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Study of Urine Treatment After BCG Intravesical Instillation Therapy — A Secondary Publication

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Abstract: *Background and methods:* Bacillus Calmette-Guérin (BCG) intravesical instillation therapy is used to treat non-muscle invasive bladder cancer. Instilled BCG is typically collected at the time of initial urination and disposed of after sterilization with 10% sodium hypochlorite or household bleach, however, these methods can have unpleasant effects, such as pungent odor, rapid foaming, and fever. We investigated whether isopropanol can be used to sterilize and dispose of urine after BCG intravesical instillation therapy since isopropanol at a concentration of 33% or higher (70% isopropanol was used in this study) has the same disinfectant and bactericidal effects against *Mycobacterium tuberculosis* as 10% sodium hypochlorite or household bleach. *Results:* The use of isopropanol eliminated the unpleasant effects experienced with sodium hypochlorite and no growth of *Mycobacterium tuberculosis* was observed in culture tests. *Conclusion:* Isopropanol is safer than sodium hypochlorite, and should be considered for sterilizing and disposing of urine after BCG intravesical instillation therapy in the future. However, fire and ventilation precautions are required.

Keywords: BCG intravesical instillation therapy; Urine treatment; Isopropanol

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1. Introduction

Bacillus Calmette-Guérin (BCG) is an intravesical injection of a live attenuated bovine tuberculosis vaccine originally intended to prevent tuberculosis. When BCG suspension is injected into the bladder, the urine contains a large amount of *Mycobacterium tuberculosis*. It is generally recommended that urine be collected in an appropriate container (e.g., urine storage container) and disinfected before disposal at the first voiding after BCG intravesical injection therapy [1,2]. According to the "Guidelines for Infection Control in Urology" [3] (hereafter referred to as the "Guidelines"), the recommended disinfection method is to add half the volume of urine to a 10% sodium hypochlorite solution or household bleach and allow it to stand for 15 minutes. However, when 10% sodium hypochlorite is added to urine, the urine may foam violently or the temperature of the solution may rise rapidly. In addition, the odor of chlorine may waft into the room, making medical personnel uncomfortable. Coughing fits and respiratory distress may occur in some healthcare workers who treat the urine. Therefore, since isopropanol with a commercial concentration of 33% or higher is effective as an alternative to sodium

hypochlorite with an action time of 15 minutes [3,4], this study investigated the use of 70% isopropanol (hereinafter referred to as "Isopro"), which is commonly used as a disinfectant for external use in the medical field, for the safe treatment of urine after BCG injection.

2. Methods

We used a household bleach, Purelox® (6% sodium hypochlorite) (n = 6), and added half the amount of Isopro (n = 8) to the urine after BCG injection, and (1) observed the state of urine immediately after injection, at 5, 10, and 15 minutes, and submitted the urine at each observation time for *Mycobacterium tuberculosis* culture test. The same sample was used for each of the three *Mycobacterium tuberculosis* culture tests. (2) At each observation time, the concentrations of chlorine and isopropanol directly above the container were measured using a detector tube gas measuring device (hereinafter referred to as "detector tube"). (3) The temperature of the urine in the container was measured at each observation time.

This study was conducted with the approval of the hospital ethics committee (Approval number: R3-9). Statistical analysis was performed by repeated measures analysis of variance using EZR (Easy R) software.

3. Results

Immediately after the addition of Purelox, bubbles appeared and bubbled violently (**Figure 1**), and a strong chlorine odor was observed, while the temperature rose (35–42°C). The chlorine concentration immediately above the container was measured using a detector tube, and the maximum concentration was 10 ppm. When Isopro was used, a characteristic odor was observed, but no bubbles were generated. The concentration of isopropanol measured directly above the container using a detector tube was below the sensitivity of the measurement. No sudden temperature increase was observed. A significant difference ($P = 7.52 \times 10^{-15}$) was observed between the temperature change over time after the addition of Purelox and that of Isopro (**Figures 2** and **3**). *Mycobacterium tuberculosis* cultures 15 minutes after the addition of Purelox and Isopro were negative in all three culture tests (**Figure 4**).

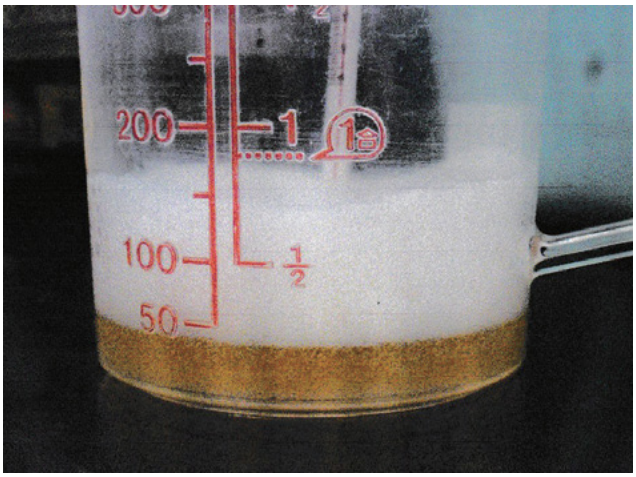

Figure 1. Condition immediately after adding Purelox to urine after BCG intravesical injection

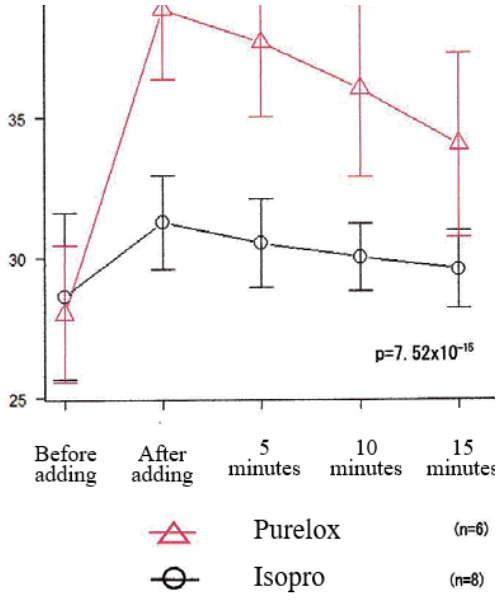

Figure 2. Temperature change over time with Purelox and Isopro ($P = 7.52 \times 10^{-15}$)

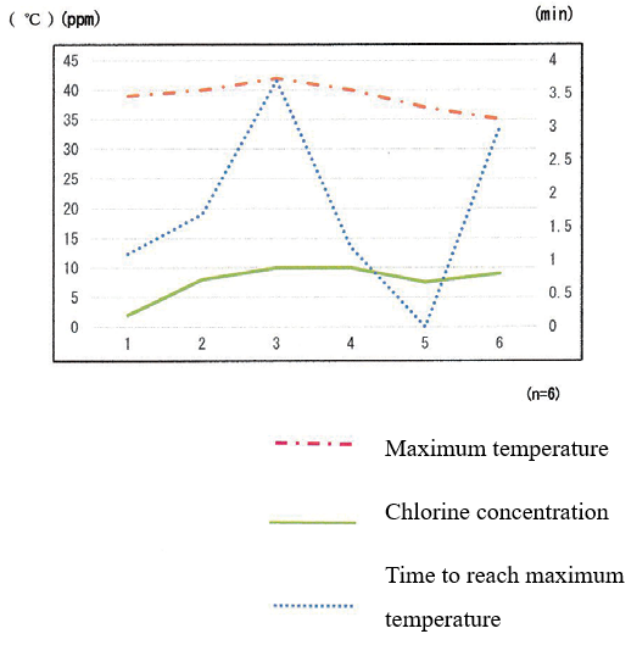

Figure 3. Maximum temperature, time to reach maximum temperature, and chlorine concentration directly above the container when Purelox is injected

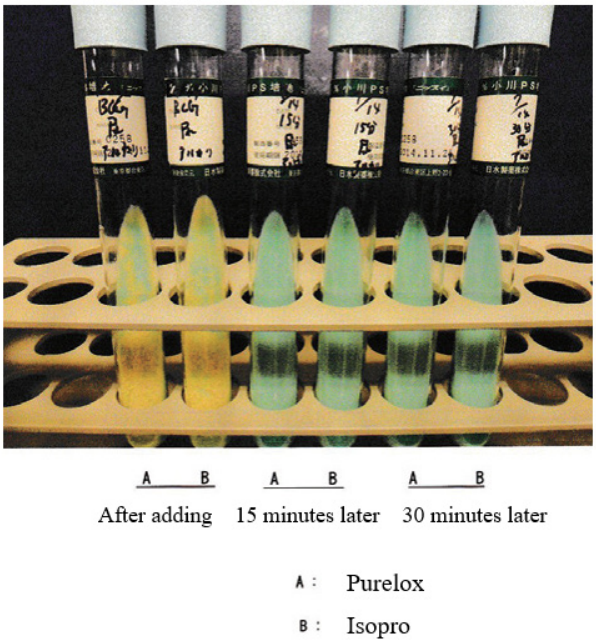

Figure 4. *Mycobacterium tuberculosis* culture after treatment with Purelox and Isopro (immediately, 15 minutes, and 30 minutes after application)

4. Discussion

The "Guideline" states that "urine after intravesical BCG injection should be disinfected and discarded to prevent infection. It is recommended that half the volume of 10% sodium hypochlorite or household bleach be added to the urine, allowed to stand for 15 minutes, and then discarded." The report states that "isopropanol is effective at a commercial concentration of 33% or more with a 15-minute action time," but because "isopropanol is flammable," "treatment with 10% sodium hypochlorite may be appropriate from the standpoint of versatility and safety." Kobayashi *et al.* [5] stated that "sodium hypochlorite generates a large amount of chlorine gas when mixed with acidic substances (e.g., acidic cleaning agents)." The chemical reaction between sodium hypochlorite and urine generates chlorine gas and bubbles, which may cause health problems for healthcare workers who treat urine. In this study, the maximum chlorine concentration measured by the detector tube directly above the container was 10 ppm. The maximum allowable concentration of chlorine is 0.5 ppm [6], and the maximum allowable concentration (the concentration at which no adverse health effects are observed in almost all workers if the exposure concentration is below this value at any time during the workday) is 0.5 ppm [7]. According to the information on poisoning for physicians published by the Japan Poisoning Information Center, chlorine concentrations of 5 to 15 ppm are considered to be moderately irritating to the upper respiratory tract. There is concern that this may have adverse effects not only on medical personnel but also on patients in daily medical practice. On the other hand, isopropanol is one of the substances classified as Volatile Organic Compounds (VOC) under the Air Pollution Control Law and is considered a cause of photochemical oxidants (a generic term for oxidizing substances in the air that cause photochemical smog). The emission standard is 400 ppmC (133 ppm) [8]. It is classified as a Class 2 Organic Solvent in the Ordinance on Prevention of Organic Solvent Poisoning under the Industrial Safety and Health Law, with a controlled concentration of 200 ppm [6] and a maximum allowable concentration of 400 ppm [7]. In this study, the concentration of isopropanol

immediately above the container was below the measurement sensitivity and was clearly lower than the emission standard, controlled concentration, and maximum allowable concentration. However, isopropanol is volatile and can be flammable. Although isopropanol has a characteristic odor, we did not use an odor meter to compare the odor in this study. The commercial price of Purelox is approximately 500 yen for 600 mL (approximately 10 yen per 10 mL), and the price of Isopro is 4.5 yen per 10 mL, making Isopro less expensive.

5. Conclusion

Isopro is safer than Purelox in the indoor environment, including medical personnel and patients, and should be considered for use in the future.

Acknowledgments

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Disclosure statement

The authors declare no conflict of interest.

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