MULTICENTER STUDY OF ENVIRONMENTAL 5-FU CONTAMINATION DURING NORMAL MIXING OF ANTINEOPLASTIC DRUGS

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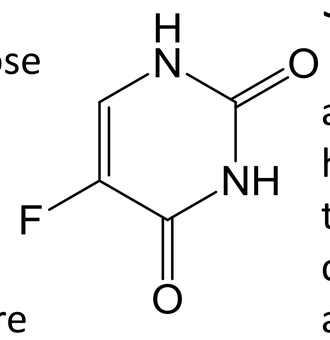
Background

Hazardous drugs

NIOSH has defined hazardous drugs as those with six characteristics (e.g., teratogenicity, carcinogenicity or reproductive toxicity) observed in humans or animals. Hazardous drugs are recommended to be prepared in biological safety cabinet (BSC) and healthcare workers need safe handling skills.



5-Fluorouracil (5-FU)

Antineoplastic drugs account for most of the hazardous drugs. Among them, 5-FU is a common cytotoxic antineoplastic drug, and can potentially cause harm if not handled properly.

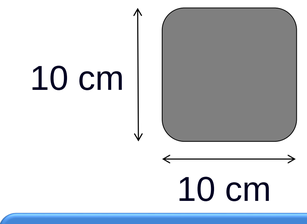
Purpose

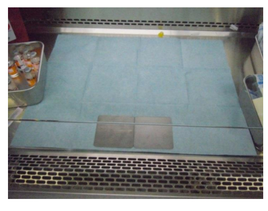
We investigated the relationship among the level of 5-FU contamination during normal mixing, the time of plate placement in the BSC, the operator's experience in mixing, the amount of 5-FU vial prepared during this study, and the number of anticancer agents prepared at each hospital.

Material and Methods

5-FU contamination

During preparation, 5-FU contamination on 2 stainless steel plates (10 cm × 10 cm) in the BSC was determined. These stainless steel plates were collected at the end of the protocol period.





Measurement

We sampled 5-FU from these 2 plates with 40 mL of 90% acetonitrile in water. Samples were analyzed by a validated liquid chromatography coupled to tandem mass spectrometry method. Limit of quantitation is 1 ng/mL.

Relative standard deviation (%CV)	
Diurnal variation	Less than 3%
Interday variation	Less than 4%

Table 1. Results of method validation

Analysis

We examined the correlation between 5-FU contamination level and the following four items:

① Amount of 5-FU prepared
② Time of plate placement in the BSC
③ Operator's experience in mixing
④ Number of anticancer agents prepared at each hospital

Results

	Average	Range
Participating institution	8 national hospitals in Japan	
Participant	16 pharmacists	
Amount of 5-FU prepared	13 vials	2 – 38 vials
Time of plate placement in the BSC	1.71 hours	0.1 – 5.5 hours
Operator's experience in mixing	35 months	1 -168 months
Number of anticancer agents prepared at each hospital in a month	1427	326 - 4500

Table 2. Characteristics of objective items

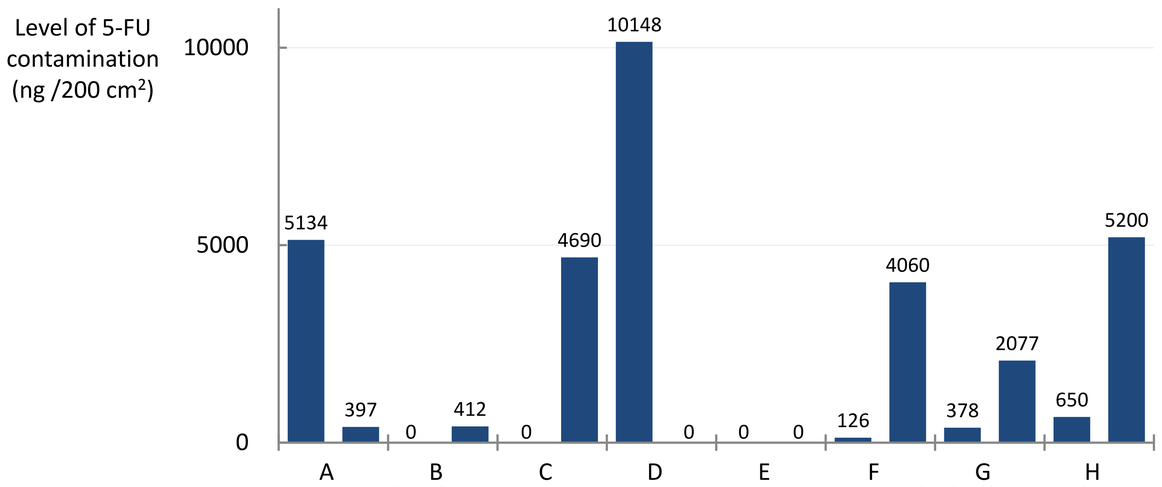


Fig 1. Level of 5-FU contamination at each hospital

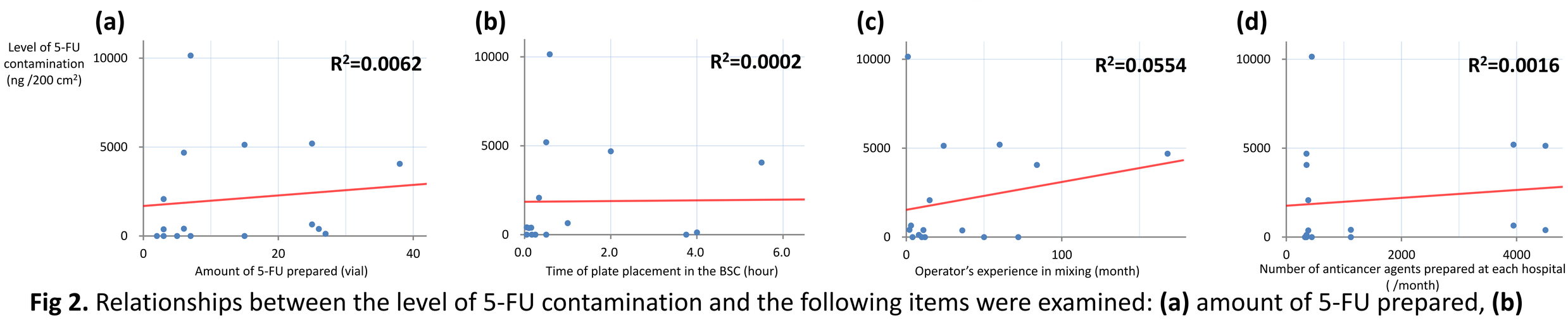


Fig 2. Relationships between the level of 5-FU contamination and the following items were examined: **(a)** amount of 5-FU prepared, **(b)** time of plate placement in the BSC, **(c)** operator's experience in mixing, and **(d)** number of anticancer agents prepared at each hospital.

Discussion

There were 5 pharmacists with 5-FU contamination at the level less than detection limit. Importantly, years of preparation experience varied among these pharmacists. These results suggested that even experienced pharmacists may underestimate the risk of environmental exposure and/or overestimate mixing skills during normal preparation. The routine training of mixing skills is needed to safety handle anticancer agents.

Conclusions

These results suggest no relationship among the level of 5-FU contamination during normal mixing, the time of plate placement in the BSC, the operator's experience in mixing, the amount of 5-FU vial prepared, and the number of anticancer agents prepared at each hospital.

Acknowledgements

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