

ISMP Canada Safety Bulletin

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ALERT: Infusion Errors Leading to Fatal Overdoses of *N*-Acetylcysteine

Acetaminophen is safely used by millions of people worldwide, but acetaminophen poisoning remains a leading cause of acute liver failure and medication-related death.¹ The antidote, *N*-acetylcysteine, can be a life-saving medication and is widely regarded to be safe, with generally mild, self-limiting adverse effects.² ISMP Canada recently received reports of fatal overdoses of intravenous (IV) *N*-acetylcysteine resulting from errors in pump programming. This bulletin is shared to alert stakeholders to the potentially fatal outcome of errors and to encourage review of the processes that support IV administration of *N*-acetylcysteine.

INCIDENT EXAMPLE

A patient arrived at the hospital with acetaminophen poisoning. IV administration of *N*-acetylcysteine was ordered, and the medication was promptly administered using a protocol that calls for a loading dose, followed by a maintenance dose to be given from the same infusion bag, but at a slower rate. The loading dose was completed, and the maintenance dose was incorrectly programmed to continue at the same rate as the loading dose. The error was noticed when the patient experienced nausea, vomiting, and seizures. The patient subsequently died.

This was one of two similar incidents of *N*-acetylcysteine overdose that were shared with ISMP Canada. Both involved patients under the age of 18 years, both involved a similar protocol for

IV administration of the antidote, both involved the pump being programmed to erroneously continue delivering *N*-acetylcysteine at the rate for the loading dose instead of the rate for the maintenance dose, and both resulted in a fatal outcome.

BACKGROUND

Serious adverse events, including death, following *N*-acetylcysteine overdose are rare but have been reported in the literature. Overdose (4- to 16-fold) of IV *N*-acetylcysteine has been linked to serious life-threatening adverse effects, including hemolysis and hemolytic uremic syndrome, cerebral edema, and seizures.³⁻⁷ Given that *N*-acetylcysteine for IV administration is prepared in 5% dextrose in water (D5W), an overdose results in the introduction of a substantial amount of fluid and other osmotically active components into the circulation; this, in itself, can lead to severe clinical harm.

DISCUSSION

Several protocols for the preparation and administration of IV *N*-acetylcysteine are in use across Canada.⁸ Preliminary review of the incidents reported to ISMP Canada has identified the pump-user interface, when following a defined protocol, as a key contributing factor.

In the incident example described above, the nurse followed an IV *N*-acetylcysteine protocol and had to

manually reprogram the pump to administer the maintenance dose after completion of the loading dose. During programming of the maintenance dose rate, the pump presented the loading dose rate as an option, which increased the likelihood that the incorrect rate would be programmed. Some smart pumps have a stepwise titration or sequential programming feature,⁹ which allows the pump to be programmed to automatically switch from the loading dose rate to the maintenance dose rate. The pump involved in the incident did not have this feature, and manual intervention was required to change the rate.

CONCLUSION

ISMPCanada continues to analyze these cases and is in the process of connecting with stakeholders, including poison centres across Canada, to identify strategies to prevent adverse events and deaths associated with IV *N*-acetylcysteine treatment errors. We encourage practitioners to report their experiences related to *N*-acetylcysteine protocols through the individual practitioner reporting portal, at https://www.ismp-canada.org/err_ipr.htm, or by email to info@ismpcanada.ca.

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