

## Transcutaneous Absorption of Iodine in Pediatric Cardiac Surgery Following the Topical Use of Povidone Iodine

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### Original Article

#### Abstract

**BACKGROUND:** There is still a controversy about the best method for preoperative skin preparation (skin cleaning). The main antiseptic solution used in the cardiac surgery room is Povidone Iodine (PI), which is used to prepare the area to be operated on.

This study aimed to determine the urinary iodine level in children (newborns, infants, and toddlers) undergoing open and closed heart surgery, in whom preoperative skin preparation was performed using PI solution.

**METHOD:** This study was conducted over eight years on a total of 212 children who underwent cardiac surgery. A form was developed for each patient in which all their details, condition, and type of surgery were recorded. A urine sample was taken after the patients were anesthetized and before they were painted with PI through the urinary catheter that had to be attached to them for the cardiac surgery. The patients were then prepped with PI and draped and the surgery was performed. Afterwards, the second and third urine samples were taken 24 and 48 hours after the surgery from the urine collection bag. The samples were transferred to polyethylene tubes with screw caps in a cold box at -20 °C and sent to the iodine reference laboratory of the Endocrinology Research Center of Shahid Beheshti University. The samples were measured using the kinetic colorimetric reaction proposed by Sandell and Kolthoff after the acid digestion of urine.

**RESULTS:** A total of 212 patients (newborns, infants, toddlers) who underwent (open and closed) cardiac surgery entered the study, including 104 (49.1%) males and 108 (50.9%) females. The patients ranged in age from 1 day to 14 years (mean = 168 months). The urinary iodine level was  $40.6 \pm 21.9$  µgr/dl in the first stage (pre-surgery),  $204.1 \pm 92.5$  µgr/dl in the second stage (24 hours post-surgery), and  $130.3 \pm 56.2$  µgr/dl in the third stage (48 hours post-surgery).

Urinary iodine levels increased dramatically after PI use, and the second-stage urinary iodine changes (24 hours post-surgery) were in the excessive range according to the WHO classification, and they decreased gradually over the next 24 hours, but did not reach normal levels until 48 hours post-surgery. The difference between the samples was significant ( $P < 0.05$ ).

The samples were also separately analyzed by age group (group A: 0-2 years and group B: 2-14 years), which showed that transcutaneous iodine absorption and urinary iodine excretion were high in both age groups.

**CONCLUSION:** In children, transcutaneous iodine absorption following preoperative skin preparation with PI (for cardiac surgery) is so high that its urinary excretion reaches an excessive level 24 hours after surgery and remains higher than normal until 48 hours' post-surgery. Furthermore, the transcutaneous absorption of iodine is similar in the 0-2 and 2-14-year-old age groups, and the iodine level following its transcutaneous absorption is excessive in both age groups.

**Keywords:** Povidone Iodine; Skin Absorption; Cardiac Surgery; Pediatric; Urine Iodine Level.

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#### Introduction

In 1956, when Povidone Iodine (PI) was introduced as an antiseptic agent, it gradually became clear that bacteria do not develop PI resistance and that this agent can kill most pathogens and even spores and

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allergies to the product are highly unlikely<sup>1-4</sup>. These properties made PI a popular antiseptic agent for color and painting before surgery. For many years, the standard preoperative preparation in most healthcare centers has included a 5-minute PIScrub; however, following reports on the transcutaneous absorption of iodine and other metals, attempts have been made to prove the transcutaneous absorption of iodine and find alternatives for PI<sup>5-10</sup>.

The extent of transcutaneous absorption of iodine in children has been discussed in a few articles<sup>11</sup>; meanwhile, most of the studies have examined burnt skin, large wounds, and percutaneous absorption through the skin and mucous<sup>8,12,13</sup>.

There have been reports on the incidence of transcutaneous absorption following the topical application of PI, and the evidence demonstrating the transcutaneous absorption of iodine involve evaluations of serum iodine levels and thyroid dysfunction<sup>14</sup>. Complications such as renal failure, metabolic acidosis, hyponatremia, hyper osmolality and hypothyroidism have also been reported<sup>15</sup>. Nevertheless, it is not yet clear whether these complications are clinically valuable.

Transcutaneous absorption of iodine has been reported in infants who tend to have thin, permeable skin even when it is healthy<sup>16</sup>. In pediatric cardiac surgery, a large area of the body (about 25-30% of the body surface area) is washed with PI which can increase the transcutaneous absorption of iodine significantly in children.

In infants, the skin is very thin and permeable<sup>17</sup>. A significant transcutaneous absorption has been reported even in the healthy skin of this age group<sup>16</sup>.

In adults, the skin is less permeable and only a few studies have reported transcutaneous absorption among them, and even then only in cases of massive exposure<sup>17,18</sup>. Meanwhile, no studies have yet been conducted to investigate transcutaneous absorption in children (ages 0-14 years). Moreover, the existing studies have measured and evaluated the iodine level only up to 24 hours after contact with PI. In the present study, the examined children's skin surface has been healthy and a relatively large surface area of their body (25-30%) has been washed with PI, and the iodine level has been measured in them three times up to 48 hours after contact.

## Methods

This study was performed over eight years from

2012 to 2020 at the pediatric cardiac surgery ward of Shahid Modarres Hospital. The study design was prospective analytical. The study group included children with congenital heart disease who required cardiac surgery (open and closed heart surgery). In closed-heart surgery, the heart and lungs continue their function in grand, their role is not taken over by the heart-lung machine. In open-heart surgery, the heart and lung system stop their function in grand, their role is taken over by a Cardiopulmonary Bypass (CPB) machine which is gradually removed after the operation is completed and the patient's heart and lung function is recovered. This study was conducted at the pediatric cardiac surgery ward of Shahid Modarres Hospital in Tehran, which is a tertiary referral hospital and educational center affiliated to Shahid Beheshti University of Medical Sciences.

The study investigated children who were diagnosed with cardiac disease by pertinent diagnostic methods and needed cardiac surgery.

The inclusion criteria were: age under 14, having a congenital heart disease requiring cardiac surgery, not having a thyroid problem, which was determined by asking the parents and the assessment of the thyroid screening conducted at birth, not having skin problems, as determined by routine examinations made by the physician in charge of their insurance, and having parental consent.

The exclusion criteria were: expiration during surgery or within 48 hours in the ICU. The sampling method was based on the patients order of referral to the pediatric cardiac surgery ward. In this study, Povidone Iodine 10% was used for cardiac surgery prepping and draping.

A sample of the patient's urine was taken after anesthesia before being painted with PI through the urinary catheter (iodine-free solutions were used to disinfect the catheter). The patient was then painted with PI 10%, the surgery was performed on them, and then the second urine sample was collected 24 hours after the surgery. The third urine sample was collected 48 hours after the surgery. A child undergoing cardiac surgery will have a urinary catheter in place from before undergoing surgery until admission to the ICU and until at least the third day after the surgery. Alcohol-based solutions were used for the patients in the ward, for venipuncture site selection, Central venous line insertion, and catheterization, and the patient's skin had not come into contact with any PI solution before taking the

first urine sample.

The second and third postoperative samples were collected from the urine collection bag containing the same day's urine. The samples were transferred to polyethylene tubes with screw caps and kept in a freezer at  $-20^{\circ}\text{C}$ . They were then sent in a cold box to the iodine reference laboratory located in the Endocrinology Research Center of Shahid Beheshti University and assessed using the kinetic colorimetric reaction proposed by Sandell and Kolthoff after the acid digestion of urine.

For ethical considerations, the parents of all the patients signed and submitted written consent for covering all the areas of the study before entering the project and after being fully briefed on it. The confidentiality of the patient information was strictly maintained, and extreme caution was taken in collecting data and reporting the results. No samples were taken without the informed consent of the child's parents. No separate urine sampling was performed, and no additional needle was injected into the patients' body and no additional invasive action was performed on any of the patients either.

Part of this study has been extracted from Dr. Saina Motahedin's pharmacist dissertation in Pharmacy entitled "Urinary iodine level in pediatric patients (newborns, infants, and toddlers) undergoing (open and closed) heart surgery using Povidone Iodine". This dissertation was carried out jointly by the Department of Cardiac Surgery of Shahid Beheshti University of Medical Sciences and Islamic Azad University, Pharmaceutical Sciences Branch, in Tehran, Iran, from 2012 to 2014, and after the dissertation was completed, the study continued by the Cardiac Surgery Department of Shahid Beheshti University of Medical Sciences until 2020.

### Statistical Analysis

Continuous and categorical variables were described as mean $\pm$ Sd and frequency (percent), respectively. A repeated measures ANOVA was used to compare the urinary iodine level at the specific time points between the groups under 24 months and over 24 months. All analyses were performed by SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc.. P value  $<0.05$  was set as statistically significant.

## Results

A total of 212 people were recruited. Among

the study population, 104 (49.1%) were male and 108 (50.9%) were female. Their mean age was  $60.05\pm 55.75$  month with an age range from 1 day to 14 years. Their weight ranged from 2.8 to 63 kg ( $18.35\pm 15.04$  Kg). The Body Surface Area (BSA) was between 0.21 and 1.60 ( $0.72\pm 0.383\text{kg}/\text{m}^2$ ).

Table 1 shows the quantitative characteristics of the patients. Table 2 presents the outcomes and complications after the surgery.

The mean urinary iodine levels were found to differ significantly in the 2<sup>nd</sup> and 3<sup>rd</sup> samples ( $P<0.001$ ), as the differences in urine levels of iodine between the 1<sup>st</sup> and 2<sup>nd</sup> samples (24 hours after surgery), between the 1<sup>st</sup> and 3<sup>rd</sup> samples (48 hours after surgery), and also between the 2<sup>nd</sup> sample (24 hours after surgery) and the 3<sup>rd</sup> sample (48 hours after surgery) were statistically significant ( $P<0.001$ ) (Figure 1).

Besides, dividing all the subjects into two groups by age, namely a group under 24 months and a group over 24 months, and measuring the mean urinary iodine during the follow-ups showed no differences in the mean urinary iodine levels on the measurement occasions and in either of the two age groups. In other words, the transcutaneous absorption of iodine was similar and along the same lines in both age groups (over and under 24 months) (Figure 2).

The transcutaneous absorption of iodine was between group under 24 months and group over 24 months ( $P<0.5$ ).

## Discussion

This study examined urinary iodine levels in pediatric patients (newborns, infants, toddlers) undergoing (open and closed) cardiac surgery with Povidone Iodine for their preoperative preparations at a pediatric cardiac surgery ward. Urine samples were taken from each patient (after anesthetization before using PI, and then 24 and 48 hours after surgery). The assessment of the results and the urinary iodine analysis showed that urinary iodine level increases significantly after using PI, and the significant changes were observed in urinary iodine levels in the third sample compared to the second sample and also in the second sample compared to the first sample. The urinary iodine levels were classified as excessive based on the WHO classification<sup>8</sup>.

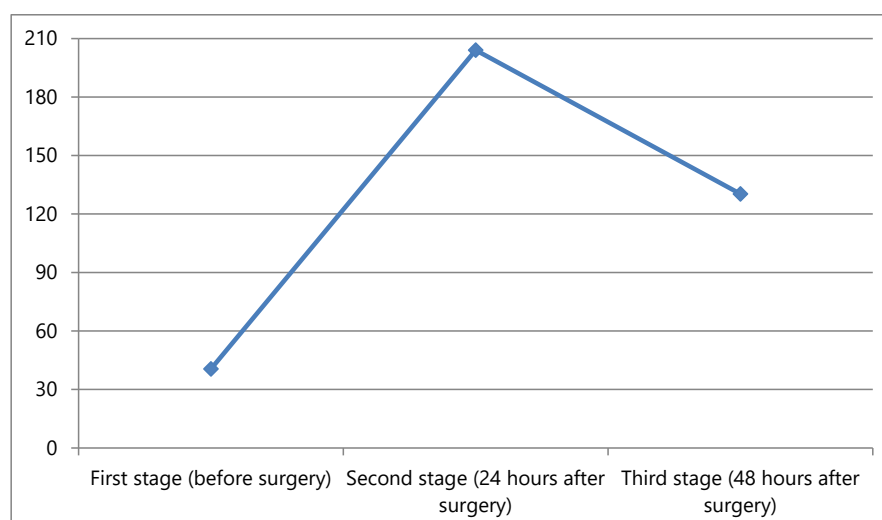
This study measured urinary iodine levels without using any invasive methods or injecting any additional needles into the children. More than 90% of the iodine entering the body is excreted by urine

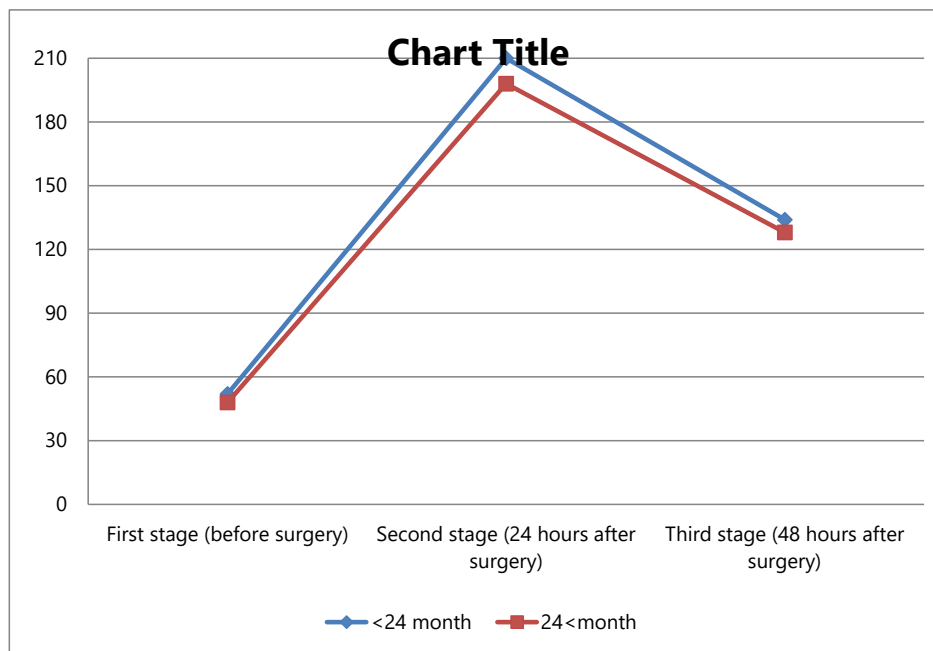
**Table 1.** The quantitative characteristics of the children with congenital heart defects undergoing cardiac surgery

Quantitative Variable	Mean $\pm$ SD N=212
Patient's age (months)	60.1 $\pm$ 55.8
Patient's weight (Kg)	18.4 $\pm$ 15.0
Body Surface Area (BSA)	07. $\pm$ 0.4
Stage-1 (preoperative) urine sample ( $\mu$ gr/dl)	40.6 $\pm$ 21.9
Stage-2 (24 hours after surgery) urine sample ( $\mu$ gr/dl)	204.1 $\pm$ 92.5
Stage-3 (48 hours after surgery) urine sample ( $\mu$ gr/dl)	130.1 $\pm$ 56.2
Duration of open-heart surgery (minutes)	172.8 $\pm$ 44.7
Duration of closed-heart surgery (minutes)	75.1 $\pm$ 26.6

**Table 2.** The qualitative characteristics of the children with congenital heart defects undergoing cardiac surgery

	Absolute Frequency	Percent Frequency (%) N=212
Gender		
Male	104	49.1
Female	108	50.9
Mortality		
Live	204	96.2
Expired	8	3.8
Bleeding after surgery		
Negative	204	96.2
Positive	8	3.8
Neurological complications		
Negative	208	98.1
Positive	4	1.9
Heart rhythm problems		
Negative	200	94.3
Positive		
RBBB	8	3.8
Tachycardia	4	1.9

**Fig. 1.** The evaluation of urinary iodine levels at the specified times in all the children( $\mu$ gr/dl)



Repeated measure analysis of variance shows there is not any significant difference between groups.

**Fig. 2.** The evaluation of urinary iodine levels between group under 24 months and group over 24 months ( $\mu\text{gr}/\text{dl}$ )

and urine sample collection is an easy process. Blood serum; however, contains iodinated compounds, such as iodinated hormones and proteins, which cause further interferences<sup>19, 20</sup>, but urine iodine assessment does not pose any problems and is more suitable for analysis.

Mitchell et al.<sup>1</sup> examined 17 infants under three months old who underwent open-heart surgery. The infants were studied in two groups: Group A consisted of 15 infants on whom PI was used for prepping, and Group B consisted of two infants on whom chlorhexidine solutions were used for prepping. In their study, urinary iodine levels were monitored at 6, 12, 18, and 24 hours after the surgery. The results showed that serum iodine level had reached a toxic level after using PI and this level lasted more than 24 hours.

In the present study, urinary iodine levels were measured until 48 hours after exposure, and the study was performed with a much larger sample size.

In one study, Chabrolle and Rossier<sup>17</sup> linked hypothyroidism to iodine absorption in some newborns whose skin was prepped with PI, which was confirmed in two subsequent studies<sup>17, 21</sup>. To prevent this complication, they recommended washing the area with normal saline after prepping

the skin of infants with PI<sup>1, 8</sup>.

Some studies<sup>1, 6, 7, 22, 23</sup> have found that the rate of infection after surgery is not different in cases using PI and PI compounds or alcohol and alcohol compounds alone. These studies; therefore, have argued that children's skin can be washed before surgery with alternative substances instead of PI.

### Conclusion

The increased urinary iodine level in infants and children following the use of PI for preoperative preparation in cardiac surgery suggests that the transcutaneous absorption of iodine occurs in large amounts and the level reaches its excessive limit based on the WHO classification. The urinary iodine level reaches its maximum 24 hours after exposure and does not return to normal in the 48 hours following surgery and remains high.

The increased transcutaneous absorption of iodine was observed in children both under 24 months (newborns and infants) and over 24 months (toddlers and children). In other words, the increased transcutaneous absorption of iodine and the increased urinary iodine excretion following the use of PI are not limited to infants and also occur in



children (2-14 years).

### Acknowledgments

Part of this study has been extracted from the dissertation of Dr. Saina Motahdin for a PhD in Pharmacy entitled “Urinary iodine level in pediatric patients (newborns, infants, and toddlers) undergoing (open and closed) heart surgery using Povidone Iodine”, which was carried out jointly by the Department of Cardiac Surgery of Shahid Beheshti University of Medical Sciences and Islamic Azad University, Pharmaceutical Sciences Branch, in Tehran, Iran, from 2012 to 2014. This study continued by Dr. Manouchehr Hekmat and Dr. Hamid Ghaderi from the Cardiac Surgery Department of Shahid Beheshti University of Medical Sciences until 2020.

### Authors' Contributions

Manouchehr Hekmat was the head of the surgical team who managed this project. Hamid Ghaderi was a member of the surgical team and also helped in data collection. S. Adeleh Mirjafari and Sayna Motahedin were a major contribution to the literature search and writing of the discussion. Alireza Omid Farzin, Seyedeh Adeleh Mirjafari, Mandana Hekmat, and Mahya Hekmat and Hamed Askarpour helped in data collection. Hamid Ghaderi was in charge of drafting the manuscript and provided administrative, technical and material support. Zahra Ansari Aval and Mahmoud Beheshti Monfared edited the final draft. All the writers reviewed and edited the final draft and gave their final approval for the manuscript.

### Ethical Considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patients gave their consent for the publication of the results of this study.

### Competing Interests

The authors declare that they have no competing interests.

### Funding/Support

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### Key Points

1. The transcutaneous absorption of iodine is very

high in children following the use of povidone iodine after preoperative skin preparation (for cardiac surgery), to the extent that the urinary excretion of iodine reaches extreme levels 24 hours after the surgery and remains higher than normal until 48 hours post-surgery.

2. The transcutaneous absorption of iodine is similar in the 0-2 and 2-14-year-old age groups, and the iodine level following its transcutaneous absorptions is excessive in both of these age groups.

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