Scientific Research Publishing

Pharmacology & Pharmacy, 2023, 14, 229-238
https://www.scirp.org/journal/pp
ISSN Online: 2157-9431
ISSN Print: 2157-9423

Comparison of Anticancer Drug Preparation Techniques between Chemotherapy Specialist Pharmacists and Non-Chemotherapy Pharmacists Using Eye-Tracking Techniques

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How to cite this paper: Miyachi, Y., Miyagi, Y., Gocho, S., Nakayama, C., Ejiri, M., Takeuchi, M., Onishi, M. and Oshima, T. (2023) Comparison of Anticancer Drug Preparation Techniques between Chemotherapy Specialist Pharmacists and Non-Chemotherapy Pharmacists Using Eye-Tracking Techniques. *Pharmacology & Pharmacy*, **14**, 229-238.
https://doi.org/10.4236/pp.2023.148017

Received: June 8, 2023
Accepted: August 15, 2023
Published: August 18, 2023

Abstract

Anticancer drug preparation by pharmacists is a critical task directly related to medical incidents. This study examined the factors influencing medical errors in chemotherapy, that is, errors by specialist pharmacists (CPh) and pharmacists in other departments (NCPh), by measuring their gaze during the preparation of anticancer drugs. The eye-tracking results showed that the gazing time of NCPh was significantly longer than that of CPh for items such as "preparation of a closed-system device" and "preparation of the syringe" and all preparation times ($P < 0.05$). The NCPh were not assigned to prepare drugs on a regular basis, indicating their lack of familiarity with the process. There was no significant difference in gaze ratio between CPh and NCPh. This outcome was suggested to be a result of the use of an anticancer drug preparation support system. The results for the pupil diameter variation rate showed that NCPh were significantly more mydriatic in the "mixing injections" category than CPh. However, CPh tended to be more mydriatic in the "checking" category. CPh exhibited a smooth workflow and focused on the important items to be checked. This study showed that the differences in procedure flow and concentration points may lead to errors. Furthermore, the results are of interest from the perspective of medical incident prevention. They will be useful in identifying potential human factors, such as where the pharmacist focuses their attention by measuring eye movements.

Keywords

Eye Tracking, Medicine Inspection, Anticancer Drug, Pharmacists

1. Purpose

Since the 1990s, hospital pharmacist services have expanded from dispensing in pharmacies to drug information management and therapeutic drug monitoring. In addition, a pharmaceutical management fee has been initiated, and ward operations have been established. Pharmacists have made significant contributions to the promotion of effective and safe drug treatment [1] [2]. The Japan Council for Quality Health Care, a neutral and scientific third-party organization, reports on the Project to Collect Medical Near-miss/Adverse Event Information 2021 Annual Report. (https://www.med-safe.jp/pdf/year_report_2021.pdf, June 2023). This report collects the number of medical accidents and near-misses at 1575 medical institutions. According to the report, approximately 33.9% of near-miss cases involved drugs, and this proportion was the highest. Thus, it indicates that drugs have a high potential to lead to serious accidents. Injections are administered directly into the body and are expected to have a rapid onset of action. Incorrect administration of injections is directly linked to medical incidents. In particular, anticancer drugs are extremely toxic and have a high potential to cause serious medical incidents. Incidents in chemotherapy have been attributed to insufficient confirmation of "laboratory data of the patient" and "concentration and route of administration after drug dissolution" [3].

In recent years, continuous patient involvement by board-certified oncology pharmacy specialists and board-certified oncology pharmacists has been encouraged [1]. Yoshida *et al.* reported that pharmacists could provide prescription support and medication guidance, including supportive care and treatment policies, in real time by attending doctor consultations and considering doctors' intentions and patients' wishes [4]. The adoption rate of prescription suggestion by long-term continuous intervention by specialist pharmacists in cancer pharmacotherapy is as high as about 98%, and improvement of symptoms by the suggested drugs was reported in about 70% of patients [5]. The result that a prescription suggestion adopted at a high rate has a certain effect on symptom improvement indicates the usefulness of pharmacological management by oncology pharmacists and suggests the need for active prescription suggestions.

Various measures have been implemented to ensure the efficacy and safety of chemotherapy. Tsuneki *et al.* established a system shared among multiple professions that can be checked at the time of prescription, dispensing, and administration of chemotherapy, thereby contributing to accident prevention [6]. In recent years, the use of artificial intelligence (AI) has also progressed, and scholars have assumed that the verification of drug matching and weighing through barcode authentication can ensure safety [7]. The use of barcode authentication has been reported to reduce healthcare costs because it provides objective confirmation and allows the reuse of leftover fluids [8].

Our laboratory has been using eye trackers using in powdered medication dispensing, and medicine inspection by pharmacists to study factors affecting medical errors [9] [10] [11]. Eye tracking enables the visualization and measurement of "what people are looking at," and eye-tracking systems are widely used in ergonomics, psychology, and medicine (https://www.nacinc.jp/, October 25, 2022). This system allows the detection of eye movement through infrared corneal reflex detection. In addition, changes in pupil diameter are caused by involuntary autonomic sphincter and pupillary dilator nerves within the iris. The pupillary sphincter, which runs in a circular pattern within the iris, is a parasympathetic nerve. Therefore, changes in pupil diameter cause the nerves to contract when the body is resting, resulting in pupil constriction. The pupillary dilator nerve runs radially within the iris and is a sympathetic nerve. Therefore, when the brain is active, such as when concentrating, the muscles contract, and mydriasis occurs [12] [13] [14].

In this study, we examined the work content of pharmacists' anticancer drug preparation using eye-tracking technology to measure human eye movements and examined the factors associated with medical incidents.

2. Method

2.1. Subjects

Four pharmacists who worked at Aichi Medical University Hospital and had experience in the chemotherapy room (experts) and four inexperienced pharmacists (non-experts) were included in the study. The number of anticancer drugs prepared at the hospital was approximately 1400 per month.

The frequency of non-exclusive anticancer drug preparations was approximately 3 h once every 2 months.

2.2. Measurement Method

Eye tracking measured the process of checking prescriptions and regimens, preparing for mixing, mixing, final check, and cleanup.

The pharmacists used a fluorouracil injection simulator and an Epirubicin hydrochloride injection simulator attached to a training kit to prepare the anticancer drugs (Japan Pharmaceutical Manufacturing Equipment Co., Ltd., Osaka). Prescriptions, process documents, and other medicines were the same as those routinely used in hospitals. Pharmaceuticals attached to training kits for the preparation of anticancer drugs were illuminated with black light. After preparing, the place of preparation, gloves, syringes, and vials was irradiated with black light.

In addition, as with routine operations, closed connecting instruments (BDPhaSeal™; Becton-Dickinson Inc.) were used. We adopted an injection drug mixing and inspection system (AddDis; TOSHO Inc.). The gaze measurement equipment used was EMR-8 (NAC Image Technology Inc.). Data on the trends of subjects' eye movements, gaze time, pupil diameter, and field of vision images were collected and analyzed. The imaging records collected through EMR-8 were analyzed using EMR-dTarget (NAC Image Technology Inc.). **Figure 1** showed an example of a gaze point.

2.3. Gaze Point

The desired gaze points within the entire work period were divided into 19 regions. From the collected data, the gaze points during the inspection were individually categorized. The gaze points used were as follows: "Prescription" and "Regimen" for the dosage plan; "Label," "Anticancer drug," "Other drugs," "Attachment of the closed-system device," "Preparation of the closed-system device," "Preparation of the syringe," "Scale of the syringe," and "System" for the injection drug mixing and inspection system; "Display" for the display of the injection drug mixing and inspection system; "Pedal" for the pedal of the injection drug mixing and inspection system; "Check (prescription)" for checking of prescription before starting preparation; "Check (regimen)" for checking of regimen before starting preparation; "Check (anticancer drug)" for checking of the anticancer drug before starting preparation; "Check (other drugs)" for checking of other drugs before starting preparation; "Check (others)" for checking of other drugs before starting preparation; "Disinfection"; and "Others."

Gaze rate (%) was determined as the percentage of gaze time for each gaze point relative to the overall gaze time.

2.4. Pupil Diameter

The mean pupil diameter was computed for each gaze category. The categorization consisted of [Prescription and process documents], [Display (display of the injection drug mixing and inspection system)], [Mixing], [Preparation check], and [Others].

Figure 1. The eye tracking video (■ : gaze point).

The rate of variation of the pupil diameter was calculated as follows:

$$\text{The rate of change}(\%) = \frac{\text{Mean pupil diameter for each category} - \text{Mean pupil diameter for all categories}}{\text{Mean pupil diameter for all categories}} \times 100$$

2.5. Statistical Analysis

Differences in each parameter were statistically evaluated by the Mann-Whitney U test. All differences were considered significant when $P < 0.01$ or $P < 0.05$.

2.6. Ethics Statements

This study was approved by the Kinjo Gakuin University Ethical Review Board (No. H17015, January 31, 2018).

3. Result

3.1. Preparation Time

Table 1 shows the pharmacist's history and total mixing time. There was no difference in years of experience between the experts and non-experts. The preparation times of non-experts were significantly longer than those of experts ($P < 0.01$).

3.2. Gazing Time

Figure 2 shows the results for gaze time. The gaze times for "Regimen," "Label," "Anticancer drug," "Other drugs," "Attachment of the closed-system device," "Preparation of the closed-system device," "Preparation of the syringe," "Scale of the syringe," "Display," and "Disinfection" of non-experts were significantly longer than those of experts ($P < 0.05$). Moreover, for all items, the gaze times of non-experts were longer than those of experts.

3.3. Gazing Rate

Figure 3 shows the results for the gazing rate. There were no significant differences in gaze points between experts and non-experts.

3.4. Changes in Pupil Diameter

Figure 4 illustrates the results of the change in pupil diameter. The rates of change in pupil diameter for "Prescription and process documents" were −4.05% and −0.91% for experts and non-experts, respectively. The pupil diameters for

Table 1. Preparation time.

	expert	non-expert
Pharmacist's history time (year)	12.8 ± 6.5	11.0 ± 6.9
Total mixing time (second)	406.9 ± 112.4	1016.0 ± 301.8*

Mean ± SD (n = 5), *$P < 0.01$.

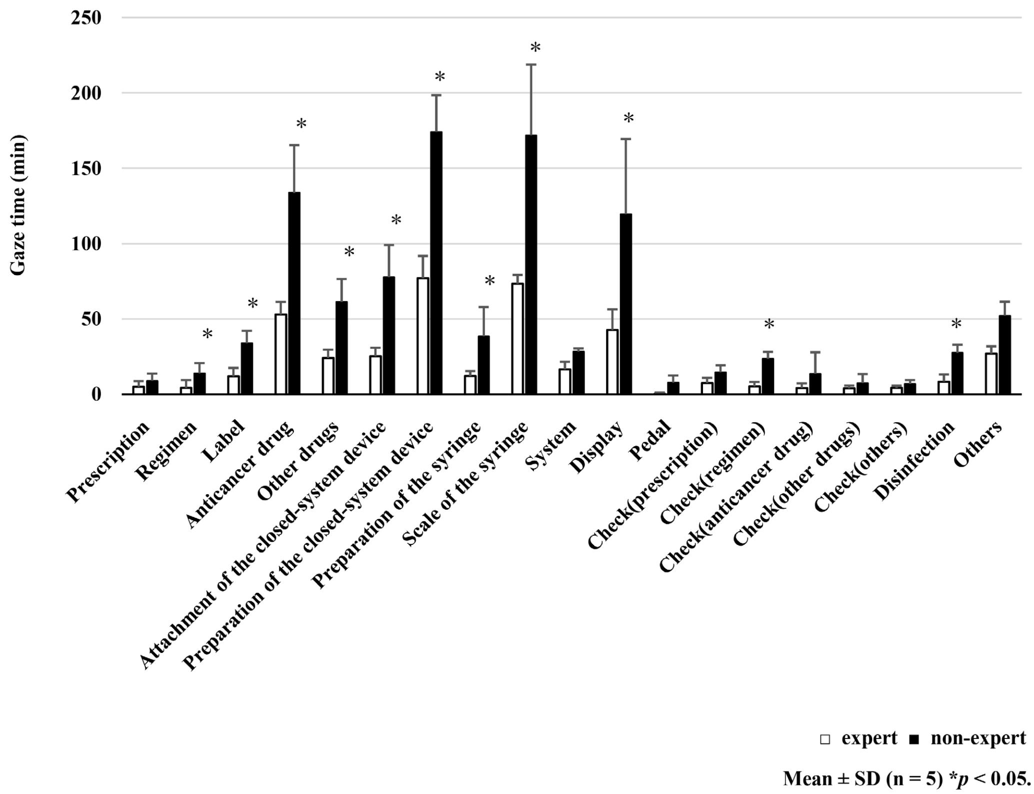

Figure 2. The gaze time of expert and non-expert pharmacists (min).

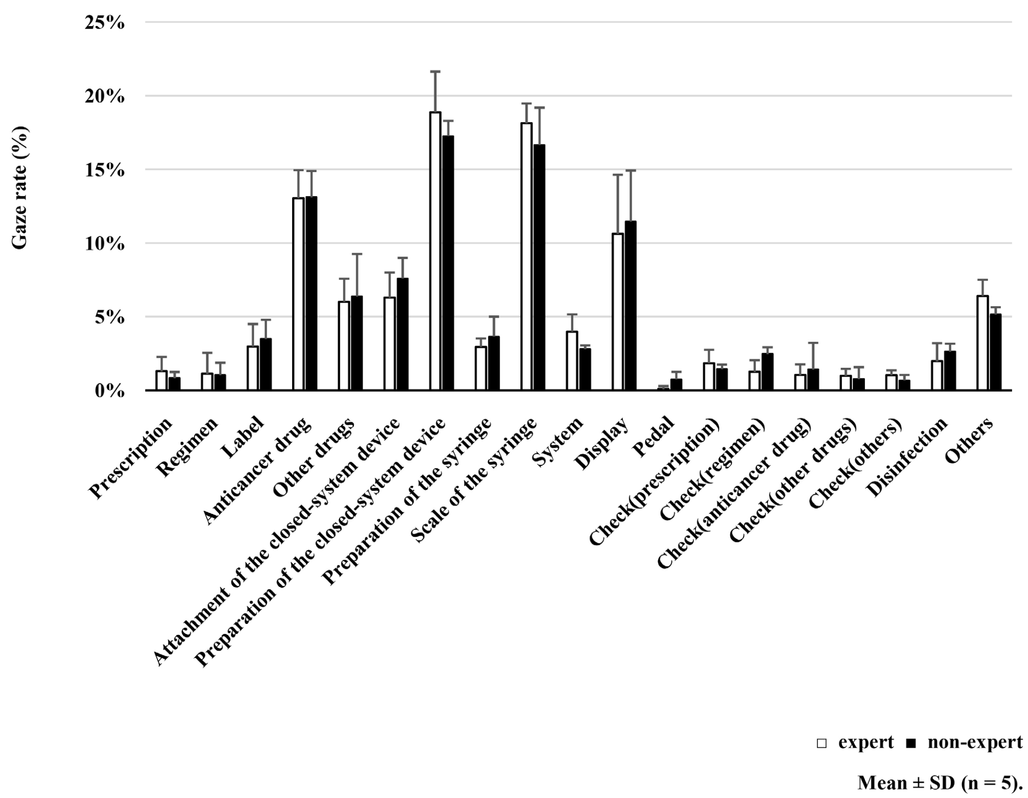

Figure 3. Gaze rateof expert and non-expert pharmacists (%).

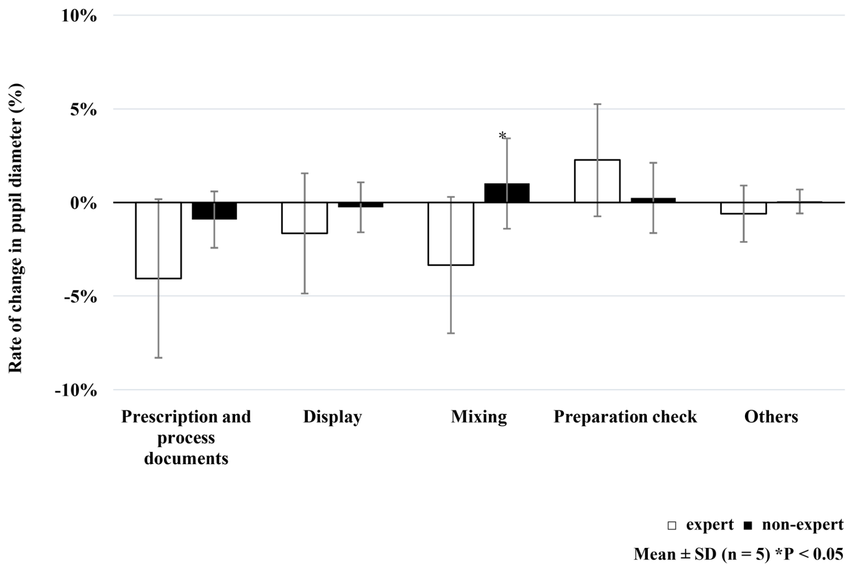

Figure 4. The rate of change in pupil diameter of expert and non-expert pharmacists (%).

"Display" were larger for non-experts (−0.25%) than for experts (−1.65%). The pupil diameter for "Mixing" of non-experts (1.02%) was significantly greater than that of non-experts (−3.34%) ($P < 0.05$). The pupil diameters for the "Preparation check" were larger in experts (2.27%) than in non-experts (0.25%).

3.5. Drug Dispersal Condition

After preparing anticancer drug mimics, dispersal conditions due to ultraviolet (UV) irradiation were checked. There was no dispersion in this study.

4. Consideration

Dosage errors and wrong dosing intervals in chemotherapy lead to adverse events. Medical error prevention measures for anticancer drug preparations are essential for pharmacists. In this study, gaze measurement of anticancer drug preparation was performed. Anticancer drug preparation techniques of expert and non-expert pharmacists were compared, and human error countermeasures were examined.

The results of gazing time showed that the total preparation time was approximately 2.5 times longer for non-experts than for experts, with non-experts having longer preparation times for all items. In particular, the preparation time of non-experts in terms of "Anticancer drug," "Attachment of the closed-system device," "Preparation of the closed-system device," "Preparation of the syringe," "Scale of the syringe," "Display," and "Disinfection" was significantly longer than that of experts. This finding indicates inexperience and reflects the unfamiliarity of non-experts with mixing. Some non-experts were unaware of the amount of lyophilized drug-dissolving solution or the capacity of the syringe to be used and were observed to divert their attention from the workbench and check with other pharmacists. On the other hand, the experts performed each task in detail, such as taking the syringe out of the encasement, attaching and detaching the closed connection device, and collecting the medicinal solution appropriately, reducing the preparation time. In a previous study comparing veteran experts and newcomers in dispensing, inconsistent dispensing arrangements among new pharmacists possibly induced human errors [10]. In this study, some situations, such as when non-experts did not comprehend the workflow, could have led to medical errors.

The gaze rate results showed no significant differences between experts and non-experts. Okayasu *et al.* reported that the injection drug mixing and inspection system prevented weighing errors and enabled accurate preparation by inexperienced personnel by displaying the necessary information [15]. Introducing the injection drug mixing and inspection system helped non-experts perform the same preparations as experts, suggesting that the system is a measure to prevent medical errors.

The rate of change in pupil diameter showed a significant difference in mixing, which included "removing the outer bag of the syringe," "attaching the needle to the syringe," "Attachment of the closed-system device," and "removing the medicinal solution." The rate of change in pupil diameter in experts decreased from the average because they were aware of the next operation, often checked the display of the injection drug mixing and inspection system, or only moved their eyes ahead of them. On the other hand, non-expert mydriasis reflected tension and concentration.

A video of non-experts showed cases in which they were interrupted during preparation. Reports have revealed that interruptions can lead to dispensing errors [16] caused by shifting the gaze to a distant area.

In verifying the drug dispersal situation, there was no dispersal due to UV irradiation in all cases, including in preliminary experiments. This finding was clearly due to the use of the closed-system BD Phaseal™ device. Consistent with previous studies [17] [18], the use of BD Phaseal™ contributed to preventing exposure to anticancer drugs during drug preparation.

For the safe implementation of chemotherapy, a third party other than the doctor planning the treatment must examine and confirm the plan. Therefore, clarifying protocols and establishing a system to check them will lead to safety measures [19]. Studies on dispensing errors have shown that "impatience," rather than "insufficient knowledge" or "inexperience," is the most common cause of dispensing errors during preparation [20]. Therefore, errors are more likely to be influenced by psychological and emotional factors than physical factors. This study revealed that injection drug mixing and inspection systems prevent dispensing errors. On the other hand, differences in procedure flow and concentration points may lead to errors. Therefore, the results were considered a step toward preventing dispensing errors. However, this study was conducted at a single target facility, and the injection drug mixing and inspection system was in place. In the future, it will be necessary to conduct this study in facilities that do not have the injection drug mixing and inspection system in place. In the future, while utilizing AI devices, safety measures must be established to prevent "impatience," which may occur in cases of concern.

Acknowledgements

We would like to thank the pharmacy staff of the Department of Pharmacy, Aichi Medical University Hospital who cooperated in this study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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