—Regular Article—

Current Status and Future Directions for Clinical Trials Pharmacy

Hyen-Oh LA,*,[a] Sun CHOI,[b] Soo-Kyung LEE,[b] Byeung-Eun RYU,[b] and Ok-Yeon HAN[b]

[a]*Department of Pharmacology, College of Medicine, Catholic University of Korea, and* [b]*Clinical Trial Pharmacy, Seoul St. Mary's Hospital, #505 Banpo-dong, Seocho-ku, Seoul, Korea*

(Received October 26, 2010; Accepted March 10, 2011)

This survey was conducted to investigate the current status and suggest future directions for clinical trials pharmacy in Korea. A 32-item survey was distributed to 96 hospital pharmacies conducting clinical trials. The questionnaire was designed to elicit information on the following: (1) general clinical trial status of each hospital, (2) Investigational Drug Service (IDS) performance status. The response rate was 59.4% and 61.8% of the respondents carried out all the regulatory IDSs. Independent of the IDS's performance, the respondent started to feel the need for reinforcement in human resources when the number of active studies crossed 35. Analyzing the workload based on the subjective need for reinforcement in CTP, the overall CTP work execution rate was significantly higher in the 'needs reinforcement' group ($p<0.05$), even though this group had a 2.3 times higher workload than that in the 'current number of CTPs is adequate' group. The 'needs reinforcement' group performed more efficiently with a better understanding of IDSs, even though the group was having difficulties due to the shortage of CTPs. The lower execution rate in the 'current number of CTPs is adequate' group can be assumed to be due to the lack of understanding of the scope of IDSs. The work of CTPs should evolve into one of the specialized hospital pharmacists' roles, and a trial institution should designate at least one CTP per 40 protocols. Furthermore, the education for CTPs should be diversified into basic course and advanced course based on the IDS's performance of each hospital.

Key words——clinical trial pharmacy, clinical trial pharmacist, human resource, Investigational Drug Service (IDS)

INTRODUCTION

A clinical trial is a core step in new drug development, as it can verify the clinical, pharmacological and other pharmacodynamic effects of an investigational drug with the objective of ascertaining its safety and efficacy. Recently, global clinical trials initiated in the Asia-Pacific region have increased significantly, a dramatic one year spurt of growth led by Japan, Korea, Taiwan and India. But this will not be an isolated incident. Countries in the region have continued to make changes for the better in their respective clinical research environments to allow for even more growth.

Korea government has put significant effort on clinical trials to be conducted according to the international standards. Korea has adopted International Conference on Harmonization-Good Clinical Practice (ICH-GCP) guidelines since the year 2000 as a part of an effort to improve the regulatory system.

Furthermore, Korea Good Clinical Practice (KGCP)[1] guidelines has unique clauses to enhance the quality of clinical trials in comparison with the other countries; 1) the head of a hospital has the responsibilities of contracting with sponsors and supervising its investigators conducting clinical trials. 2) Only Korea Food and Drug Administration (KFDA)-accredited hospitals can conduct clinical trials. 3) The responsibility of managing the investigational drugs is assigned to the clinical trial pharmacist (CTP) while the overall responsibility of the clinical trial lies on the Principal Investigator or the institution. Consequently, all the clinical trial institutions have to designate more than one pharmacist as the CTP.

With strong government support and timely regulatory changes, the number of multinational clinical trials approved by the KFDA has steadily increased. However, the clinical trial infrastructure in Korea faces challenges which have come along with growth in the number of clinical trials.

Narrowing the scope on the challenges faced by clinical trial pharmacists and considering the regulation enforced do work for CTPs, number of the actual working pharmacist in the field are limited and they relatively lack the specific field experience. To elaborate this perception, a survey was conducted to provide the current status in terms of work load (assigned trials), tasks (required or not required by

*e-mail: blue27@hanmail.net

regulation) performed, assessment of clinical trial tasks (resource and knowledge situation); of hospital pharmacy-based Investigational Drug Service (IDS) and to suggest future directions for CTPs.

METHOD

From August 2009 to October 2009, the survey was distributed to 96 hospitals conducting clinical trials in Korea and was retrieved *via* e-mail or fax. This survey was designed to investigate the current activities of CTP in hospital pharmacy. Ninety-six hospitals were selected based on the following criteria.

Inclusion Criteria −By August 2009, should have been designated as a clinical trial institution by the Korean government, −Should belong to the Korean Society of Health System Pharmacist (KSHP), −Should have more than one pharmacist, and their pharmacists should have been doing the actual activities in hospital pharmacy field.

Exclusion Criteria Specialized hospitals for limited medical fields, such as: ophthalmology, psychiatry, herbal medicine.

Study Design The survey was designed to elicit information on the current status of clinical trials pharmacy of each hospital.

The contents of the questionnaire were as mentioned below:

1) General clinical trial status of each hospital: (1) Hospital size by staffed beds, (2) The number of active clinical trial protocols and investigational drugs (ID), (3) The number of clinical trial pharmacists (CTP) and the need for reinforcement of CTPs, (4) Fee charged for IDS management.

2) IDS performance status: Evaluation of IDS performance was divided into 2 major categories: Regulatory tasks and Initiative IDS. 'Regulatory IDSs' were those works specified as the responsibilities of CTP in the KGCP guidelines. Among the works of CTPs, those that were not the obligation of CTP as per the KGCP guidelines and needed some initiative taking on the part of the CTP were categorized as 'Initiative IDSs'. These works are described as pharmaceutical service or pharmacist's role as an investigator in the ASHP guidance on clinical drug research.[2)]

(1) Regulatory IDSs
- −Maintaining accurate ID receipt and dispensing record
- −Managing ID inventory and storage
- −Preparing, monitoring, auditing and inspection of clinical trial conducting status
- −Educating the patients and monitoring therapy
- −Preparing a descriptive summary of the ID management for the Principal Investigator regularly

(2) Initiative IDSs
- −Attending an Investigator pre-meeting
- −ID data sheet development
- −Consult on ID management
- −Participating in Protocol development

Data Analysis

Classification of the Hospitals The surveyed hospitals were general hospitals. According to the Korean Medical Law, a general hospital requires to have more than 100 staffed beds. The general hospitals are again classified into three groups by the number of staffed beds, medical departments, and medical specialists. Hospitals with less than 500 staffed beds are classified into Group I. Hospitals with more than 500 staffed beds are classified into Group II. Hospitals conducting educational functions and having more than 20 medical departments & their specialists are classified into Group III; the advanced general hospital.

Calculation of Full-Time Equivalent (FTE) Pharmacists Due to fast growth of the clinical trials field in Korea, in many cases pharmacists working in the clinical trials field also perform the functions of a conventional pharmacist. Therefore, a calculation method was developed to estimate the work hours of a part-time pharmacist for that of a full-time pharmacist. The number of Full-Time Equivalent (FTE) pharmacists is calculated by the total work hours of all the pharmacists involved in the IDS divided by 8, which are the standard work hours per day.

Analysis of Work Performance The performance status of the regulatory IDS's and initiative IDSs was determined. In addition, the possible effect factors for the work performance were investigated.

Statistical Analysis The obtained data were analyzed by the SAS Ver. 9.1 program. Common descriptive statistics were used to characterize the data by the group size. Kruskal-Wallis one-way analysis and *t*-test were used to verify the difference and correlation between the IDS performance and each effect factor. In each case, an alpha level of 0.05 was set as the priori level of significance.

RESULTS

General Characteristics of the Respondents

Overall Status of the Clinical Trial The overall response rate was 59.4% (57/96). Among the hospitals surveyed, 45.8% (44/96) belonged to Group III, and their response rate was the highest at 70.5% (31/44), while the other groups showed a 50% response rate (Table 1).

The general status classified by hospital grade is summarized in Table 2. For each measure, the median values of each clinical status factor for each group were significantly different from each other ($p<0.0001$). Especially, Group III showed statistically higher values than the other groups when multiple comparison was done ($p<0.05$). The median value of the total number of FTE pharmacists was different according to the hospital grade ($p<0.0001$).

The total number of FTE CTPs showed a significant positive correlation with the total number of active protocols ($r=0.7$, $p<0.0001$) and the total number of IDs ($r=0.8$, $p<0.0001$) in each hospital.

IDS Management Fee 77.2% of the respondents charged IDS management fee to the sponsors at about 1% to 15% of the research fund. On an average 5.1% percent of the research fund was charged as the IDS management fee.

Table 1. Distribution of the Respondents among the Groups (n=number of hospitals)

	Respondents ($n=57$)	Non-respondents ($n=39$)
Group I ($n=18$)	9	9
Group II ($n=34$)	17	17
Group III ($n=44$)	31	13
Total	57	39

Group I; <500 staffed beds, Group II; >500 staffed beds, Group III; advanced general hospital.

Experience and Training of CTP's Among the 127 CTP's who responded, 61.4% (78/127) of the respondents had more than 1 year of experience in the clinical trials field. 24.4% (31/127) of the respondents had less than 1 year of experience. Training programs for CTPs were offered by 91.9% (50/55) of the hospitals. Only three hospitals offered internal programs and the other 47 offered external training programs. External training programs include the various government supported programs such as KSHP CTP SPG program.

IDS Performance Status Each IDS performance status is summarized in Table 3. 61.8% (34/55) of the respondents performed all the KGCP required services. The most uncommonly performed services were 'Preparing the descriptive summary of the ID management for the Principal Investigator regularly' (67.3%, 37/55) and 'Educating the patients and monitoring therapy' (81.8%, 45/55) in an ascending order. Among the initiative IDSs, 'Attending an Investigator pre-meeting' showed the highest performance rate (98.2%).

Respondents Assessment

Workload According to Subjective Property of CTP Number Regarding the question on ''whether the current number of CTPs is adequate,'' 49.1% (27/57) of the respondents answered as 'Yes.' The correlation analysis between this subjective property of the number of FTE CTP's and the number of protocols per 1 FTE CTP revealed that if the number of protocols per 1 FTE CTP exceeded 30, the shortage of FTE CTPs was felt ($p<0.0001$).

The total number of active protocols and IDs per 1 FTE CTP, total prescriptions per day were significantly different between the respondents who answered as 'Yes' and those who answered as 'No' (Table 4). The answered as 'No, needs reinforcement'

Table 2. Status of the Clinical Trial According to the Hospital Grade (Mean±S.D.)

Respondents Number	Group I ($n=9$)	Group II ($n=17$)	Group III ($n=31$)	p value[1]
Total number of protocols	9.1±9.9	24.6±35.6	91.8±98.7	<0.001
Total number of IDs[2]	7.3±6.1	35.4±62.9	130.5±137.7	<0.001
Total prescriptions per day	2.0±2.2	4.1±6.9	21.5±26.4	<0.001
Total Number of FTE[3] CTP in one hospital	0.3±0.2	0.5±0.5	1.8±1.8	<0.001
Total number of pharmacists in one hospital	7.6±2.2	17.9±6.5	38.1±29.8	<0.001

[1] Kruskal-Wallis one-way analysis of variance. [2] ID; Investigational drugs. [3] FTE; Full-time equivalent.

group had; 2.3 times more workload than the mean number of total protocols per 1 FTE CTP in the 'Yes, adequate (current number of CTPs is adequate)' group (79.9 *vs.* 35.1), 3.0 times more number of total IDs than the mean number of total IDs per 1 FTE CTP in the 'Yes, adequate' group (120.6 *vs.* 40.6), and 1.5 times more total prescriptions per day than the mean number of total prescriptions per day in the 'Yes, adequate' group (11.8 *vs.* 7.8) ($p<0.05$).

Table 3. List of the Investigational Drug Services (IDSs) Performed at the Hospital Pharmacy

List of IDSs	Performance rate of the respondents [% (number)][a]
Regulatory IDSs	
Maintaining accurate ID receipt and dispensing record[b]	100 (55)
Managing ID inventory and storage[b]	98.2 (54)
Preparing, monitoring, auditing and inspection[b]	90.9 (50)
Educating the patients and monitoring therapy[b,c]	81.8 (45)
Preparing a descriptive summary of ID management for the Principal Investigator regularly	67.3 (37)
Initiative IDSs	
Attending an Investigator pre-meeting	98.2 (54)
ID data sheet development[b]	67.3 (37)
Consult on IDs management[c]	61.8 (34)
Participating in protocol development[c]	43.6 (24)

[a] Respondents were instructed to select all the performed IDS. Total number of respondents was 55. [b] Described as a pharmaceutical service in ASHP guidelines. [c] Initiative CTP work, these works could be included for the pharmacists' serving as an Investigator, Manager, or Co-ordinator within the research team as per the ASHP guidelines.

Table 4. Workload According to the Subjective Property of the Number of CTPs (mean±S.D.)

Respondents answers to the property of current CTP number	Yes, adequate ($n=27$)	No, needs reinforcement ($n=30$)	p value[1]
Total number of protocols per 1 FTE CTP	35.1±60.7	79.9±95.5	0.038
Number of total IDs[2] per 1 FTE CTP	40.6±64.0	120.6±143.3	0.0085
Total prescriptions per day	7.8±4.6	11.8±8.1	0.0288

[1] t-test analysis of variance. [2] ID; Investigational drug.

Correlation between the Subjective Property of the Number of CTP's and the Work Performance

When work performance rate was compared between the groups that answered as 'Yes, adequate' and 'No, needs reinforcement', the work performance rate of all the 'regulatory IDS' and all the 'initiative IDS' were significantly higher in the group that answered as 'No, needs reinforcement' ($p<0.05$).

Main Obstacle for Work Performance and the Way of Improving the Work of CTPs Regarding the question on the major difficulties in the work of CTPs, 57.9% of the respondents pointed out ''shortage of CTPs'' and 40.4% of the respondents pointed out ''lack of understanding on the work of a CTP in the pharmacy department.'' Regarding the question on the way of improving the present difficulties, 80.4% of the respondents pointed out that more detail standards, such as maintaining the minimum ratio between a CTP and an active protocol, by the regulation of human and facility resources is necessary.

Table 5. Work Performance Rate of All the 'Regulatory IDSs' and 'Initiative IDSs'[a]

Respondents answer to the property of the number of current CTPs	Yes, adequate ($n=27$)	No, needs reinforcement ($n=30$)	p value[b]
Regulatory IDSs	48.1% (13/27)	70.0% (21/30)	<0.05
Initiative IDSs	29.6% (8/27)	53.3% (16/30)	

[a] % of respondents who perform all the asked IDS's. [b] One way repeated ANOVA (all Pair wise Multiple Comparison Procedures with Tukey Test).

Table 6. Main Obstacle for CTP Work Performance[a]

Property of the current number of CTP's (N)	Yes, adequate ($n=27$)	No, needs reinforcement ($n=30$)	Total
Understaffed hospital pharmacy	37.0% (10/27)	63.3% (19/30)	50.9% (29/57)
Shortage of CTPs	25.9% (7/27)	86.7% (26/30)	57.9% (33/57)
Lack of knowledge on clinical trials	51.9% (14/27)	30% (9/30)	40.4% (23/57)
Lack of understanding of work of CTPs in a pharmacy department	48.1% (13/27)	33.3% (10/30)	40.4% (23/57)

[a] Respondents were instructed to select all the obstacles for CTP works. Total number of respondents was 57 ($p>0.05$).

DISCUSSION AND CONCLUSION

Work Distribution The first observation of the survey is that the number of IDS and FTE CTP has a proportional relationship with the grade of the hospital. Group III (Educational general hospital) had more active studies, IDSs and FTE CTP as compared to Group II (>500 staffed beds), and Group II had more active studies, IDSs and FTE CTP as compared to Group I (>300 and ≤500). This shows that these educational hospitals in Group III, had more opportunities for conducting clinical trials and they conducted clinical trials more actively. The fast growth of the clinical trials field in Korea has led to the allocation of clinical trials to the front runners in Group III. Even though the resources and facilities are sufficient to run the trials, the proportional distribution of clinical trials to the other groups may take more time, thereby striking a balance in this field.

Performance Analysis and Adequacy The second observation of the survey is from the analysis of the execution rate of IDS's. When categorized into the regulatory IDSs and initiative IDSs, 61.8% of the hospitals carried out all the regulatory IDSs and only 43.6% of the hospitals carried out all the other initiative IDSs.

Independent of the IDS's carried out, the respondent started to feel the need for reinforcement in human resources when the number of active studies crossed 35. This result is similar with that of the previously reported 40–50 studies[3] on the saturation range for a FTE. Apart from these numbers, the subjective view of the respondents on the adequacy of their work load brings up some additional interesting findings. Though the workload in the 'No, needs reinforcement in CTP' group was 2.3 times higher than that in the 'Yes, current number of CTPs is adequate' group (the mean values of the total number of active protocols per 1 FTE CTP were 79.9 *vs.* 35.1, respectively), the overall CTP work execution rate was significantly higher in the 'No, needs reinforcement in CTP' group than the 'Yes, current number of CTPs is adequate' group ($p<0.05$). The higher execution rate of CTPs in the 'No, needs reinforcement' group can be explained by the fact that even though the group was having difficulties due to the shortage of CTPs, the group performed more efficiently with a better understanding of IDSs. The lower execution rate while having a lesser work load in the 'Yes, current number of CTPs is adequate' group can be assumed to be due to the fact that the group lacked the understanding of the scope of IDSs, but still evaluated the number of CTPs as 'adequate.' These interpretations are supported by the results wherein the 'No, needs reinforcement in CTP' group pointed out 'shortage of CTPs' as the 'main obstacle' for the CTP work while 'lack of knowledge of clinical trials' was pointed out as the 'main obstacle' by more than half of the 'Yes, current number of CTPs is adequate' group.

As previously reported, despite their critical role in clinical trials, Investigational Drug Services (IDSs) in hospital pharmacy have been thought of in terms of cost and risk to the institutions. Institutions hesitate to dedicate full-time equivalents (FTEs) to IDS because of the fear of increasing costs for intangible benefits to the institution.[4,5] Nevertheless, pharmacy departments of leading hospitals in the clinical trials field should recognize the CTP's work as one of the important areas in hospital pharmacy. IDS's are very individualized tasks according to each study,[6] and managing ID's and preparing ID prescriptions in compliance with their protocols needs more time and effort than just dispensing of the general medications.[7] Accordingly, proper staffing is one of the key factors for conducting clinical trials successfully, and the pharmacy manager should consider a systematic support through proper staffing.[8] Besides this, simple supplementation of CTPs, implementation of a computerized ID management system could also be considered. According to this survey (data not shown), 47.7% (27/57) of the respondents have used computerized ID management system and this system was mainly used to prescribe the clinical trials medications. There is certainly a scope for improvement in the ID management system in many hospitals, such as management of the inventory of IDs and administrative affairs. As Sweet BV *et al.* pointed out there are some challenges even [*e.g.*, generally ID management is very company-specific, and the possibility of dual system (manual and computerized system)]. Such a computerized system could improve the daily operations of IDS, enhance efficiency,[9] and help CTPs to expand their work to more specialized fields.

Future Directions These days clinical trials conducted in Asia-Pacific region are in the transition phase of quantitive expansion to qualitative growth. To advance the role of CTPs from basic management of the investigational drugs to being a core member of

the research team, there is a need to diversify the improvement methods according to the enviroment of each hospital.

Based on the results of this survey, we suggest proper staffing and standardized education for CTPs according to the working environment of each group of general hospitals as follows: Firstly, the main standard for staffing and education level should be based on the size of the clinical trial being conducted.

1) Staffing of Clinical Trial Pharmacy

We recommend that every clinical trial institution should designate at least one clinical trial pharmacist per 40 protocols. It is desirable that these CTPs should be exclusively responsible for the IP management; especially those CTPs who are working in the hospitals conducting more than a total of 40 clinical trials.

2) Education program for CTPs

It is needed to diversify the CTP education program into basic mandatory course and advanced course based on the CTP's work performance. The contents of basic mandatory course should comprise of applied regulations and basic practice skills of CTPs.

Accordingly in the intial stages, hospitals and practitioners should themselves take more efforts to deepen their understanding of their role as a CTP through such a basic mandatory education program. Furthermore, considering that over 20% of CTPs of the respondent hospitals had less than 1 year of experience in the clinial trials field, standardized and continuous basic training of CTPs is also needed.[10]

The advanced course should comprise of those items that help a CTP to develop the ability to consult a clinical trial team, regarding the IP management and related documents from the viewpoint of the pharmacist.

Some demonstration-based education programs have been under testing at the Korean Food and Drug Administration and KoNECT. For years, the Korean government has supported various educational programs for clinical trials specialists, such as CTTA (Clinical Trials Training Academy)− Training programs for professional human resource by KoNECT (Korea National Enterprise of Clinical Trial). KSHP had also participated in this special program through the CTP SPG program. Based on these experimental training courses, an official certification course for CTPs should be introduced.

Till the issue of the official educational organization for CTPs is settled, clinical trial pharmacies of educational hospitals like those in Group III could act as the main training institutions.

In summary, as the other general role of hospital pharmacists, shortage of staff across the hospital pharmacy is one of the major limitation factors in CTP's work. However, the work of a clinical trial pharmacist should evolve into one of the specialized hospital pharmacists' role. To achieve this, proper staffing and standardized education for CTPs according to the working environment of each hospital are needed.

Acknowledgements The statistical analyses performed in this article were advised by Catholic Research Coordinating center. We thank Hyeon-Woo, Yim, M.D., Ph.D. and Seung-Hee, Jeong, M. PH. This study was supported by a grant from the Korea Health 21 R&D Project (A070001), Ministry of Health & Welfare, Republic of Korea.

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