Health Education and Care

Research Article ISSN: 2398-8517

Current situation of clinical trials in Nanchang, China

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Abstract

Purpose: Recently global clinical trials are conducted vigorously and rigorously in line with the guideline of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use of Good Clinical Practice. Since to confirm the current situation of clinical trials in Asia is critical for improving the practice of global clinical trials, we conducted the research in Beijing and in Shanghai consequently. But China is such a huge country that it is difficult for us to evaluate the whole country's situation by evaluating data of two largest cities. Therefore the purpose of this study is to conduct the research on the detail of current situation of clinical trials in Nanchang, 25th largest city in China.

Methods: Questionnaires were administered to medical doctors belonging to institutes affiliated to Nanchang University in Nanchang, 25th largest city in China.

Results: The questionnaires were administered to 192 medical doctors and 172 of them were analyzed. There were significant differences between institutes in relation to getting reports from the external authorities after audits and inspections by external authorities. In total, 70.0%, 88.0%, and 100.0% of respondents from Institute A, Institute B, and Institute C, had a report from external authorities after audits and inspections conducted by external authorities in a year, respectively.

Conclusion: Our research suggests clinical trials not only in Shanghai and Beijing but also in Nanchang, are conducted vigorously and are appropriately monitored by audits and inspections conducted internally by the local institutes and/or by an external authority.

Abbreviations: ICH-GCP: The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use of Good Clinical Practice; GCP: Good Clinical Practice; PMDA: The Pharmaceutical and Medical Devices Agency of Japan; CROs: The contract research organizations; CRC: Clinical Research Coordinator; CRFs: case report forms; SFDA: The State Food and Drug Administration of China

Introduction

Recently global clinical trials have been conducted not only in developed countries but also in developing countries based on the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use of Good Clinical Practice (ICH-GCP) guidelines [1-7]. To deliver the new, effective drugs to patients as rapid as possible, the guidelines have been playing the very important role to ensure the quality of clinical trials. For example, in developing countries, even though there are few places in sub-Saharan Africa with the necessary infrastructure and expertise to support clinical trials in compliance with the ICH-GCP, the Clinical Research Unit of Nanoro was founded in 2008 to provide a much-required Good Clinical Practice (GCP)-compliant clinical trial platform for an imminent large-scale phase 3 malaria vaccine trial in line with the ICH-GCP guidelines [8]. On the other hand, transparency on the results of inspection by the external authorities of Japan has been guaranteed based on the concept of regulatory science advocated by the Pharmaceutical and Medical Devices Agency of Japan (PMDA) [9-13] and the review reports are available on the PMDA homepage [14-16]. The concept is also supported by the U.S. Food and Drug Administration and medical industry in USA [17,18]. However, to the best of the authors' knowledge, the inspection result from other Asian countries is not accessible.

Since we believe that confirming the current situation of clinical trials in Asia is essential to improve the quality of global clinical trial practices, we conducted research on the current situation of clinical trials in Beijing and Shanghai consequently [19,20].

These two studies showed that clinical trials in both Shanghai and Beijing were conducted vigorously and were monitored appropriately by way of audits and inspections by concerned institute and/or by an external authority. However, China is such a large country that it may be difficult for us to evaluate the whole country's situation just by evaluating data from two of its largest cities. Fortunately, we had the chance to conduct a similar study in Nanchang, the 25th largest city in China, using the same questionnaire method as cooperative study. The aim of this study was to conduct research on the details of the current situation of clinical trials in Nanchang, China.

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Key words: *good clinical practice, regulatory science, global clinical trial, asian clinical trial network, Nanchang*

Received: April 04, 2017; **Accepted:** April 27, 2017; **Published:** April 29, 2017

Materials and methods

The subjects were doctors who had been working in medical institutes that had conducted clinical trials in Nanchang. The research in Nanchang was conducted using the questionnaires that had been employed in Beijing and Shanghai [19,20]. The study was conducted from April 10 to May 21, 2014. The questionnaires were distributed among 192 doctors, randomly selected by the Nanchang University research team at four medical institutes in Nanchang, all of which had been conducting clinical trials. The Nanchang University research team initially obtained the names of all doctors who had conducted research involving human subjects, such as medicine and medical devices, within the past one year, in each selected medical institute and coded them using digital numbers. The doctors answered the questionnaires, after having been informed by the Nanchang University research team. All 192 questionnaires were collected, but twenty answer sheets, with logical errors and missing three or more answers, were deleted. Therefore, 172 out of 192 (response rate 89.6%) were analyzed. The three categorized, affiliated institutes were the First Affiliated Hospital of Nanchang University (described as Institute A), the Second Affiliated Hospital of Nanchang University (Institute B), People's Hospital of Jiangxi Province and the Chinese Medicine Hospital of Jiangxi Province (Institute C). Since the People's Hospital of Jiangxi Province and the Chinese Medicine Hospital of Jiangxi Province are both operated by the Jiangxi Province government, the respondents of these two hospitals were merged as Institute C. Paper-based informed consents were obtained from the respondents, and complete confidentiality was assured. Before data collection, the study protocol was approved on February 18, 2014 by the Ethics Committee of the Graduate School of Medicine Nagoya University (approval number: 2013-0192-2). The main contents of the survey forms comprised the general characteristics of respondents (e.g. GCP education opportunities), activity of the contract research organizations (CROs), global clinical trials, benefits of participation in clinical trials, audits and inspections, and deficiencies found by audit and inspection. Raw data was sent to Nagoya University and was analyzed with SPSS version 20. χ^2-test and U-test were applied. All values were expressed as percentages or as mean ± standard deviations.

Results

General characteristics of respondents

The questionnaires were administered to 192 medical doctors and 172 of them were analyzed. As shown in table 1, these 172 questionnaires included 91 responses from Institute A, 63 from Institute B, and 18 from Institute C. A significant difference among institutes was the possession of a Ph.D. with 37.4% (34 out of 91) and 38.1% (24 out of 63) of respondents from Institute A and Institute B, respectively, had a Ph.D. compared with 5.6% (1 out of 18) of respondents from Institute C. In total, 34.3% of respondents had a Ph.D. Further, there was a significant difference among institutes in the number of clinical trials respondents participated in as a principle investigator (PI). Respondents from Institute C participated in the highest number of clinical trials (3.1 ± 5.0). Respondents from Institute A and Institute B participated in a lesser number of clinical trials (1.1 ± 2.1 and 1.5 ± 3.0, respectively). In total, the average number of clinical trials the respondents participated in as a PI was 1.5 ± 2.9.

There were no significant differences among institutes in gender, age, duration of work, duration of participation in clinical trials or the number of years in which the respondents had participated in clinical trials, and duration of participation in clinical trials as a PI.

GCP education opportunities and activity of CRO

There was no significant difference in the participation in GCP education seminars organized annually by institutes. A total of 96.8% (61 out of 63) of respondents at Institute B and 88.9% (16 out of 18) of respondents at Institute C participated in an annual GCP education seminar. However, only 84.6% (77 out of 91) of respondents at Institute A had participated in an annual GCP education seminar. In total, 89.5% of respondents had participated in an annual GCP education seminar. On the other hand, there were no significant differences in the degree of participation of Clinical Research Coordinator (CRC) and participation and activity of CROs among institutes.

The benefits of participation in clinical trials

Table 2 shows the benefits of participating in clinical trials. Multiple answers were invited from the respondents for every question. Therefore, the final percentage was calculated based on multiple answers. The benefit identified by most respondents was the ability to provide the most up to date drugs to patients (82.6%). The second most common identified benefit was the ability to acquire information on the success of such drugs (81.4%). Improvements in drug therapy at a clinical level after executing a clinical trial (62.2%), potential publication of data obtained from clinical trials of drugs in scientific journals (61.1%), and the ability to obtain further funding by the sponsor of a clinical trial (26.7%) were also identified as potential benefits.

Audits and inspections by institutes and authorities

Table 3 shows that there were significant differences between institutes in relation to getting reports from the external authorities after audits and inspections conducted by them. In total, 70.0%, 88.0%, and 100.0% of respondents from Institute A, Institute B, and Institute C, respectively, had a report from external authorities after audits and inspections conducted by them in a year. On the other hand, there were no significant differences among institutes in relation to participation in audits and inspections conducted by the institute itself in a year, by external authorities in a year, and reports from the institute itself after audits and inspections conducted by institute itself in a year.

Table 4 reports deficiencies identified by audits and inspections

Table 1. General characteristic of respondents.

Institute	n	Sex			Possession of Ph.D.*			Age (years)	Duration of work (years)	Duration of participation of clinical trial (C.T.) (year)	No. of C.T. in which participated	Duration of participation of C.T. as principal investigator (P.I.) (year)	No. of C.T. in which participated as P.I.*
		Male	(%)	Female	Yes	(%)	No						
A	91	58	63.7	33	34	37.4	57	37.2±8.6	12.4±9.1	6.2±4.8	5.4±4.1	1.5±2.7	1.1±2.1
B	63	38	60.3	25	24	38.1	39	39.6±8.8	15.4±9.9	6.7±4.9	5.4±4.2	1.7±3.2	1.5±3.0
C	18	15	83.3	3	1	5.6	17	39.8±10.6	15.3±10.1	6.7±5.0	7.4±7.6	2.1±2.7	3.1±5.0
Total	172	111	64.5	61	59	34.3	113	38.4±8.9	13.8±9.6	6.4±4.8	5.6±4.6	1.6±2.9	1.5±2.9

*: χ^2 test $p < 0.05$

Table 2. Benefits of participation in clinical trials.

Merit	Response (No. of respondents=172)		Case Percentage (%)
	n	Percentage (%)	
Ability to acquire information on the latest drugs and treatments	140	25.9	81.4
Provision of the latest drugs and treatments to patients	142	26.2	82.6
Contribution to scientific research by using the data obtained from clinical trials	105	19.4	61.1
Improving clinical expertise by participating in clinical trials	107	19.8	62.2
Enabling future clinical trials by investing the funds of the present clinical trial	46	8.5	26.7
Others	1	0.2	0.6

Table 3. Current situation of audits and inspections conducted by institute itself and external authorities.

Institute	Participation of audits and inspections conducted by institute itself in a year			Reports from the institute itself after audits and inspections conducted by institute itself in a year			Participation of audits and inspections conducted by external authorities in a year			Reports from external authorities after audits and inspections conducted by external authorities in a year*		
	Yes (%)	No (%)	Total (%)	Yes (%)	No (%)	Total (%)	Yes (%)	No (%)	Total (%)	Yes (%)	No (%)	Total (%)
A	69(75.8)	22(24.2)	91(100.0)	63(91.3)	6(8.7)	69(100.0)	50(54.9)	41(45.1)	91(100.0)	35(70.0)	15(30.0)	50(100.0)
B	51(81.0)	12(19.0)	63(100.0)	48(94.1)	3(5.9)	51(100.0)	25(39.7)	38(60.3)	63(100.0)	22(88.0)	3(12.0)	25(100.0)
C	17(94.4)	1(5.6)	18(100.0)	16(94.1)	1(5.9)	17(100.0)	11(61.1)	7(38.9)	18(100.0)	11(100.0)	0(0.0)	11(100.0)
Total	137(79.7)	35(20.4)	172(100.0)	127(92.7)	10(7.3)	137(100.0)	86(50.0)	86(50.0)	172(100.0)	68(79.1)	18(20.9)	86(100.0)

*: χ^2 test $p < 0.05$

Table 4. Deficiencies found by audits and inspections conducted by institute itself and external authorities.

Item of deficiencies	Response (No. of respondents=127)		Case Percentage (%)	Response (No. of respondents=68)		Case Percentage (%)
	n	Percentage (%)		n	Percentage (%)	
Deviations from the protocol to recruit a patient to clinical trial	57	19.1	44.9	31	20.7	45.6
Deviations from the protocol to prescribe contraindicated combination treatment	19	6.4	15.0	8	5.3	11.8
Deviations from the protocol to conduct the test	47	15.8	37.0	14	9.3	20.6
CRFs filled incorrectly	64	21.5	50.4	47	31.3	69.1
CRFs filled insufficiently	93	31.2	73.2	42	28.0	61.8
Inappropriate informed consent	17	5.7	13.4	7	4.7	10.3
Others	1	0.3	0.8	1	0.7	1.5

conducted by the institute itself or by an external authority. Since multiple answers were invited from the 172 respondents for every question, the final percentage was calculated based on multiple answers. The most common reported failure identified by such audits and inspections, performed by the institute itself, was insufficient completion of case report forms (CRFs) (73.2%), and followed by incorrect filling in of CRFs (50.4%). Deviations from the protocol for entering a patient into a clinical trial (44.9%), deviations from the protocol for conducting tests (37.0%), and deviations from the protocol to contraindicated combination treatment (15.0%), inappropriate informed consent (13.4%), and others (0.8%) were also reported.

The most common failure identified in audits and inspections, performed by an external authority in the 68 respondents, was incorrect filling in of CRFs (69.1%), followed by insufficient CRFs (61.8%). Deviations from the protocol for entering a patient into a clinical trial (45.6%), deviations from the protocol for conducting the test (20.6%), deviations from the protocol for contraindicated combination treatment (11.8%), and inappropriate informed consent (10.3%) were also reported. The "Others" option was selected by one respondent, with the following associated comment: "deviations from general principle."

Global clinical trials

Table 5 shows that there was a significant difference among institutes in their participation in global clinical trials with 60.3% and 59.3% of respondents from Institute B and Institute A, respectively, reported having had an opportunity to participate in such a trial compared with 5.6% of the respondents from Institute C. In total, 54.1% of respondents reported participation in global clinical trials. Moreover, 94.5%, 95.2% and 94.4% of respondents from Institute A, Institute B, and Institute C, respectively, reported a wish to participate in such a trial. In total 94.8% of respondents reported that they would like the opportunity to be involved in a global clinical trial.

Table 5. Issues related to participation in global clinical trials.

Institute	n	Participation to the global clinical trial**		Wish to participate the global clinical trial	
		Yes (%)	No (%)	Yes (%)	No (%)
A	91	54 (59.3)	37 (40.7)	86 (94.5)	5 (5.5)
B	63	38 (60.3)	25 (39.7)	60 (95.2)	3 (4.8)
C	18	1 (5.6)	17 (94.4)	17 (94.4)	1 (5.6)
Total	172	93 (54.1)	79 (45.9)	163 (94.8)	9 (5.2)

**: χ^2 test $p < 0.01$

Discussion

Recently, global clinical trials have been conducted throughout the globe in line with the guidelines of the ICH-GCP [1-7]. On the other hand, the inspection result from other Asian countries has not yet been accessible. We think that clarification of the current situation of clinical trials in Asia is one of the most important things to improve the quality of global clinical trial practices. Therefore, we have conducted the research on the current situation of clinical trials in Beijing and in Shanghai, and basically the State Food and Drug Administration of

China (SFDA) and its affiliated local authorities conduct audits and inspections in China, but China is such a large country that it is difficult to evaluate a whole country's situation by evaluating data only from its two largest cities. Therefore, this study was conducted to evaluate the details of the current situation of clinical trials in Nanchang, the 25th largest city in China, using a questionnaire method.

In our study, a total of 34.3% of respondents had a Ph.D. with a significant difference among institutes in Nanchang. The study also indicated that the average number of clinical trials in which respondents participated as PI was 1.5 ± 2.9 per year, again with a significant difference among institutes. The previous study showed that duration of work and participation in clinical trials were approximately two-fold in Shanghai. These differences may have strongly influenced the subsequent performance indicators. Between Beijing and Shanghai almost all tested parameters indicated significant differences between the two cities [19,20]. We assumed that these discrepancies were because of differences in experience and duration of conducting clinical trials in both the cities. Compared with the two big cities in terms of possession of a Ph.D., the Nanchang study showed that the Nanchang data was just between Shanghai's (46.3%) and Beijing's (31.3%). Furthermore, in terms of the average number of clinical trials in which respondents participated as PI, the Nanchang study also showed that the Nanchang data was just between Shanghai's (5.3 ± 7.5 years) and Beijing's (0.6 ± 1.3 years). Therefore based on this research we speculate that clinical trials were also conducted vigorously in the four medical institutes of Nanchang.

The study clearly revealed that respondents perceived two primary benefits from participation in clinical trials: the ability to provide the latest treatment to a patient and the ability to acquire information on the success of such drugs. The previous study also showed that respondents in both Beijing and Shanghai thought that they obtained benefits from participation in clinical trials, i.e., providing the latest treatment to patients, acquiring information on the success rate of such drugs, improving clinical status by attempting to execute a clinical trial, and contributing to scientific research.[19,20] We think these merits led medical doctors to be vigorously involved in clinical trials not only in Beijing and Shanghai but also in the four medical institutes of Nanchang. Our results in Nanchang confirmed that 79.7% of respondents participated in audits and inspections conducted by their institute with significant difference among institutes and 92.7% reported receipt of the findings of such audits and inspections each year, again with significant difference among institutes.[19,20] In addition, 50.0% of respondents participated in audits and inspections conducted by an external authority with significant difference among institutes and 79.1% reported receipt of the findings of such audits and inspections each year, again with significant difference among institutes. The most commonly reported failure identified by institutional audits and inspections was insufficient completion of CRFs, followed by incorrect completion of CRFs. The most commonly reported failure identified in audits and inspections conducted by an external authority were also incorrect completion of CRFs, followed by insufficient completion of CRFs.

Our previous research confirmed that in total 30.9% of respondents participated in audits and inspections conducted by an external authority, and in total 24.2% reported receipt of the findings of such audits and inspections each year in Beijing and Shanghai. Compared with these data, each percentage in the four medical institutes of Nanchang is larger than that of Shanghai and Beijing. Further, we think that these numbers show that the audits and inspections were conducted rigorously in the four medical institutes of Nanchang. This shows now the four medical institutes of Nanchang acquire the know-how regarding clinical trial through the experiences of audits and inspections.

In this study, 54.1% of doctors belonging to an institute affiliated to Nanchang University were involved in a global clinical trial each year, with a significant difference among institutes. More than 90% reported that they would like to participate in a global clinical trial. In Shanghai and Beijing, 46.1% and 25.2% of respondents were involved in a global clinical trial each year, with significant difference among institutes respectively. To enhance the quality of global research, similar studies should be expanded to other countries in Asia and the world.

Global clinical trials have played a very important part in research and development by carrying out rapid and effective delivery of state-of-the-art drugs to patients worldwide. Therefore, we believe that an Asian clinical trial network should be organized promptly to make it possible to perform global clinical trials in Asia more efficiently.

Although 10 medical institutes in Nanchang conduct clinical trials, which are approved and registered by SFDA, this study was conducted at four medical institutes affiliated to the Nanchang University. This is one of the limitations of this study.

Conclusion

It is still difficult for us to evaluate the situation of the clinical trials in China as a whole, but this study shows that not only in Shanghai and Beijing but also in Nanchang, clinical research is conducted vigorously and rigorously, and is appropriately monitored by audits and inspections conducted internally by the local institutes and/or by an external authority.

Ethics approval and consent to participate

Paper-based informed consents were obtained from the respondents, and complete confidentiality was assured. Before data collection, the study protocol was approved on February 18, 2014 by the Ethics Committee of the Graduate School of Medicine Nagoya University (approval number: 2013-0192-2).

Availability of data and material

Data formatted by SPSS are available.

Authors' contributions

YY carried out the planning the conception and design of the research, the analyzing and conducting the interpretation of data, the preparing the draft manuscript, the contributing the finalization of the manuscript. SF carried out the acquiring data in Nanchang, the analyzing and conducting the interpretation of data, the contributing the finalization of the manuscript. YY carried out the analyzing and conducting the interpretation of data, the contributing the finalization of the manuscript. ZY carried out the acquiring data in Nanchang, the analyzing and conducting the interpretation of data, the contributing the finalization of the manuscript. All authors read and approved the final manuscript.

The competing interests

The authors declare that they have no conflicts of interests. Consent for publication is not applicable, since this manuscript does not contain any individual persons' data.

Acknowledgements

This study was partially supported by a Grant-in-Aid for Science Research B (B 22406002) from the Japan Society for the Promotion of Science.

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