Abstract


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This study reviewed the clinical protocols for new drug development, approved by the Ministry of Health and Social Affairs from 1994 to July, 1996, with respect to scientific integrity. 61 clinical protocols out of total 79 were reviewed.

To investigate scientific integrity, statistical considerations in clinical trials were reviewed for study design, random allocation, blinding, statistical basis for sample size estimation and the decision criteria of patients included and statistical methods for its analysis.

About 30 cases were approved annually and among them the phase 3 study was 68.9% (42 cases). Type of the drug was antibiotics, anticancer, other circular drug and antihypertension in order.

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The results concerning scientific integrity were summarized as follows:

Non-comparative study was more frequent than comparative study (59%: 36 cases vs 41%: 25 cases). In the phase 3 clinical protocols, the proportion of non-comparative study was 52.3%. The phase 3 study, the final stage of new drug development to confirm efficacy and safety, is usually with comparative study design. The results indicated that statistical significance of the comparative study design in clinical trials should be primarily recognized to improve scientific integrity.

Comparative studies were classified into parallel design, cross over design and historical control design(22, 1 and 2 cases, respectively).

In the comparative studies(23 cases) except the historical control design, random allocation was applied in 91.3%(21 cases) and blinding in only 56.5%(13 cases).

After the KGCP(Korean Good Clinical Practice) was implemented on 1 Oct. 1995, the number of comparative study design did not increase but random allocation and blinding increased.

44.6%(25 cases) of the clinical protocols simply adopted the sample size described in the government regulation, while only 32.2%(18 cases) showed statistically reasonable sample size estimation method. Since the KGCP implementanation, sample size estimation on the basis of rather reasonable statistical consideration was observed more frequently.

42.6%(26 cases) discussed the decision criteria of patients inclusion for only safety evaluation and there was no change since the KGCP implementation.

Any statistical analysis plan was never mentioned in 24.6%(15 cases) and 16.4%(10 cases) mentioned only descriptive analysis. The analysis plan was
improper in 8.2%(5 cases). And it was proper but described based on weak statistical concept in 34.4%(21 cases). To summarize, neither importance of the statistical analysis is well recognized nor statistical concept is sufficient yet. Since the KGCP implementation, cases with statistically proper analysis increased.

Consequently, this study indicated scientific integrity of clinical protocols is still not satisfactory yet, but tends toward improvement since the KGCP implementation.

Key words: Clinical trials, Clinical Protocol, Scientific Integrity, Statistical Consideration