

# Inadvertent intrathecal administration of vincristine

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This new feature is designed to help protect your patients with updates on adverse events related to various cancer treatments.

**D**espite its boxed label warning, there have been a number of cases in which vincristine was inadvertently administered intrathecally. When given in this way, vincristine causes central nervous system (CNS) toxicity, producing progressive ascending myeloencephalopathy. The first sign is evident in the neurons that innervate the distal lower extremity; it is characterized by leg weakness, leg pain, and loss of the tendo calcaneus reflex.<sup>1</sup> Autonomic dysfunction may follow with urinary retention. Symptoms of meningitis such as stiffness in the neck and high fevers may also occur. Generalized inflammation and dysfunction of the CNS lead to respiratory failure and death. Attempts to mitigate the toxic effects with cerebrospinal fluid lavage and glucocorticosteroids remain largely unsuccessful.<sup>1</sup>

## Where reported

The first reported case of intrathecal administration of vincristine sulfate occurred in the United States in 1968 in a 23-month-old girl diagnosed with acute lymphocytic leukemia who was prescribed intrathecal methotrexate along with intravenous vincristine.<sup>2</sup> Inadvertently, 3 mg of vincristine was given intrathecally.

This mistake was recognized a short time later, and 200 mL of cerebrospinal fluid was exchanged with 200 mL of saline as medical management. Despite these efforts, the patient displayed thrashing movements and an opisthotonic posture the following day. On day 3, the patient developed respiratory paralysis, became comatose, and died.

The reasons for this medication error are not clear, but contributing factors may have included premature removal of the drug from its over-wrap packaging, unfamiliarity with cancer drugs and protocol, or failure to check physicians' orders by health-care workers. The autopsy report revealed evidence of neuronal changes produced by the effects of intrathecal vincristine.<sup>2</sup>

The Research on Adverse Drug Events and Reports (RADAR) project of Northwestern University conducted a review of the literature published from 1968 to June 2006. Since 1968, 55 cases of inadvertent intrathecal vincristine have been reported worldwide. In addition to cases in the US, intrathecal administration of vincristine has occurred in the UK, Australia, Israel, Saudi Arabia, and Singapore. While 32 cases have been documented in the literature, only 13 have been reported to the FDA MedWatch. Of those 32 cases, 27 (84%)

deaths have resulted (Table 1). Based on the literature findings, the three most frequently cited types of error were:

- physician/nurse and pharmacy error (69%);
- pharmacy error only (19%);
- physician-nurse error only (12%; Table 2).

In cases of physician/nurse and pharmacy error, reports show that intrathecal administration of vin-

## Fast Facts

### VINCRIStINE

Vincristine is an alkaloid isolated from the Madagascar periwinkle (*Catharanthus roseus*). Because vincristine sulfate has low octanol:water solubility, it results in low oral bioavailability and poor penetration of the CNS. Therefore, it is labeled for intravenous administration. The drug is used in both children and adults to treat a variety of hematologic malignancies and solid tumors including acute lymphoblastic leukemia, Hodgkin's lymphoma, and non-Hodgkin's lymphoma. Vincristine exerts its cytostatic effects on mitotic spindle fibers causing cell cycle arrest during metaphase.

Common side effects associated with intravenous vincristine include abdominal cramps and constipation, a temporary change in taste, bruising/bleeding, and neurotoxicity, which may be irreversible.

**TABLE 1**

Number of published case reports and deaths from inadvertent intrathecal administration of vincristine by region since 1968

Year	USA/ Canada	Europe	Australia	Asia	Total	Deaths
Prior to 1985	7	0	0	1	8	8 (100%)
1986-1990	1	0	1	0	2	1 (50%)
1991-1995	2	2	1	1	6	4 (66%)
1996-2000	4	1	0	3	8	6 (75%)
2001-2005	2	5	1	0	8	8 (100%)
Total	16	8	3	5	32	27 (84%)

cristine occurred most often because of inadequate communication between pharmacy and medical staff. In these situations, the pharmacy mistakenly delivered vincristine syringes with syringes containing intrathecal medications and physicians or nurses wrongly administered vincristine intrathecally. In cases of pharmacy error alone, the mislabeling of syringes was a common mistake, whereas physician/nurse error alone usually resulted from failure to read syringe labeling

**TABLE 2**

Number of cases of inadvertent intrathecal administration of vincristine attributed to each source of error reported since 1968

Year	Physician/ nurse + pharmacy	Pharmacy	Physician/ nurse
Prior to 1985	5	2	1
1986-1990	1	0	1
1991-1995	3	2	1
1996-2000	5	2	1
2001-2005	5	3	0
Total	19 (59%)	9 (28%)	4 (13%)

or to check physicians' orders.

Additional errors that contributed to the inadvertent intrathecal administration of vincristine include:

- Administration of other chemotherapy agents in combination with vincristine;
- Premature removal of the drug's overwrap packaging;
- Lack of awareness regarding labeling and dispensing requirements;
- Lack of familiarity with chemotherapy drugs and protocols.

### Recommendations

All of these cases involved a combination of human and system errors occurring in the medical, nursing, and pharmacy professions. Strategies and guidelines exist to prevent inadvertent intrathecal administration of vincristine. The most effective strategy is to sequester the intrathecal administration of chemotherapy drugs.<sup>3</sup> Thus, *intrathecal* administration of chemotherapy drugs should not occur at the same time or in the same location in the facility where *intravenous* adminis-

tration of chemotherapy drugs occurs.

In the US, the recommendations for preventing this error include:

- Clearly labeling vincristine as "FATAL IF GIVEN INTRATHECALLY. FOR INTRAVENOUS USE ONLY. DO NOT REMOVE COVERING UNTIL MOMENT OF INJECTION."
- Properly training healthcare workers to prepare, deliver, and administer vincristine or any chemotherapy drug.
- Implementing a formal checking procedure or "time out" at each institution.<sup>4</sup>

Intrathecal administration of vincristine is a fatal yet preventable error that needs to be fully understood. With clear labeling, proper awareness, and training of pharmacists, physicians, and nurses, this medication misadventure can be avoided.

### References

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