

Fatal Factors Related to Abuse of Propofol (Diprivan) A Case Report and Review of the Literature

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프로포폴 남용과 관련된 사망 사례 및 문헌 고찰

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We report the case of the death of a 38 year-old male plastic surgeon found dead at his own hospital. The only notable reason for his death was intravenously administered propofol. An ampoule of propofol of 20 ml was discovered beside him. Although the pharmacokinetics of propofol would not allow the abuser to insert more than one bolus injection before losing consciousness, the infusion would be continuous in this case via fluid agent. However, the blood concentration of propofol was within therapeutic level, we concluded that death was the result of side effects rather than an overdose similar to other cases of propofol fatalities. In the present case, a continuous infusion contributed the most to the lengthy apnea. As medical professionals are a high incidence group of propofol abuse for recreational use, it would be necessary to investigate on the factors that could cause amplified side effects in cases of propofol fatalities unrelated to overdose.

Key words : propofol, fatality, abuse

Introduction

Propofol is a quickly acting intravenous agent widely used in induction and maintenance of anesthesia. There have been a few reports in forensic areas about abuse, accidental, suicidal and homicidal overdose. Although mainly abused for its sedative and relaxing properties,¹ propofol could also be abused for sexual illusions and disinhibitions causes while awakening from the narcotic-induced sleep.²

Since propofol has a rapid onset and short action period,³⁻⁵ deaths related to self-abuse are rarely suspected as a result of overdose.⁶⁻⁹ Not only has the quick narcotic action of propofol allowed the user of only one bolus injection,⁹ but also the short half-life and high clearance rate of propofol makes it

impossible for the concentration of propofol to accumulate in the blood. Consequently, several reports that deal with fatality of propofol self-abuse commonly report blood concentrations to be within therapeutic ranges (for inducing anesthesia, normally 2.0-2.5 mg/kg, blood concentration 2-6 mg/L), and conclude that death was the result of side effects such as apnea.⁹ In our case, the scene of death suggested that propofol could have been infused for a long time with fluid agent inserted in the dorsal vein of the hand. However, propofol concentration was within therapeutic range and even lower than many of previously reported cases of propofol abuse.

Case Report

A 38-year-old male plastic surgeon was found dead

in the recovery room of his own hospital around 3:30 am, with fluid agent pinned into the dorsal vein of his hand. He was reported to have bought the medicine, which he himself had prescribed, the day before around 6:00 pm under the name of his assistant nurse. He was known to have taken the medicine with alcohol. The weight of the deceased was 74 kg, and the height was 167 cm. He had a puncture in the right dorsal vein of the hand. Lividity was observed strongly on the posterior surface of the body, with medium level of rigor mortis. Several petechial bleedings were found on the palpebral conjunctiva.

The main autopsy findings were mild fatty liver and dark-semisolid clots in the heart while the coronary arteries, aorta, brain and kidney were not specific except from moderate congestion. Microscopic examinations revealed the grade I steatosis in the liver and congestion in other organs.

During the autopsy, blood and gastric contents was taken for toxicological tests. With the routine screening of organic poisons, high performance liquid chromatography was performed. The analysis showed 0.72 mg/L of propofol in femoral blood. However, blood alcohol concentration was found to be lower than 0.01%. Metallic poisons, CNS agents, opioid derivatives were all negative.

The overall consideration of the fact that the deceased was found dead alone, the testimony that propofol was connected to the bag of liquid agent which was inserted into vein, the absence of disease or any trace of external force, and the propofol found in the blood lead to concluding the cause of death to be propofol poisoning.

Discussion

Propofol, a short acting intravenous agent (2,6-disopropylphenol), was put into practical use in 1977 for inducing anesthesia.¹⁾ Like other CNS inhibitors

(barbiturates, etomidate) propofol is known to activate the chloride ionophore complex of GABAA receptor. The advantages compared to other anesthetics are its rapid onset, short action period,¹⁰⁻¹²⁾ and lower occurrence of emesis and nausea.¹⁰⁾ However, the occurrence rate of apnea when using propofol as an anesthetic is quite high.^{11, 13)} Also, propofol has a greater effect in depressing the respiratory system compared to thiopental sodium,¹²⁻¹⁴⁾ which is widely used.

In this case of propofol fatality, the question seems to be not the dosage the deceased consumed, but rather the multiple factors that caused the severe side effects. Petechial bleedings, dark-red semisolid clots, and organ congestion seem to imply suffocation, which could be caused by apnea, usually a minor side-effect of propofol. However, as some reports deem propofol to present no practical side effects,¹⁵⁾ it is important to find out the factors which amplified minor side effects, thereby causing fatality. To assess the relevance of side effects as a cause of death, previous cases of propofol fatalities have been compared to our case.

Our case seems to have lower blood concentration of propofol than most of the other fatality cases (Table 1). Although it might be possible that blood concentration levels had dropped from the time of death until being discovered, considering that postmortem hepatic blood flow decreases, blood concentration would not greatly differ from the original level. Since it was reported that a high level of blood concentration leads to higher frequency and longer period of apnea,^{3, 4)} blood concentration level should not have been a critical factor in lengthening the period of apnea.

One of the noticeable aspects of this case compared to other previous cases is that the induction of propofol was done via Ringer's lactate solution rather than a bolus injection. In the case of using fluid agent,

Table 1. Propofol Concentration in Blood and Liver Tissue in this Case and in those Reported in the Literature

	Drummer ⁶⁾	Chao ⁷⁾	Iwersen-Bergmann ⁹⁾	Kranioti ⁸⁾	Our Case
Blood concentration (mg/L)	0.22	2.5	5.3	2.4	0.72

the injection speed, lower than normal bolus injection. It was reported that the lower the injection speed, the less likely it is for the apnea to be lengthy.⁵⁾ Therefore, the speed of injection could be irrelevant to fatality.

However, it is noticeable that the infusion time was longer than most cases due to use of fluid agent. The amount of propofol required for the induction decreases as injection speed decreases.¹⁶⁾ Therefore, with low infusion rate, the deceased would have been unconscious with less amount of propofol than required in most of the other inducing. Additional continuous infusion to aforementioned state would have been more than a sufficient dose for the deceased. Although the amount of dosage in itself does not trouble any restrictions or recommended therapeutic dose of propofol, a higher amount of injection would lead to higher frequency and longer period of apnea.^{5, 17)} Thus, a lengthy infusion time could be suspected as the fatal factor of causing apnea.

Age may be considered as another factor. In aged people, the required amount for induction is less.¹⁸⁾ Because the hepatic blood flow decreases in aged person, the central clearance decreases. Furthermore, the volume of central compartment in the three-compartment model decreases as age increases, and thereby creates the initial peak of blood concentration. Age could affect the frequency of apnea as a side effect of propofol injection. 9.1% of the people under 65-year-old had apnea, while 19% had apnea for those who were over the age of 65.¹⁸⁾ However, the deceased was 38 year-old, and would not have been affected significantly by age. Although there were number of factors which might have caused the side effects of propofol to be critical, lengthy infusion of propofol via Ringer's lactate solution could be the main cause for heavy respiratory depression in this case.

요 약

본인 소유의 의원 침대에서 정맥 주사를 삽입한 상태로 사망한 38세 남자 의사에 대해 사후 검사를 실시하였다. 부검에서 결막의 점상출혈, 암적색 혈액 및 고형 장기의 울혈 등의 질식

의 일반적인 소견이 관찰되었으나 다른 장기에서의 특이 사항은 관찰되지 않았다. 넓다리의 말초 정맥혈의 검사결과 프로포폴의 농도는 0.72 mg/L의 수치로 치사량 이내로 측정되었다. 이에 저자들은 프로포폴이 링거액과 함께 투여 시간이 길어질 경우 질식 등의 부작용이 나타날 수 있음을 문헌을 통해 고찰하였다. 프로포폴은 의료 전문가에 의해 남용이 되는 대표적인 약물로, 투여시간, 연령 등의 다양한 원인에 의해 치사량 이내에서도 부작용에 의해 사망할 가능성이 있음을 보고한다.

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