journals: mean, SD, median, interquartile range	IF < 1.5 (n=47)	1.1 ± 0.4; 1.4; 0.7	0.000*
	IF ≥ 1.5 (n=39)	4.3 ± 1.7; 3.9; 2.1	

* significant difference; SD – Standard deviation

3. Discussion and Conclusions

Our study showed that difference in number of satisfied criteria among the groups was not significant, however, number of citations was significantly higher in the group of studies published in high-impact factor journals. The studies published in low-IF journals less frequently used pseudo replication and more often randomized their units of observation than studies published in high-IF journals. The details of the analysis of preclinical studies are presented in our previous publications (4-6). The presentation of the meta-analysis approach is very valuable since in most cases it provides an explanation of statistical methods, their meaning, purpose and ultimate impact on the interpretation of meta-analysis. It is demonstrated in our study which showed similarity in methodological quality between the high and low impact factors journals cited in WoS and Pubmed. Prevalence of experimental preclinical studies that did not implement completely basic principles of research design was high in both low- and high-impact factor journals, raising suspicion to validity of their results. Although much more cited, studies published in high-impact factor journals bore the same risk of incorrectness, bias, and consequent misleading future authors to conduct fruitless research that will waste precious resources.

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