

# Use of povidone–iodine during the first trimester of pregnancy: a correct practice?

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Povidone–iodine (PVP-I) has been widely used as an antiseptic agent during invasive procedures for prenatal diagnosis. Women have been reported of thyroid dysfunction after simple exposure to PVP-I. We studied the effect on thyroid function and urinary iodine excretion after a single topical application of PVP-I in 31 women who had a miscarriage during the first trimester of pregnancy. PVP-I is absorbed through the skin and the vaginal

mucosa, resulting in a sudden increase in the urinary excretion of iodine and a short-term variation in concentrations of thyroid hormones in maternal serum. This metabolic effect could have consequences for the embryo and the fetus during crucial stages of development.

**Keywords** Iodine deficiency, povidone–iodine, pregnancy.

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## Introduction

Povidone–iodine (PVP-I), in a 10% aqueous solution, is a commonly used antiseptic to disinfect the surgical field in different types of surgery because of its antiseptic power and broad-spectrum microbicide. Most centres that carry out invasive prenatal diagnostic techniques use PVP-I on the skin of the abdomen in amniocentesis, chorionicentesis and trans-abdominal chorionic villus sampling as well as for vaginal irrigation prior to a transcervical chorionic villus sampling.<sup>1</sup>

The effects of exposure to PVP-I, both acute and chronic, on urinary iodine excretion and the thyroid hormones, in both adults and young children, especially premature infants,<sup>2</sup> have been known for some time. Women have been reported of thyroid dysfunction, both hypothyroidism and hyperthyroidism, after exposure to massive doses of iodine and, more specifically, after transcutaneous absorption of a single or multiple application of PVP-I.<sup>3</sup>

These effects have been reviewed elsewhere, with special emphasis on the induction of transitory hypothyroidism in newborn infants after exposure of their mothers to PVP-I during delivery. Its use, therefore, is discouraged in delivery rooms and newborn wards.<sup>2</sup> However, few studies have evaluated the effects of exposure to PVP-I during the first

trimester of pregnancy, either on maternal thyroid metabolism or regarding the possible consequences to the embryo and fetus.<sup>4,5</sup>

The aim of this study was to assess the effect of an application of PVP-I on urinary iodine concentrations and levels of thyroid-stimulating hormone (TSH) and free thyroxine (T<sub>4</sub>) during the course of antiseptic treatment prior to uterine evacuation by dilatation and curettage in first-trimester miscarriages.

## Materials and methods

This prospective study, undertaken between July and September 2006, involved 31 women with nonviable first-trimester pregnancies admitted to the Gynaecology and Obstetrics Service of the Hospital de la Merced, Osuna, Seville, Spain. We examined the absorption of PVP-I through the skin and the vaginal mucosa during uterine evacuation by dilatation and curettage in first-trimester miscarriages, which is similar to what occurs in invasive prenatal diagnostic techniques.

All the women underwent transvaginal ultrasound to confirm the diagnosis of miscarriage and the indication for uterine evacuation by dilatation and curettage. The gestational age in all the women was less than 14 weeks of amenorrhoea

(range 7<sup>+1</sup> to 13<sup>+2</sup> weeks), and the ultrasound gestational age was less than 12 weeks (range 6–11<sup>+3</sup> weeks). None of the women had any known chronic or acute disease at the time of diagnosis. Women were excluded if they had been taking micronutrient complexes containing iodine or potassium iodide supplements during gestation. A sample of blood and urine was taken from each woman immediately before the procedure.

Prior to the uterine curettage, sterile swabs were dipped into a 10% aqueous solution of PVP-I and applied immediately before surgery to the skin of the vulva and the vaginal mucosa as a surgical field antiseptic. It was generally not possible to exceed a total amount of 10 ml of antiseptic with all the swabs used to perform the antiseptics.

The following day further samples of blood and urine were obtained. The iodine concentration in urine samples was measured by the modified Benotti and Benotti technique.

The thyroid hormones were measured in a MODULAR ANALYTICS E170 (Roche Diagnostics GmbH, Mannheim, Germany). The intra-assay coefficient of variation of the free T<sub>4</sub> was 1.7%.

The women were informed verbally of the nature of the study and signed an informed consent form, which was authorised by the Ethics and Clinical Research Committee of the Hospital de la Merced, Osuna. (This Committee did not approve the study in normal pregnancies).

### Statistical study

The data are presented as the mean and SD. The distribution of frequencies of all variables included in the study was adjusted to the normal distribution (Kolmogorov–Smirnov test) ( $P > 0.05$ ). Differences between means were measured with the Student's *t* test (for paired data). The level of rejection of a null hypothesis was  $\alpha = 0.05$ . The study included 31 women. With this sample size, for an  $\alpha = 0.05$  and  $\beta = 0.80$  (for one tail), the study was able to detect statistically significant differences of at least 50 mg/l of iodine in the urine; this difference is clinically relevant and less than that found in the study.

### Results

Most of the women had a baseline urinary iodine concentration lower than 100 (Table 1), with thyroid hormone levels within normal ranges. Only one woman with undiagnosed subclinical hypothyroidism was found (low serum T<sub>4</sub> levels with raised serum TSH); this person was excluded from the study.

The topical application of PVP-I to the vulva and vaginal mucosa led to a very significant increase in urinary iodine in all the women (before: mean 67.51 ± 72.55 micrograms/l; after: 381.72 ± 156.45 micrograms/l). In some cases, the increase was greater than 30 times the baseline value and more

**Table 1.** Urinary iodine excretion (micrograms/l)

Patient	Iodine before	Iodine after	Iodine after/before
1	72.94	315.93	4.33
2	85.38	140.53	1.65
3	122.68	324.71	2.64
4	79.89	129.67	1.62
5	100.5	580.75	5.77
6	10.89	398.11	36.55
7	18.92	520.18	27.49
8	42.08	341.68	8.11
9	20.61	546.64	26.52
10	37.61	498.56	13.25
11	28.49	286.13	10.04
12	34.32	520.18	15.15
13	62.69	618.42	9.86
14	3.03	580.75	191.66
15	14.12	54.31	3.84
16	31.08	172.34	5.54
17	91.34	510.58	5.59
18	37.24	303.94	8.16
19	345.59	608.02	1.75
20	251.98	312.1	1.23
21	67.91	510.58	7.52
22	23.71	307.53	12.97
23	133.64	447.2	3.34
24	20.01	359.82	17.98
25	48.29	342.54	7.09
26	62.24	247.49	3.97
27	51.04	543.54	10.64
28	35.89	180.97	5.04
29	44.73	239.76	5.36
30	12.90	511.27	39.66
31	41.28	379.05	9.18

intense in those women who had lower urinary iodine levels before the procedure (<50 micrograms/l)

The levels of free T<sub>4</sub> fell significantly 24 hours after the application of PVP-I (before: 16.92 ± 2.5 pmol/l; after: 16.49 ± 2.5 pmol/l;  $P = 0.05$  by Wilcoxon), with no significant change in TSH levels (before: 1.94 ± 2.42 µU/ml; after: 1.94 ± 2.21 µU/ml;  $P =$  not significant).

### Discussion

The main finding of this study was that just one single dose of PVP-I applied during preparation for uterine curettage resulted in a 30-fold increase in urinary iodine concentrations and a slight, but nevertheless significant reduction in free T<sub>4</sub> within 24 hours of application.

Numerous studies have shown that the cutaneous or mucosal absorption of PVP-I results in a series of transitory and reversible changes in thyroid metabolism, especially a state of transitory hypothyroidism, known as the acute

Wolff–Chaikoff effect.<sup>6</sup> Below *et al.*<sup>3</sup> calculated the systemic absorption of different concentrations of PVP-I for conjunctival and periorbital antiseptics during cataract operations. According to their calculations, the application of 1 ml of 10% PVP-I to the skin and mucous membrane represented an increase in free urinary iodine of 1000 micrograms/g of creatinine, whereas when it was just applied to the conjunctiva, the amount of free iodine in the urine only rose by half (500 micrograms/g of creatinine).

The overload represented by simple exposure to PVP-I causes a sharp rise in urinary iodine excretion as well as functional blockade in the thyroid gland, with temporary inhibition of the biosynthesis and secretion of thyroid hormones. This effect is dose dependent and is more intense and prolonged in persons who have a nutritional iodine deficiency.<sup>6</sup>

Iodine deficiency remains the most common endocrine disorder worldwide and the most frequent cause of preventable mental retardation,<sup>7</sup> and it is a special public health problem in Europe, which may contribute to a negative balance in maternal iodine. Escape from the acute Wolff–Chaikoff effect takes about 2 days, although it may last longer in states of chronic iodine deficiency or immaturity of the thyroid gland (preterm infants and neonates).<sup>6</sup>

A previous study undertaken by our group in 520 pregnant women<sup>8</sup> found a urinary iodine concentration during the first trimester of 70.22 micrograms/l and a free T<sub>4</sub> of 14.80 pmol/l. These figures are in agreement with those found in the present study prior to exposure to PVP-I.

The application of iodine antiseptics in pregnant women and the subsequent absorption of the iodine release it into the maternal circulation. This not only has known embryotoxic effects in mouse embryos at all concentrations tested (even 1:100 000) and worsens outcome of *in vitro* fertilisation,<sup>5</sup> but at the same time, the metabolic effect of the suppression of thyroxin synthesis during the first trimester of pregnancy may lead to a transitory state of maternal hypothyroxinaemia. Maternal hypothyroxinaemia during the first trimester is associated with permanent and irreversible lesions in the cytoarchitecture of the cerebral cortex in the embryo and fetus.<sup>7</sup>

Although the reduction in the plasma concentration of free T<sub>4</sub> found in our study was slight, it should be remembered that T<sub>4</sub> has a half-life of 5–7 days, with biologically significant amounts still showing even 20 days later. The measurement of hormones in blood 24 hours after exposure, therefore, only detects the start of changes in plasma concentration. Moreover, this reduction in maternal T<sub>4</sub> occurred at a time of embryonic development prior to the onset of fetal thyroid function when its function is vital to determine neuronal migration and the neocortical cytoarchitecture of the embryo.<sup>7</sup>

Maternal transfer of T<sub>4</sub> has an important protective role in fetal neurodevelopment, and exposure to chemical, pharma-

cological or environmental agents that interfere in the maternal plasma concentration of free T<sub>4</sub> during the first trimester of pregnancy must be identified and avoided, if possibly.

A solid body of evidence now exists on the importance of an adequate intake of iodine during pregnancy as well as the deleterious effect of excessive amounts of iodine on thyroid function. However, questions such as the difference in absorption of iodised disinfectants between the vaginal mucosa and the skin or the effect on cognitive maturation of one single exposure to PVP-I during pregnancy still remain to be answered in full. Nevertheless, with our current knowledge, the use of iodine antiseptics (especially PVP-I) might be considered with special caution during the first trimester of pregnancy.

### Disclosure of interest

The authors declare that they have no conflict of interest associated with this study.

### Contribution to authorship

I.V., S.N. and C.L.-P. enrolled the women and performed curettages. M.J.G. and E.G.-F. performed the analyses of thyroid hormones and urinary iodine concentrations. I.V. and F.S. designed the study, analysed the data and wrote the paper.

### Details of ethics approval

This study needed two extra blood samples from each woman. It had the approval of the Research Department of the Hospital de la Merced (Osuna) and the Regional Ethics Commission (Andalusia). Documents have been included.

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