INTRODUCTION

Recently, many oral anticancer drugs have been developed, facilitating cancer treatment at home [1]. When performing such treatment for patients who are unable to take tablets or capsules due to dysphagia, non-health care professionals, such as family members, tend to administer the anticancer drugs using a tube for tubal feeding. Therefore, the simple suspension method [2] may be useful for safely administering cytotoxic medicines, such as anticancer drugs, considering the risk of drug-administering persons’ exposure. However, non-health care professionals’ knowledge regarding the handling of anticancer drugs or administration procedures is unclear; health damage related to anticancer-drug exposure resulting from a lack of knowledge or skills must be avoided. In Japan, characterized by the rapid aging of society, persons aged over 60 years account for approximately 70% of family caregivers [3], raising a social issue: Nursing for elderly persons by elderly caregivers. Therefore, the tubal administration of anticancer drugs by elderly persons, whose motor function is reduced in comparison with young person [4], without sufficient knowledge or skills may further increase the risk of exposure.

For evaluation of the anticancer drug exposure of persons who administer drugs, a method using fluorescein sodium has been previously reported [5]. Anticancer drug exposure of health-care professionals is evaluated using this method and measures to reduce exposure are taken based on the results. On the other hand, anticancer drug exposure of non-health care professionals who administer drugs has not been investigated in detail. The detection of very low exposure levels and micro spots using the fluorescein sodium method is difficult because it requires measurement of the number of plots emitting fluorescence induced by ultraviolet light irradiation [6]. Moreover, to quantitatively evaluate scattered fluorescein sodium, it is necessary to collect it by washing with purified water and measure it using a fluorescence spectrophotometer. Thus, we devised a method to quantitatively evaluate the anticancer drug exposure level using Indian ink, which is safe and can be easily obtained, without the use of ultraviolet light and expensive devices such as a fluorescence spectrophotometer. We investigated the influence of the age and syringe used on anticancer drug exposure of non-health care professionals who administered drugs through a tube, which has not previously been reported.

METHODS

The subjects

The subjects were 10 volunteers aged 22-24 years (20-year-old group), 10 aged 45-54 years (50-year-old group), and 10 aged 75-84 years (80-year-old group).

The study contents

Initially, the grip strength was measured to collect basic data, and then, this study was conducted according to the following procedures: The study outline is shown in Fig. 1.

Initially, the subjects wore gloves and administered 20 mL of Indian ink to an adult training model (Sakura II, Kyoto Kagaku Co., Ltd). For administration, 5 kinds of syringe (Syringes A to E) produced by different manufacturers (Table 1) were used, and administration was performed twice using the respective syringes.

In the phase of preparation, we (investigators) placed Indian ink to an adult training model (Sakura II, Kyoto Kagaku Co., Ltd). For administration, 5 kinds of syringe (Syringes A to E) produced by different manufacturers (Table 1) were used, and administration was performed twice using the respective syringes.

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The count of pixel numbers
Subsequently, the gloves were cut to open them flat using scissors, and images of them were input into a personal computer using a scanner. After monochromatic processing with Gimp 2.8 (The GIMP Team), pixels at the sites of ink attachment were counted using a pixel counter (Hals Factory), and used as a parameter of exposure to anticancer drugs. When the resolution is 300 ppi, the number of pixels per 1 cm is 118, and thus, the number per 1 cm$^2$ is 13,924. Referring to this number, the area was calculated from the number of pixels and used as an index of anticancer drug exposure.

The ethical consideration
Before this study, its contents were sufficiently explained to the subjects using an explanatory document, and written informed consent was obtained. The protocol of this study was approved by the Ethics Review Board of Hyogo University of Health Sciences (Approval No. 14034).

Statistical analysis
For statistical analysis, IBM SPSS version 22.0 software was used, and the Games-Howell method was adopted. A p-value of 0.05 was regarded as significant. Date was represented as mean ± standard deviation.

RESULTS
The data for grip strength
The mean ages of the subjects in the 20-, 50-, and 80-year-old groups were 22.7±0.8, 49.9±2.5, and 78.4±3.2 years, respectively. In the 20-year-old group, the mean grip strength of the left and right hands was 29.2±9.1 and 31.3±10.9 kg, respectively. In the 50-year-old group, the values were 26.0±10.3 and 27.8±9.5 kg, respectively. In the 80-year-old group, they were 24.1±8.1 and 26.0±7.5 kg, respectively.

The number of pixels among the syringes
We compared the total number of pixels on the first and second sessions of administration among the syringes regardless of age. The number of pixels for Syringe B was the lowest (11.8±3.1 cm$^2$) showing a significant difference in comparison with Syringe E (p=0.006, Fig. 2d). With respect to age, the number of pixels for Syringe B was the lowest (0.8±0.3 cm$^2$) in the 20-year-old group, showing a significant difference in comparison with Syringe E (p=0.01, Fig. 2a). In the 50-year-old group, the number of pixels for Syringe B was the lowest (7.1±2.4 cm$^2$), showing a significant difference in comparison with Syringe E (p=0.001, Fig. 2b). In the 80-year-old group, there were no significant differences among the syringes (Fig. 2c).

The number of pixels with respect to the frequency of administration
With respect to each syringe, we compared the number of pixels on the first session of administration with that on the second session. Overall, the number of pixels for Syringe B on the first session was 14.4±4.7 cm$^2$ and that on the second session was 9.1±4.0 cm$^2$, showing a significant decrease (p=0.04, Fig. 3d). Furthermore, the number of pixels for Syringe C on the first and second sessions was 27.6±7.0 cm$^2$ and 18.2±8.7 cm$^2$, respectively, showing a significant decrease (p=0.016, Fig. 3d). With respect to age, the number of pixels for Syringe E on the first and second sessions in the 20-year-old group was 43.6±16.4 cm$^2$ and 9.6±4.0 cm$^2$, respectively, showing a significant decrease (p=0.014, Fig. 3a). In the other groups, no syringe showed any significant differences between the first and second sessions (Fig. 3b and 3c).

The number of pixels for all syringes
We compared the total number of pixels for all syringes on the first and second sessions among the groups. In the 20-year-old group, it was the
lowest (10.9±2.3 cm²) showing significant differences in comparison with the other groups (p=0.002, p<0.001, Fig. 4).

In each group, the total number of pixels for all syringes was compared between the first and second sessions of administration. In the 20-year-old group, the number of pixels on the first session was 15.5±4.1 cm², and that on the second session was 6.3±1.9 cm², showing a significant decrease (p=0.037, Fig. 5). In the 50-year-old group, it was 29.1±5.5 and 23.1±5.4 cm², respectively, showing a significant decrease (p=0.002, Fig. 5).

DISCUSSION

Other than the method using fluorescein sodium, a method using aqueous dye-based red ink has been reported but this also requires washing of the red ink-stained region and measuring the absorbance of the washing solution. In contrast, our method analyzes the Indian ink-stained area using free software being simpler than previously reported methods. In addition, exposure can be visually confirmed without using any specific device, showing that the method is very useful. Furthermore, visually presenting the risk of exposure to patients’ families, who are non-health care professionals, may be very effective.

When comparing the number of pixels among the syringes, that for Syringe B was markedly lower than for the other syringes. As shown in Table 1 and Fig. 6, we compared the characteristics of the respective syringes. Concerning Syringe B, the inner diameter of the syringe nozzle (a) was wider than that of its neck (b), differing from the other syringes; pressure in the nozzle on pushing the syringe pump may be minimized. This may have prevented liquid leakage at the connecting part between the syringe nozzle and tube, resulting in a small volume of Indian ink attachment. Concerning Syringe E, the syringe nozzle was present on the unilateral side, and not at the center. In addition, its length was 2.0 cm shorter than those of the other syringes; the subjects may have been frequently exposed to liquid on connecting the syringe nozzle with a tube, leading to a large volume of Indian ink attachment.

With respect to the influence of the frequency of administration, the number of pixels on the second session was lower than on the first session regardless of the age, suggesting that skills improve with the frequency of administration. However, in the 80-year-old group, the difference was less marked than in the other groups, and there was no significant difference. This was possibly associated with an aging-related reduction of memory and understanding [7]. Therefore, it may be necessary to review administration procedures or educational tools with respect to the age.

In the 80-year-old group, the number of pixels was high regardless of the type of syringe, and there was a variation, suggesting that
administration skills reduce with aging meaning that caregivers are exposed to anticancer drugs. Kinugasa et al. reported that 80-year-old persons showed a ≤30% reduction of the exercise capacity involved in the motor skills of the fingers, regarding the exercise capacity at 20 years of age as 100 and that they showed a 40 to 60% reduction of the exercise capacity such as grip strength [8]. Therefore, an aging-related reduction in the motor skills of the fingers may have influenced syringe operations. On the other hand, there was no correlation between the subjects’ grip strength and number of pixels; therefore, drug-administering persons’ grip strength may not influence the degree of exposure.

Several studies have reported that, when administering drugs through a tube using the simple suspension method, the dose depends on the type of syringe or administration procedures [9,10]. This study suggests that these factors influence anticancer-drug exposure. However, the subjects were health-care professionals, and syringes of the same manufacturer with different shapes were used for comparison in these studies. Therefore, simple comparison with our study results is difficult but it was suggested that the syringe type and administration techniques influence the anticancer drug exposure level in non-health care professionals, similarly to those in health-care professionals.

Furthermore, the number of pixels did not reach zero in any subject based on the results of this study. This suggests that all subjects may be exposed to anticancer drugs when administering them through a tube regardless of the type of syringe or age.

CONCLUSION

When introducing the simple suspension method for home care, health-care professionals guide patients’ families responsible for drug administration so that they can acquire the necessary skills. Since there has been no report on the exposure of non-health care professionals to anticancer drugs administered through a tube, the findings of this study cannot be compared with previous data. However, it was clarified that the anticancer drug exposure level markedly varies depending on the syringe type and age. These findings may be very useful basic data to investigate methods to select a syringe appropriate for persons who administer drugs and educate them regarding administration techniques in consideration of their age. It was also clarified that the anticancer drug exposure evaluation method using Indian ink devised by us is capable of quantitatively evaluating exposure simply and visually, being very useful.

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REFERENCES