

The Potential Risk of Povidone-Iodine in Sperm Quality: A Case Report

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ABSTRACT

To report a rare case of severe oligoasthenoteratozoospermia which seems to be associated with long-term topical povidone-iodine (PVP-I) therapy. A 45-year-old man with secondary infertility was diagnosed with mild asthenospermia before undergoing in vitro fertilization (IVF). A repeat sperm analysis (SA) on June 30, 2022, after 3 months of using compound PVP-I liniment to treat fungal infection under a fingernail and toenail, revealed severe oligoasthenoteratozoospermia. After 77 days of drug withdrawal, sperm concentration, and normal morphology gradually returned to normal, but motility was only partially restored. It seems that the usage of PVP-I has a side effect of causing a decline in sperm quality. Although the exact mechanism of this adverse effect of PVP-I is unclear, men who are in fertility treatment should be informed of the potential risks.

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INTRODUCTION

Compound PVP-I liniment is a widely used over-the-counter dermatology drug indicated in the treatment of fungal or bacterial infections of the skin or nails, in which each milliliter contained 30 mg of PVP-I and 120 mg of aspirin. The auxiliary materials used are glycerin, polyethylene glycol, phenol, ethanol, and povidone K30. PVP-I is a complex of polyvinylpyrrolidone and iodine and its bactericidal component is the free iodine.¹ It has the ability to penetrate microorganisms quickly and oxidize proteins, nucleotides, and fatty acids,

eventually causing cell death.² Several adverse effects have been reported for PVP-I, including allergic reactions,³ kidney failure, and hypothyroidism.^{4,5} No studies, however, have reported an adverse effect of PVP-I on sperm quality. There is evidence in this case report that PVP-I negatively impacts male reproductive function.

CASE

A 45-year-old man and his 37-year-old female partner experienced secondary infertility for 5 years following a spontaneous

TABLE 1.

Changes in Sperm Parameters

Date (Drug withdrawal period)	Days of abstinence	"Semen volume (ml)"	"Sperm concentration (×106/ml)"	"Total spermatozoa in ejaculate (×106)"	"Total motility (%)"	"Progressive motility (%)"	"Total progressive motile sperm in ejaculate (×106)"	"Sperm morphology (%)"
09/09/2019	3	2.6	31.6	82.2	30	22	18.1	4
03/15/2021	5	2.0	165.2	330.4	42	26	83.6	7
06/30/2022(0)	5	1.2	0.8	1.0	0	0	0	1
07/04/2022(4)	2	1.3	2.9	3.8	0	0	0	1
07/18/2022(18)	5	1.8	25.6	46.1	3	2	0.9	None
08/12/2022(43)	5	2.3	17.6	40.5	5	3	1.2	None
09/04/2022(66)	6	2.0	11.7	23.4	31	16	3.8	None
09/15/2022(77)	5	2.1	23.4	49.1	22	11	5.5	10
Reference values*	--	≥1.5	≥15	≥39	≥40	≥32	--	≥4

*Reference values accordingly to World Health Organization, 2010.

abortion in June 2017. According to the sperm classification established by the WHO (WHO, 2010), his sperm concentration and morphology in 2019 and 2021 were normal, except for a slight reduction in motility (Table 1). It was diagnosed in 2021 that his female partner had a low ovarian reserve. They have undergone 3 cycles of in vitro fertilization (IVF) procedure at another IVF center since May 2021. Due to only one matured follicle, the first cycle was eventually canceled. After retrieving one mature oocyte from the second cycle, fertilization occurred normally and an 8-cell embryo of good quality grade 1 was obtained on day 3. His wife was not pregnant after frozen embryo transfer (FET). One mature oocyte was retrieved in the last cycle, resulting in normal fertilization and a good quality day 3 embryo (7 cells, grade 1). Finally, his wife did not become pregnant after undergoing FET.

He came to our center in June 2022 seeking treatment for Assisted Reproductive Technology. He reports no drinking or smoking habits, no family history of infertility, and no difficulties with sexual function. No previous medical or surgical history has been reported. In physical examination of the scrotum, there was no sign of varicocele. Using Prader orchidometry, the left testis volume was measured to be 15 mL and the right to be 14 mL. At our center, the patient's first sperm analysis (SA) was carried out on June 30, 2022, and showed a 0.8×10^6 sperm/mL concentration, a 1% normal sperm morphology rate, and 100% type D spermatozoa. As of this time, the patient reported having used compound PVP-I liniment on his left index fingernail and right fourth toenail for 3 months because of fungal infection (Figure 1). He used this drug twice a day. Each time he applied the liniment, he rubbed the infected nails with a metal nail file, and frequently bleeding. The liniment did not cause any complications during the treatment. PVP-I liniment was the only medication he was using during that time. The patient voluntarily suspended the antifungal treatment to see if it contributed to the severe oligoasthenoteratozoospermia. The SA was repeated after 4 days and showed a 2.9×10^6 sperm/mL concentration, a 1% normal sperm morphology rate, and still no sperm motility. Eighteen days after the medication was interrupted, a new SA showed a sperm concentration of 25.6×10^6 sperm/mL, and 3% sperm motility. On days 43, 66, and 77 after discontinuation of the liniment, the SA was repeated, respectively (Table 1). Sperm

concentration and morphology gradually returned to normal, but sperm motility did not return to baseline levels.

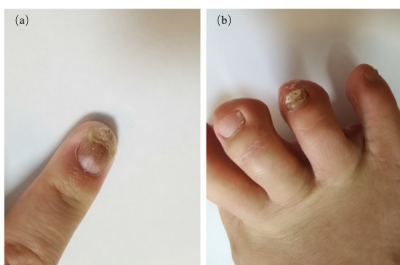
One week before discontinuation, the patient underwent thyroid hormone measurements during his annual health check-up, which showed normal thyroid-stimulating hormone (TSH), serum thyroxine (T4), triiodothyronine (T3), free thyroxine (FT4), and free triiodothyronine (FT3). Results: TSH 1.438 μ IU/mL 3.3-4.5 μ IU/mL, T4 7.63 μ g/dL (4.9-13.8 μ g/dL), T3 1.27 ng/mL (0.75-1.96 ng/mL), FT4 0.93 ng/dL (0.75-1.6 ng/dL), and FT3 2.37 pg/mL (1.8-4.3 pg/mL). On the 77th day of drug termination, the patient's sex hormone test showed a mild decrease in serum testosterone levels, the results are as follows: luteinizing hormone (LH) 4.94 IU/L, follicle-stimulating hormone (FSH) 3.55 IU/L, total testosterone (TT) 8.43 nmol/L, total estradiol (E2) 158.90 pmol/L, prolactin (PRL) 248.70 mIU/L.

DISCUSSION

We experienced a rare case of a patient suffering from severe decreased sperm quality due to topical treatment with PVP-I. Despite its safety in skin and mucosa, excessive iodine absorption from PVP-I can cause toxicity.⁶ It is estimated that one-third of the iodine entered into the body is absorbed by thyroid tissues and thyroid hormones, and the rest is distributed in various tissues such as breast tissue, eyes, gastric mucosa, cervix, prostate, testes, ovaries, and salivary glands, increasing the risk of organ toxicity.^{7,8} As a result of rubbing infected nails with a metal nail file, the mucosa was exposed, even bleeding, which facilitated the absorption of iodine. It is possible for excess iodine to damage reproductive organs.⁹ As a result of excess iodine, semen quality declines,¹⁰ sperm counts decline,¹¹ and dead spermatozoa and abnormal sperm morphology occur.⁹ Despite this, there are still no reports of sperm quality declining after topical application of PVP-I. In this case report, based on the changes in SA before and after drug withdrawal, we speculate that long-term use of PVP-I liniment may have serious consequences for sperm quality. Germ cells need nearly 76 days to complete their maturation, it would take approximately this time to recover normal sperm production after impaired spermatogenesis. In this case, the patient's sperm quality was partly restored after 77 days of PVP-I interruption. Therefore, whether this adverse effect is completely reversible needs further observation.

Reactive Oxygen Species (ROS) may contribute to the correlation between iodine excess and semen quality. Iodine accumulation causes an imbalance in antioxidant and pro-oxidant levels in the testis, resulting in excessive ROS production, which promotes apoptosis through the mitochondrial pathway.^{7,12} A high amount of iodine can disrupt the blood-testis barrier and cytoskeleton, as well as disrupt the communication between Sertoli cells and Sertoli cells and germ cells, leading to the loss of structural and functional support required for germ cell development.⁷

FIGURE 1. Fungal infection of left index fingernail (A) and right fourth toenail (B).



CONCLUSION

To our knowledge, this is the first case of adverse effects on sperm quality associated with PVP-I use. Caution should be advised against the use of PVP-I in male partners of couples who are attempting to become pregnant. Considering that this study is a case report, further experimental studies are required to investigate the effect of PVP-I on sperm quality.

DISCLOSURES

The authors certify that they are not involved in any organization with any financial or nonfinancial interest, in the subject matter discussed in the manuscript.

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