

# Transcutaneous Iodine Absorption in Adult Patients with Thyroid Cancer Disinfected with Povidone-Iodine at Operation

Chisato Tomoda,<sup>1</sup> Hiroya Kitano,<sup>2</sup> Takashi Uruno,<sup>1</sup> Yuuki Takamura,<sup>1</sup> Yasuhiro Ito,<sup>1</sup> Akihiro Miya,<sup>1</sup> Kaoru Kobayashi,<sup>1</sup> Fumio Matsuzuka,<sup>1</sup> Nobuyuki Amino,<sup>1</sup> Kanji Kuma,<sup>1</sup> and Akira Miyauchi<sup>1</sup>

Povidone-iodine is used as disinfection in patients undergoing many kinds of operations. Several cases of thyroid dysfunction induced by transcutaneous absorption of povidone-iodine have been reported in small infants. However, transcutaneous absorption was not clearly reported in adults. The aim of this study was to assess transcutaneous absorption of iodine in patients who received single topical application with povidone-iodine and serial changes of urinary iodine excretion under the condition with a simple iodine-restricted diet in Japan, an iodine-sufficient area. Sixty-eight patients with thyroid carcinoma undergoing total thyroidectomy received single skin disinfection with either povidone-iodine (group A;  $n = 47$ ) or chlohexidine gluconate, a noniodine containing biguanide (group B;  $n = 21$ ). In group A, urinary iodine excretion on the first day after operation increased up to 7 times that of the preoperative value. The amounts of urinary iodine correlated positively with operating time. Increased urinary iodine, however, returned to preoperative values on the third or fifth day after operation. In group B, there was no increase in urinary iodine excretion and urinary iodine excretion was ranged from 54 to 193  $\mu\text{g/g}$  of creatinine on the third day of operation. In conclusion, a large amount of povidone-iodine was absorbed through healthy skin even in adults. This may possibly interfere with scintigraphy or radioactive iodine treatment, or cause thyroid disinfection in susceptible patients.

## Introduction

**P**VIDONE-IODINE is an effective, safe antiseptic, and therefore is used frequently in various fields as a broad-spectrum topical disinfectant (1,2). In burn patients (3,4) and infants (5,6), the skin is very thin or permeable, and marked transcutaneous iodine absorption has been reported. However, in adults, healthy skin is much less permeable. There has been no report of transcutaneous iodine absorption in adults undergoing surgery.

The aim of this study was to assess transcutaneous iodine absorption in patients who have single topical application with povidone-iodine and the serial changes of the urinary iodine level after total thyroidectomy in patients with thyroid carcinoma. To avoid the influence of an iodine rich diet, patients were kept on a iodine-restricted diet after admission. It has been reported that the diet in Japan customarily includes foods rich in iodine and the mean urinary iodine excretion with a customary diet was 420–1760  $\mu\text{g/g}$  of creatinine (7).

## Materials and Methods

Total thyroidectomy was performed in 68 patients with thyroid carcinoma between September 2002 and December 2002. Informed consent was obtained from all participating patients. All operations were performed on the second or third day after admission. Patients received skin sterilization with either povidone-iodine (ISOJIN, Meiji Pharmaceutical Co., Tokyo, Japan) (group A;  $n = 47$ ) or chlohexidine gluconate (Maskin R, MARUISHI Pharmaceutical Co., Ltd., Osaka, Japan), a noniodine containing biguanide (group B;  $n = 21$ ), before their operations. Experimental protocol was performed prospectively and selection of sterilizing selection was done randomly, if not contraindicated. The mean ages of 47 patients (40 women, 7 men) in group A and 21 patients (19 women, 2 men) in group B were  $52.5 \pm 15$  (mean  $\pm$  standard deviation [SD]) and  $55.9 \pm 13$  years old, respectively. The difference in age or gender between the two groups was not significant.

Urinary iodine values were measured on the day of ad-

<sup>1</sup>Kuma Hospital, Kobe, Japan.

<sup>2</sup>Department of Otolaryngology, Head and Neck Surgery, Faculty of Medicine, Tottori University, Tottori, Japan.

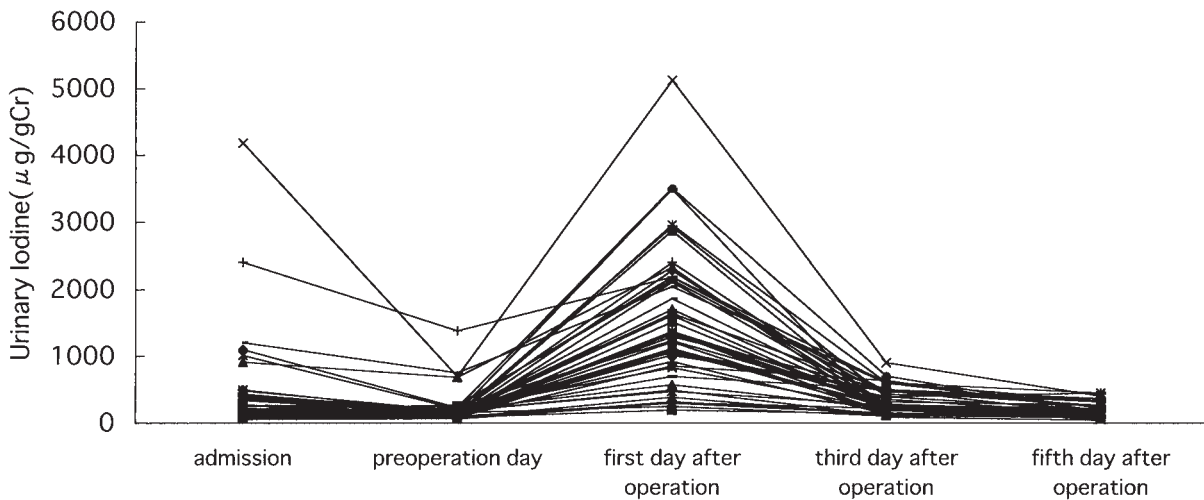


FIG. 1. The level of urinary iodine ( $\mu\text{g/g}$  of creatinine [Cr]) after povidone-iodine skin preparation.

mission (2 to 3 days before surgery), preoperatively and the first, third, and fifth day after skin preparation in both groups. Urinary iodine concentration was measured by a microplate method using Sandell-Kolthoff reaction (8). Because the urinary concentration in morning single specimens reflected dairy urinary iodine excretion (8), morning single urinary specimens were obtained from every patient. The iodine concentrations was expressed as microgram of iodine per gram of creatinine. Skin preparation was carried out in a standard fashion. Skin from the chin to the level of nipple was prepared with one of the disinfectants. The volume used for disinfection of povidone-iodine and chlohexidine gluconate was  $10 \pm 1.3$  mL (mean  $\pm$  SD). To avoid the influence of an iodine-rich diet, patients were kept on a iodine-restricted diet after admission. Iodine-restricted diets avoid seaweed and soup, which is used as a base for Japanese soup made by laminaria japonica. One bowl of soup can contain as much as 5 mg of iodine. There was no further contact with povidone-iodine or any other iodine containing compound after the operation. Also, after total thyroidectomy no patient received thyroid replacement medications throughout

the period of this study. Statistical analysis was performed by the Mann-Whitney *U* test and a *p* value less than 0.05 was considered significant.

**Results**

Serial changes of urinary iodine concentrations in individual patient of groups A and B are shown in Figures 1 and 2, respectively.

Table 1 shows the exact values of averages and standard deviation of urinary iodine excretion ( $\mu\text{g/g}$  of creatinine) in each group. Urinary iodine concentrations on admission ranged from 59 to 4182 (mean  $\pm$  SD :  $429.5 \pm 1077.3$ ). Individual values greatly varied. On the second or third day after admission, the urinary iodine concentrations were lower than the values on admission day, because of the iodine restricted-diet.

The urinary iodine levels after povidone-iodine skin preparation (group A) were significantly greater than the preoperative levels in each patient, and the mean level of urinary iodine rose nearly seven times. Also, the mean of uri-

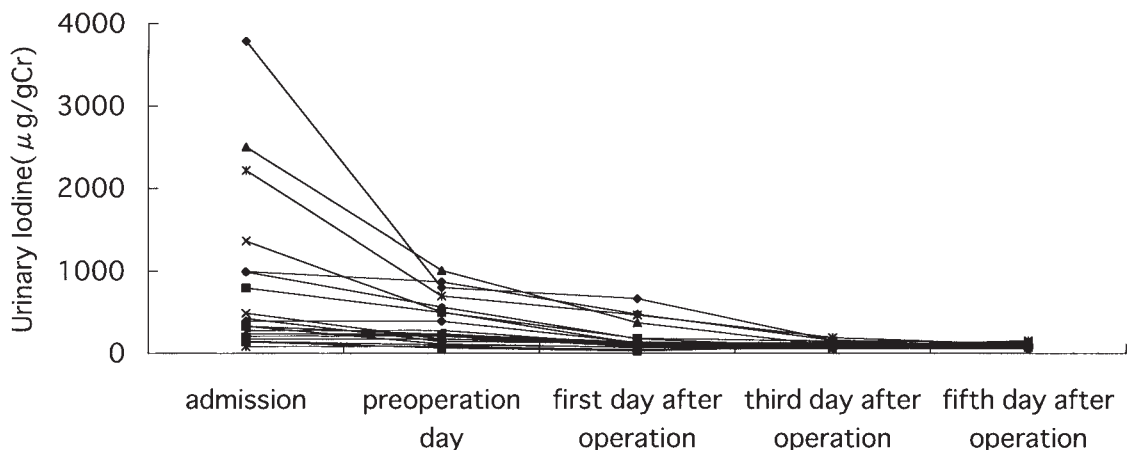


FIG. 2. The level of urinary iodine ( $\mu\text{g/g}$  of creatinine [Cr]) after chlohexidine skin preparation.

TABLE 1. URINARY IODINE LEVELS BEFORE AND AFTER USAGE OF STERILIZING SOLUTION

Sampling time	Povidone iodine (group A)	Chlohexidine gluconate (group B)	p value
Admission day	428.3 ± 690.3 (83–4182)	587.8 ± 819.41 (59–3787)	0.1779
Preoperation day	205.2 ± 230.7 (62–1381)	301.5 ± 271.9 (64–1008)	0.0891
First day after operation	1504.7 ± 984.9 ± (193–5120)	176.6 ± 169.5 (29–667)	< 0.0001
Third day after operation	319.7 ± 189.3 (85–904)	99.7 ± 39.1 (54–193)	< 0.0001
Fifth day after operation	177.8 ± 107.5 (44–451)	96.2 ± 26.5 (55–153)	0.0004

Values indicate  $\mu\text{g/g}$  of creatinine (Cr).

Results are expressed as mean  $\pm$  standard deviation (SD).

Data in parentheses indicate the range of distribution.

nary iodine concentration on the first day after operation in group A was significantly greater than that in group B. The amount of transcutaneous iodine absorption was calculated as follows: urinary iodine level in the first postoperative day minus urinary iodine level in preoperative day. Absorbed iodine amounts were positively correlated with operating time in Group A (Fig. 3). The levels of urinary iodine in group A returned to preoperative values on the third or fifth day after operation during the hospital-supplied iodine-restricted diet. In contrast, in group B, there was no increase in urine iodine concentration over the 24-hour period after operation. Urinary iodine excretion ranged from 54 to 193  $\mu\text{g/g}$  of creatinine on the third day after operation and there was little change after that.

## Discussion

Elevated urinary or serum iodine levels were found in many reports in patients treated with povidone-iodine preparation. Almost all cases were small infants undergoing operations (5) or neonates receiving skin cleansing (9). In adults, however, the skin is much less permeable, and thus transcutaneous absorption seems negligible. Elevated

urinary or serum iodine levels were reported in patients who had received a preoperative preparation for vaginal disinfection (10), daily vaginal douching (11), and for gargling (12,13). Similar results were obtained in burn patients (3,4). There was no report about transcutaneous iodine absorption in adults undergoing surgery. In this study, the urinary iodine levels after skin single preparation of povidone-iodine increased nearly 7 times the preoperative urinary level and ranged from 193 to 5120 (mean  $\pm$  SD :  $1504.7 \pm 984.9$ ) ( $\mu\text{g/g}$  of creatinine). Hyperthyroidism and hypothyroidism caused by a single absorption of iodine in infants undergoing operations (5) and elderly patients undergoing nonionic contrast radiography (14) have been reported in endemic iodine-deficient areas. The use of large quantities of povidone-iodine for irrigation of the mediastinum for 2 weeks also induced hyperthyroidism in iodine-sufficient area (15). In this study, patients had total thyroidectomy, so we could not determine whether thyroid dysfunction was caused by single administrations of povidone-iodine. However, the amounts of transcutaneous iodine absorption undergoing operations were not low. This raises the possibility that skin sterilization with povidone-iodine causes thyroid dysfunction in patients, particularly

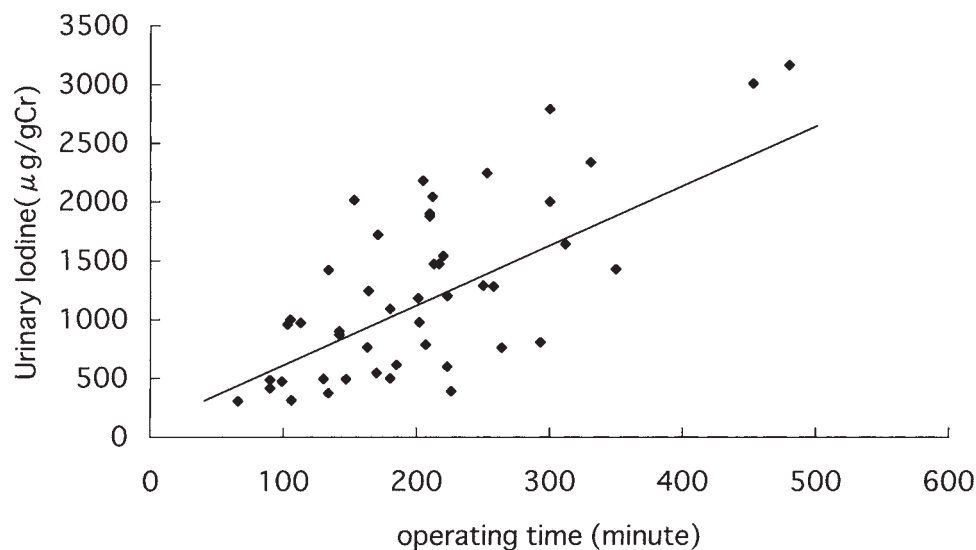


FIG. 3. Correlation of absorbed iodine amounts and operating time. Absorbed iodine amounts estimated as urinary iodine level in the first day after operation minus urinary iodine level in preoperative day. Absorbed iodine amounts and operation time were positively correlated ( $r = 0.72$ ,  $y = 6.0x + 11.2$ ).

those with preexisting thyroid disease who have iodine deficiency goiter and multinodular goiters.

We often attempt to keep the serum iodine levels low, for example, radioiodine-131 therapy after thyroidectomy for thyroid cancer. In general, a low-iodine diet for preparation is needed 1 or 2 weeks prior to the diagnostic radioiodine therapy. The kinds of restricted foods and the restricted terms vary in each country and hospital. However, in most cases, skin sterilization by povidone-iodine is not restricted. The amount of iodine incorporated after skin sterilization using povidone-iodine cannot be neglected. We must restrict not only foods but also the use of povidone-iodine when serum iodine needs to be limited.

In Japanese consuming Japanese-style meals, the urinary level of iodine is approximately 420–1760  $\mu\text{g/gCr}$  (7), and this iodine intake is higher than the World Health Organization (WHO) recommended daily intake of 150  $\mu\text{g}$ . Furthermore, daily urinary iodine excretion in each subject varies greatly according to the quantity and the frequency of ingestion of an iodine-rich diet. Patients were instructed to avoid seaweeds and soups that may be high in iodine, to avoid confounding the data. In this study, to avoid the influence of these iodine-rich diets, a simple iodine-restricted diet, by avoiding seaweed, was designed for inpatients. In our simple hospital-supplied low-iodine diet, mean levels of urinary iodine in patients in group B were lower than the 150  $\mu\text{g}$  that WHO recommended 7 to 10 days after admission, but did not reach the level of the low-iodine diets that are needed for preparation for radioiodine therapy, typically providing 50  $\mu\text{g}$  dietary iodine per day.

In summary, we have demonstrated marked transcutaneous absorption of iodine after skin preparation with povidone-iodine in adults undergoing a thyroid operation. If it is necessary for iodine in serum to be limited, for example, in radioiodine therapy, we should avoid preparation of the skin with povidone-iodine.

## References

1. Flynn J 2003 Povidone-iodine as a topical antiseptic for treating and preventing wound infection: A literature review. *Br J Commun Nurs* 8:36–42.
2. Georgiade GS, Georgiade NG, Grandy RP, Goldenheim PD 1990 The effect of povidone-iodine solutions used as surgical preparations on the bacterial flora of the skin. *Adv Ther* 7:1–8.
3. Lavelle KJ, Doedens DJ, Kleit SA, Forney RB 1975 Iodine absorption in burn patients treated topically with povidone-iodine. *Clin Pharmacol Ther* 17:355–362.
4. Rath T, Meissl G 1988 Induction of hyperthyroidism in burn patients treated topically with povidone-iodine. *Burns Incl Therm Inj* 14:320–322.
5. Mitchell IM, Pollock JC, Jamieson MP, Fitzpatrick KC, Logan RW 1991 Transcutaneous iodine absorption in infants undergoing cardiac operation. *Ann Thorac Surg* 52:1138–1140.
6. Brown RS, Bloomfield S, Bednarek FJ, Mitchell ML, Braverman LE 1997 Routine skin cleansing with povidone-iodine is not a common cause of transient neonatal hypothyroidism in North America: A prospective controlled study. *Thyroid* 7:395–400.
7. Nagataki S 1993 Status of iodine nutrition in Japan, In: DeLange F (ed) *Iodine Deficiency in Europe*. Plenum Press, New York, pp. 141–148.
8. Ohashi T, Yamaki M, Pandav CS, Karmarkar MG, Irie M 2000 Simple microplate method for determination of urinary iodine. *Clin Chem* 46:529–536.
9. Chabrolle JP, Rossier A 1978 Goitre and hypothyroidism in the newborn after cutaneous absorption of iodine. *Arch Dis Child* 53:495–498.
10. Vorherr H, Vorherr UF, Mehta P, Ulrich JA, Messer RH 1980 Vaginal absorption of povidone-iodine. *JAMA* 244:2628–2629.
11. Safran M, Braverman LE 1982 Effect of chronic douching with polyvinylpyrrolidone-iodine on iodine absorption and thyroid function. *Obstet Gynecol* 60:35–40.
12. Nobukuni K, Kawahara S 2002 Thyroid function in nurses: The influence of povidone-iodine hand washing and gargling. *Dermatology* 204:99–102.
13. Ader AW, Paul TL, Reinhardt W, Safran M, Pino S, McArthur W, Braverman LE 1998 Effect of mouth rinsing with two polyvinylpyrrolidone-iodine mixtures on iodine absorption and thyroid function. *J Clin Endocrinol Metab* 66:632–635.
14. Martin FI, Tress BW, Colman PG, Deam DR 1993 Iodine-induced hyperthyroidism due to nonionic contrast radiography in the elderly. *Am J Med* 95:78–92.
15. Rajatanavin R, Safran M, Stoller WA, Mordes JP, Braverman LE 1984 Five patients with iodine-induced hyperthyroidism. *Am J Med* 77:378–384.

Address reprint requests to:  
Chisato Tomoda, M.D.  
Kuma Hospital  
8-2-35 Shimoyamate-dori  
Chuo-ku, Kobe 650-0011  
Japan

E-mail: tomoda@kuma-h.or.jp