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Preventing Vincristine Sulfate Medication Errors

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Purpose/Objectives: To review the clinical pharmacology of vincristine sulfate, describe three types of medication errors associated with its use, and suggest strategies for vincristine sulfate medication error prevention.

Data Sources: Published books and journal articles, online newsletters and documents, pharmaceutical manufacturers' package inserts, and personal experience.

Data Synthesis: Medication errors involving vincristine sulfate include overdosage (wrong dose), name confusion (wrong drug), and incorrect administration (wrong route).

Conclusions: Vincristine medication errors are preventable errors that usually result in serious patient harm and often are lethal.

Implications for Nursing: Nurses need to be aware of the types of medication errors that can occur with chemotherapy agents and be familiar with clinical signs and symptoms associated with these errors. Nurses also need to promote patient safety by implementing specific strategies to prevent vincristine medication errors.

Since its introduction in 1963, vincristine sulfate, or vincristine as it is commonly known, has been used to treat a variety of cancers, such as acute lymphocytic leukemia, Hodgkin disease, non-Hodgkin lymphomas, rhabdomyosarcoma, neuroblastoma, and Wilms tumor. Because it has very limited efficacy as a single agent, this drug is given as a component of multidrug chemotherapy regimens (Rowinsky & Donehower, 2001; U.S. Food and Drug Administration [FDA], 2004).

Vincristine has been used widely for many years, and, as a result, most oncology nurses are very familiar with it. However, despite its extensive long-term use, vincristine has been associated repeatedly with various medication errors. This article reviews this agent and these errors, which include overdosage (wrong dose), name confusion (wrong drug), and incorrect administration (wrong route).

Clinical Pharmacology

Vincristine sulfate is the salt of an alkaloid obtained from a flowering herb, the Madagascar periwinkle plant (*Catharanthus roseus*, formerly classified as *Vinca rosea* Linn, which caused it to be called a vinca alkaloid) (Greuter et al., 1999). Vincristine inhibits microtubule formation in the mitotic spindle, re-

Key Points . . .

- Vincristine is administered by IV only.
- The major toxicity associated with vincristine is neurotoxicity that is dose related. Neurotoxicity usually is reversible with discontinuation of the drug.
- Vincristine overdoses cause sensory impairment and motor nerve involvement that can be debilitating and even fatal.
- Inadvertent intrathecal vincristine administration is usually fatal, and every effort to prevent this type of medication error should be employed.

Goal for CE Enrollees:

To enhance nurses' knowledge about the causes of and measures to prevent vincristine sulfate medication errors.

Objectives for CE Enrollees:

- On completion of this CE, the participant will be able to
1. Review the clinical pharmacology of vincristine sulfate.
 2. Describe the types of medication errors that most commonly occur during vincristine sulfate administration.
 3. Discuss strategies that may decrease the risk of medication error during vincristine sulfate administration.

sulting in the arrest of dividing cells at the metaphase stage and, because of this action, sometimes is referred to as an antimicrotubule agent. Vincristine has a triphasic serum decay pattern; the initial, middle, and terminal half-lives are 5 minutes, 2.3

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hours, and 85 hours, respectively. The primary route for excretion is the liver. Approximately 80% of a dose of vincristine appears in the feces, and 10% can be found in urine. Within 15–30 minutes following vincristine administration, about 90% of the bioavailable drug is distributed from the blood into the tissue, where it remains tightly bound (Facts and Comparisons, 2004; Rowinsky & Donehower, 2001).

Intended for IV use only, vincristine is supplied as a sterile, preservative-free solution at a concentration of 1 mg/ml in 1 mg and 2 mg vials that are refrigerated until use. The pH of vincristine ranges from 4–5; however, the drug should not be diluted in solutions that raise or lower the pH outside the range of 3.5–5.5. Prepared solutions must be refrigerated and protected from light. Vincristine can be given by IV bolus into the tubing of an infusing IV fluid or added to 50 ml infusion bags of 0.9% saline or 5% dextrose in water and rapidly infused (Facts and Comparisons, 2004; Gensia Sicor Pharmaceuticals, Inc., 1999; Mayne Pharma [USA Inc.], 2004).

Extravasation of vincristine results in irritation and tissue necrosis (Facts and Comparisons, 2004). Therefore, vesicant precautions are used when administering this drug. These precautions include ensuring the presence of a blood return before, during, and after vincristine administration; continuously monitoring patients for signs and symptoms of an extravasation while vincristine is being administered; avoiding the use of infusion pumps for vesicant administration; and educating patients about extravasation prevention and detection (Brown et al., 2001).

The major toxicity associated with vincristine is neurotoxicity, which may be dose limiting. Typically occurring as a symmetric peripheral neuropathy that is dose related, this toxicity usually can be reversed by discontinuing the drug. A common presenting symptom is paresthesia of the hands or feet. Further neurologic toxicity, including loss of deep tendon reflexes, severe pain, muscle weakness, foot or wrist drop, and rarely paralysis, can develop. Vincristine-induced autonomic dysfunction also may occur; symptoms include abdominal pain and constipation and, in severe cases, paralytic ileus (Gensia Sicor Pharmaceuticals, Inc., 1999).

The usual dose of vincristine for children weighing 10 kg or more is 2 mg/m² once a week. The adult dose is 1.4 mg/m², usually not to exceed 2 mg per dose. Dose reduction (usually 50%) may be required for patients with hepatic impairment (e.g., serum bilirubin > 3 mg/dl) (Gensia Sicor Pharmaceuticals, Inc., 1999; Mayne Pharma [USA Inc.], 2004).

Overdosage

Accidental overdoses of vincristine often have been attributed to omitted or unclear decimal points in the dose prescribed. This type of medication error results in a 10-fold overdose of the drug. For instance, in an early case report of a vincristine overdose, a decimal point was omitted from a handwritten order for a 3.2 mg dose of vincristine; as a result, a dose of 32 mg was administered. The overdose was discovered on the day following treatment when the 12-year-old patient experienced pain in her legs and bled from previous venipuncture sites. Marked abdominal distention developed, followed by confusion, stupor, seizures, and a coma. Supportive measures were ineffective, and the patient died 33 hours after the overdose of vincristine was administered (Kaufman, Kung, Koenig, & Giammona, 1976).

From 1970–2002, 18 case reports of patients who inadvertently received overdoses of vincristine were published. Vincristine overdoses resulted from decimal errors or errors in dose calculation or administration schedule. Signs and symptoms of vincristine overdose included sensory impairment and motor nerve involvement beginning within hours of the overdose. Involvement of cranial nerves III, IV, V, VI, VII, and X was reported, which caused loss of corneal reflexes, facial weakness, jaw pain, and hoarseness. Most patients developed a paralytic ileus, and two experienced atony of the bladder. All patients experienced some degree of cerebral dysfunction, including insomnia, agitation, confusion, and, occasionally, hallucinations and coma. Eleven patients had generalized seizure activity one to seven days following the overdose. Vincristine overdosage also caused severe bone marrow depression and inappropriate antidiuretic hormone (ADH) secretion. Presumably, vincristine acts on the hypothalamic nuclei to stimulate release of ADH. Fever also reportedly occurred. Although its exact mechanism is not known, fever may be related to direct hypothalamic stimulation. Patients who received large overdoses of vincristine did not survive. Causes of death included widespread hemorrhage and overwhelming infection. Two patients who received small overdoses recovered, but they had symptoms that were slower in onset and milder than those observed in patients who received 10-fold overdoses of vincristine (Berenson, 1971; Casteels-Vann Daele, Beirinckx, & Baines, 1977; Chae, Moon, & Kim, 1998; Grush & Morgan, 1979; Jochimsen, 1982; Kaufman et al., 1976; Kosmidis et al., 1991; Maeda et al., 1987; Stones, 1998; Thomas, Braat, Somers, & Goudsmit, 1982; Wakem & Bennett, 1975).

Not all vincristine overdoses are published in the literature; therefore, the extent of this type of medication error is unknown. The author is aware of two unpublished incidents of lethal vincristine overdoses that occurred in 2000 and 2002 that prompted legal action.

Vincristine has no antidote. Three of the patients in the published case reports were treated with leucovorin (two patients received 15 mg eight times daily for three days starting 48 hours after the vincristine overdose, and one patient received 12 mg four times daily for five days starting 24 hours after the vincristine overdose), based on the observation of a protective effect of leucovorin in mice that were given a lethal dose of vincristine. Despite leucovorin administration, one patient died from bone marrow aplasia and hemorrhage 68 hours following a 10-fold vincristine overdose. The two patients who also received leucovorin following a 10-fold vincristine overdose recovered, although a more rapid recovery time was not observed when they were compared retrospectively to patients who survived a vincristine overdose but did not receive leucovorin (Grush & Morgan, 1979; Thomas et al., 1982).

Because vincristine is metabolized rapidly by the liver and its metabolites are excreted primarily via the biliary system to the feces, only very small amounts of the drug appear in dialysate. Therefore, hemodialysis is not considered to be helpful following a vincristine overdose (Gensia Sicor Pharmaceuticals, Inc., 1999).

Treatment of a vincristine overdose is symptomatic and supportive. Close patient monitoring is necessary, and seizure precautions should be implemented. Because myelosuppression typically occurs, daily complete blood cell counts are

indicated, and blood product support may be required. Serum electrolytes and fluid balance are monitored closely to promptly detect inappropriate ADH secretion. The patient's abdomen is observed for distention and auscultated for bowel sounds, and abdominal x-rays are indicated when an ileus is suspected.

Vincristine overdoses are preventable medication errors. Healthcare providers need to be familiar with chemotherapeutic agents and their usual dose range and administration schedule. Any dose containing a decimal point needs to be written clearly or, preferably, typed or electronically entered. Trailing zeros, as in 2.0 mg, need be avoided; 2 mg should be used instead to avoid confusion and potential overdose. Each page of order forms that contain multiple layers needs to be inspected to ensure that orders are clear and complete (e.g., a decimal point may not be visible because the person writing the orders did not press down hard enough while writing). Orders that are unclear about the administration schedule or do not specify the length of treatment need to be clarified; vincristine overdoses also have occurred when the drug was administered daily instead of weekly as prescribed (Jochimsen, 1982).

Name Confusion

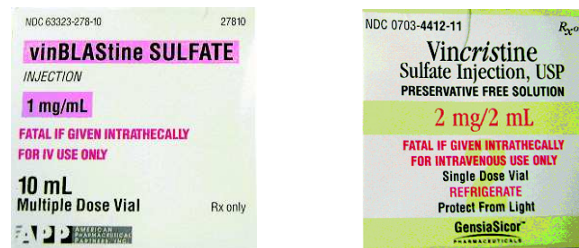
The vinca alkaloids represent a group of drugs that have been called "look-alike, sound-alike" drugs (Hoffman & Proulx, 2003). The vinca alkaloids include agents with similar sounding names: vincristine, vinblastine, vindesine, and vinorelbine. When these drug names are handwritten on order sheets, especially in script, the drugs being prescribed may be unclear. Confusion over similar names and inadvertent selection of the wrong product when drugs with similar names are stocked closely together has been reported to cause "wrong drug" chemotherapy medication errors (Boyle, Schulmeister, Lajeunesse, & Anderson, 2002; Schulmeister, 1999).

Strategies to prevent wrong drug errors for look-alike, sound-alike drugs have been developed by pharmaceutical manufacturers and healthcare providers. For instance, manufacturers highlight or emphasize a certain part of a drug's name on its label. Mayne Pharma (USA Inc.) in Paramus, NJ, uses what is termed "tall man" lettering when labeling its vials (e.g., vinCRISTINE Sulfate Injection), whereas Gensia Sico Pharmaceuticals, Inc., in Irvine, CA, uses italics (e.g., Vincristine Sulfate Injection) to more clearly distinguish vincristine from vinblastine (see Figure 1). To reduce potential confusion among the vinca alkaloids, healthcare providers who do not use automated dispensing systems should avoid stocking look-alike, sound-alike drugs in close proximity to one another and label storage bins with high-alert warning stickers. Education also is paramount so that everyone who prescribes, transcribes, prepares, handles, and administers chemotherapy is well informed about vinca alkaloids and the potential for name confusion.

Incorrect Route of Administration

Inadvertent Intramuscular Injection

Vincristine is given by IV *only*. In published anecdotal accounts, the drug has been injected inadvertently into the thighs of three children and into the gluteal muscle of a fourth. This type of medication error occurred as a result of a mix-up be-



Note. Italics are used in the word "vincristine" to help distinguish it from vinblastine.

Figure 1. Example of "Tall Man" Lettering on Vinblastine Sulfate Label to Help Distinguish the Drug From Similarly Spelled Vincristine Sulfate

tween a syringe containing vincristine and a syringe of L-asparaginase that each of the patients was scheduled to receive on the same day. The three children who received injections in the thigh were treated topically with cold compresses and an injection of 8.4% sodium bicarbonate to the affected areas. One of these children experienced pain after the inadvertent injection of vincristine, but none experienced any delayed adverse sequelae. For the fourth child who received the gluteal injection of vincristine, hot compresses were applied for 16 hours, beginning about six hours after the injection. Slight pain and erythema developed at the injection site but resolved completely within two weeks (Clark, Gallegos, & Bleyer, 1997; Olcay & Safak, 2003).

Because it is a vesicant, vincristine has the potential to cause tissue necrosis if inadvertently given subcutaneously or intramuscularly. Nurses giving chemotherapy should carefully read chemotherapy orders and drug labels, especially when multiple syringes are prepared for one patient, and administer the drugs per the correct route of administration.

Heat application is recommended for vincristine extravasations (Brown et al., 2001). In contrast, cold was applied (along with infiltration of the areas with sodium bicarbonate) to the injection areas of the three children who had been injected inadvertently with vincristine in their thighs (Clark et al., 1997). The authors of these case reports noted that tissue breakdown did not occur. Although sodium bicarbonate was used as a vincristine antidote, its role in managing vincristine extravasations or injections into the tissue has not been established. Hyaluronidase administered subcutaneously in a circumferential manner around the needle site has been used as an antidote for vinca alkaloid extravasations since the mid-1980s (Dorr & Alberts, 1985). Menzel and Farr (1998) postulated that hyaluronidase repairs tissue damage by promoting cell turnover, remodeling the tissue's extracellular matrix components, and stimulating angiogenesis (i.e., the formation of capillaries).

From 2001–2004, the injectable formulation of hyaluronidase was available only through pharmacies that compound the drug. Wyeth-Lederle (now Wyeth-Ayerst in Philadelphia, PA) discontinued manufacturing the drug in 2001. On May 5, 2004, the FDA approved Vitrase® (hyaluronidase for injection, Cardinal Health, Albuquerque, NM) as an adjuvant treatment to increase the absorption and dispersion of other injected drugs. The product is provided in vials containing 6,200 units of hyaluronidase that are being distributed as samples. FDA permission to market the product in vials containing 150

units of hyaluronidase in 1 ml of a ready-to-use solution is pending. After permission is obtained (estimated by December 2004), commercial sale of the product will begin (American Society of Health-System Pharmacists® [ASHSP], 2004a, 2004b).

Hyaluronidase also can be obtained from pharmacies that compound the drug. However, compounded drugs are not FDA-approved products because the FDA has no control over the quality or consistency of the manufacturing process. In addition, compounding practices and the legal restrictions on these practices vary from state to state (ASHSP, 2004a). Clinicians need to screen suppliers that compound hyaluronidase injection and inquire about their quality control practices.

Recommendations for managing the inadvertent injection of vincristine cannot be made because few case reports have been published and patients have been treated in different ways. However, healthcare professionals should assess injection sites as well as pain in patients who inadvertently receive vincristine intramuscularly rather than by IV. Applying heat with warm compresses and elevating and resting the affected area also may be helpful.

Inadvertent Intrathecal Administration

Administration of vincristine via the spinal route (intrathecally via a lumbar puncture or intraventricularly via an Ommaya reservoir) rather than by IV as prescribed causes severe neurologic damage and often is fatal. In addition to harming patients, inadvertent intrathecal administration of vincristine has prompted legal action, including malpractice and manslaughter charges. In a review of 17 lethal incidents that occurred in the United Kingdom from 1970–1999 that resulted in physicians being charged with manslaughter, two were incidents in which vincristine was given intrathecally (Ferner, 2000).

The first reported account of inadvertent intrathecal vincristine administration was published in 1968 (Schochet, Lampert, & Earle, 1968). Since then, at least 20 deaths from inadvertent intrathecal vincristine administration are known to have occurred in the United States, Canada, the United Kingdom, Germany, Saudi Arabia, Singapore, and Korea. In the United Kingdom alone, the National Health Service recorded 14 incidents of inadvertent intrathecal vincristine administration that occurred from 1986–2001 (Woods, 2001). Lethal inadvertent intrathecal vincristine administration is documented to have occurred as recently as 2003 in the United States (Institute for Safe Medication Practices [ISMP], 2003).

The incidence of inadvertent intrathecal vincristine administration is not known. Some of these incidents, particularly lethal events, prompt publication. Sometimes these incidents are reported to organizations such as the ISMP but are not published as case reports. Inadvertent intrathecal vincristine administration also occasionally has received media attention.

In a February 2001 editorial in the *BMJ*, Donald Berwick, president and chief executive officer of the Institute for Healthcare Improvement in Boston, described his frustration in learning of repeated accounts of inadvertent intrathecal vincristine administration by writing, “Again, a young patient with leukemia is dying, not from his disease, but from an erroneous intrathecal injection of vincristine, intended for intravenous use. Again, the newspapers express outrage . . . the

hospital apologizes again . . . and steps will be taken, again” (Berwick, 2001, p. 247). Berwick raises the interesting question of how could this error happen—again and again?

Inadvertent intrathecal vincristine administration usually has occurred when a syringe containing vincristine intended for IV administration was confused with another syringe containing a drug to be given intrathecally (usually methotrexate or sometimes cytarabine). On other occasions, healthcare providers assumed vincristine was an additional intrathecal drug to be injected when syringes were mislabeled (Fernandez, Esau, Hamilton, Fitzsimmons, & Pritchard, 1998). Although intrathecal chemotherapy typically is administered by physicians and, in some cases, advanced practice nurses, this procedure often involves other nurses or healthcare personnel, such as medical assistants. Nurses or medical assistants may be responsible for preparing patients to receive intrathecal chemotherapy, setting up the required equipment and supplies, and assisting during the procedure. Presence during intrathecal chemotherapy administration provides nurses with an opportunity to verify that the correct drug and dose are being administered.

In published accounts, the typical course of events after inadvertent intrathecal vincristine administration was rapid sensory and motor dysfunction followed by encephalopathy, coma, and death. Early signs and symptoms included tremors, disorientation, and nausea and vomiting. Progressive deterioration ensued, and patients became unresponsive within one week. Ascending paralysis occurred in six patients. The time to death ranged from 7–83 days and averaged 10 days for the 17 patients who died (al Fawaz, 1992; Bain, Lantos, Djurovic, & West, 1991; Dettmeyer, Drier, Becker, Wiestler, & Madea, 2001; Fernandez et al., 1998; Gaidys, Dickerman, Walters, & Young, 1983; ISMP, 1998, 2000, 2003; Kwack et al., 1999; Lau, 1996; Manelis, Freundlich, Ezekiel, & Doron, 1982; Meggs & Hoffman, 1998; Shepherd, Steuber, Starling, & Fernbach, 1978; Slyter, Liwnicz, Herrick, & Mason, 1980; Williams et al., 1983).

The patients who lived the longest were a three-year-old (time to death 83 days) (Alcaraz, Rey, Concha, & Medina, 2002) and a 59-year-old woman with acute lymphocytic leukemia who inadvertently received 2 mg of vincristine intrathecally (cytarabine was intended to be injected into her Ommaya reservoir and vincristine was intended to be given by IV). She became deeply comatose on day 11 and died on day 40 without regaining any neurologic function (Meggs & Hoffman, 1998).

Upon autopsy, typical findings caused by inadvertent intrathecal vincristine administration included grossly edematous and congested brain and spinal cord tissue with axonal degeneration and myelin loss of the spinal nerves (Kwack et al., 1999; Williams et al., 1983). Lau (1996) summarized this type of finding by describing it as “brain death.”

One report of a patient surviving inadvertent intrathecal vincristine administration involved a seven-year-old with acute lymphocytic leukemia who, one year after diagnosis, received maintenance chemotherapy that included IV vincristine and intrathecal methotrexate. She inadvertently received her usual vincristine dose intrathecally, and the error was detected halfway through the injection (the patient received approximately 0.5 mg vincristine). Immediate neurosurgical intervention included an exchange of cerebrospinal fluid (CSF) with Ringer’s lactate. The patient then was taken to the

operating room in an upright position, and an intraventricular drain was inserted. After surgery, the patient was responsive and was taken to the intensive care unit where her subarachnoid space was flushed continuously with Ringer's lactate for 24 hours. She also received 10 g of glutaminic acid IV followed by oral doses of 500 mg three times daily. Five days postoperatively, the patient experienced lower extremity pain and weakness that progressed to complete paraplegia. She also developed a neurogenic bladder that required intermittent catheterization. Seven years later, she remained in remission but did not regain motor function of her legs and continued to have a neurogenic bladder (Iqbal, Abdullah, Tuner, & Al-Sudairy, 2002). The researchers could not determine whether this patient's survival occurred as a result of undergoing immediate CSF fluid exchange or if she survived because, unlike other patients who received a full dose of IV vincristine intrathecally, she received about half of the vincristine dose.

Another patient who inadvertently received a partial dose of vincristine intrathecally survived but experienced continued neurotoxicity, including a neurogenic bladder, 24 months following the incident (Zaragoza, Ritchey, & Walter, 1995). The only published account of survival following a full dose of vincristine inadvertently administered intrathecally was a 23-year-old patient with lymphoblastic lymphoma who underwent immediate CSF drainage; however, he developed ascending paralysis and became comatose after two days. The patient remained comatose for 10 months at which point his disease recurred but was not treated (Bleck & Jacobsen, 1991).

The three-year-old who inadvertently received intrathecal vincristine and died 83 days later also received CSF drainage and CSF fluid exchange. Her unusually prolonged time to death following inadvertent intrathecal vincristine administration was attributed to the immediate detection of the error and prompt CSF drainage and lavage (Alcaraz et al., 2002).

The rationale for immediate CSF drainage and lavage is to dilute and remove the inadvertently administered vincristine, thus limiting neurologic damage. This is the only known anecdotally documented treatment (Al Ferayan, Russell, Al Wohaibi, Awada, & Scherman, 1999). Its success appears to be contingent on immediate detection of the error and likely is influenced by the amount of vincristine inadvertently administered intrathecally.

Because the consequences of inadvertent intrathecal vincristine administration are catastrophic, every effort to prevent this type of medication error should be used. In the United Kingdom, the Department of Health has taken a leading role in preventing accidental intrathecal vincristine administration by issuing mandates designed to promote the safe administration of all intrathecal chemotherapy (see Figure 2).

Not as much has been done in the United States to help prevent inadvertent intrathecal vincristine administration. Data from deaths resulting from inadvertent intrathecal vincristine administration have led to changes in United States Pharmacopeial Convention, Inc. (USP), requirements for manufacturers and pharmacies that package and prepare ready-to-use doses of vincristine. Each dose of vincristine now has specific cautionary labeling. A label that states "FATAL IF GIVEN INTRATHECALLY. FOR INTRAVENOUS USE ONLY" is adhered to all syringes (see Figure 3). Each syringe then is placed in an overwrap that also contains this warning (see Figure 4) (Williams, 2002). However, despite

- Qualifications of staff who order, prepare, handle, and administer intrathecal chemotherapy are delineated.
- Specialized training in intrathecal chemotherapy administration is required.
- A separate order form specifically for intrathecal chemotherapy is used.
- IV vincristine is labeled "FOR INTRAVENOUS USE ONLY—FATAL IF GIVEN BY OTHER ROUTES."
- For children 10 years of age and older, vincristine is diluted to a concentration of 0.1 mg/ml and doses are provided in a 10 ml or larger syringe.
- For children younger than the age of 10, vincristine is provided undiluted at a concentration of 1 mg/ml in a syringe that is size appropriate for measurement of the dose.
- Intrathecal drugs are issued and received by designated staff.
- Intrathecal drugs are packed and transported separately from IV or other drugs.
- "Do not disturb" signs are posted while intrathecal chemotherapy is administered.
- Compliance checklists are completed routinely.

Figure 2. Key Components of the United Kingdom's Department of Health Guidelines for Safe Administration of Intrathecal Chemotherapy

Note. Based on information from Department of Health, 2003.

this USP standard, another fatality occurred after vincristine was dispensed without this warning label on the syringe and outer wrapper; the drug inadvertently was administered intrathecally along with the prescribed intrathecal chemotherapy (ISMP, 2003).

In Australia, most hospitals prepare vincristine in a small-volume infusion bag of 50 ml normal saline as opposed to a syringe. Then, the drug is administered to adults over 5–10 minutes. The same approach is used for pediatric patients, but with a smaller volume and slower rate of infusion (Stefanou & Dooley, 2003). According to Stefanou and Dooley, "This is the only method of completely eradicating the risk of this drug accidentally being given intrathecally . . . since all published reports of intrathecal vincristine administration have been associated with preparation of the drug in a syringe" (p. 2044).

Womer and Bickert (2003) reported that routinely diluting vincristine and administering it as a short infusion have been debated in national pharmacy meetings and Internet mailing lists. The researchers did not advocate this approach, noting that, in pediatric patients, administering vincristine through a peripheral IV and a vincristine infusion, rather than bolus administration, greatly increases the risk of extravasation injury.

In developing an institutional policy for intrathecal chemotherapy administration, several concepts warrant inclusion. First, chemotherapy of any kind should be given only

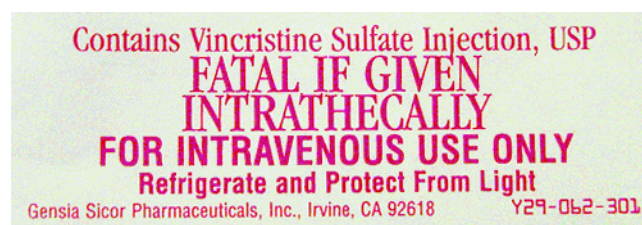


Figure 3. Example of Syringe Label That Is Affixed to Prepared Doses of Vincristine

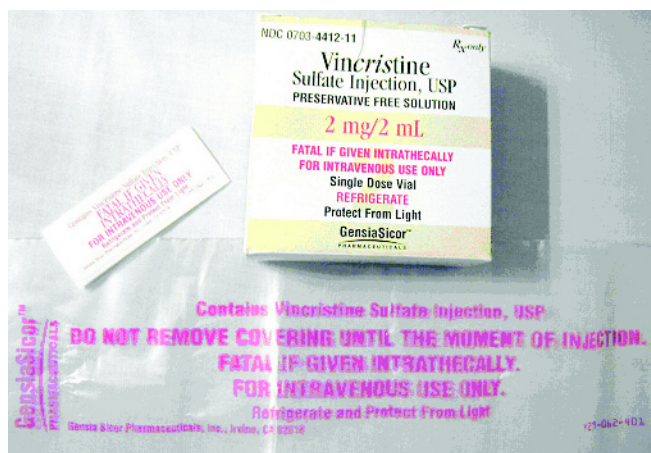


Figure 4. Example of Vincristine Box Label, Syringe Label, and Plastic Overwrap

by appropriately trained staff. Intrathecal and IV chemotherapy should never be dispensed or delivered together. When a patient is scheduled to receive intrathecal and IV chemotherapy treatment, the treatment should be viewed as two distinct procedures that are to be performed at different points in time. At least two clinicians should independently verify intrathecal medications prior to their administration. Intrathecal chemotherapy should be given in designated locations only, and, ideally, the pharmacy staff should deliver intrathecal chemotherapy immediately before use. Prepared intrathecal chemotherapy never should be stored or placed on a counter on a patient care unit or in a patient's room (Dyer, 2001; ISMP, 2003; Root & the British Oncology Pharmacy Association, 2001). In addition, Laws (2001) suggested that medical product manufacturers should develop syringes and equipment for epidural use that are noninterchangeable with IV products.

Creation of a specific IV vincristine administration policy may be warranted in facilities where both IV vincristine and intrathecal medications are administered. Adherence to the USP vincristine labeling standard is essential. Methods to distinguish vincristine from intrathecal medications also can be considered. Dispensing vincristine in small-volume infusion bags or diluting the dose to at least 10 ml to help differentiate it from intrathe-

cal drugs, for which such a large volume is not given, may help to reduce the potential for inadvertent intrathecal vincristine administration.

A disturbing trend in the literature regarding inadvertent intrathecal vincristine administration is the use of "intrathecal vincristine" without the word "inadvertent." Titles of journal articles, such as "Intrathecal Vincristine: Fatal Myeloencephalopathy Despite Cerebrospinal Fluid Perfusion" (Alcaraz et al., 2002) or "Intrathecal Vincristine: Long-Term Survivor of Potentially Fatal Chemotherapeutic Error" (Iqbal et al., 2002), in some ways make it sound as if intrathecal vincristine is an accepted treatment. To avoid confusion, clinicians and authors should consistently refer to this type of medication error as "inadvertent intrathecal vincristine administration," "accidental intrathecal vincristine administration," or "erroneous intrathecal vincristine administration."

Summary

"The system of medical care, like all other systems, is safe only if human error is recognized as inevitable and the system is designed to minimize the consequences" (Ferner, 2000, p. 1215). In many instances, human error is responsible for, or contributes to, serious medication errors. Medication errors involving the chemotherapeutic agent vincristine, which has a very short half-life and is rapidly tissue bound, can be debilitating or even fatal. Its primary toxicity is neurologic, and symptoms of neurotoxicity are amplified when overdoses of vincristine are administered inadvertently. In addition, vincristine is not a myelosuppressive agent, but when overdoses are administered inadvertently, patients are at high risk for bleeding and infection. Accidental injection of vincristine, a drug intended for IV use only, into the CSF or ventricle of the brain results in profound neurologic sequelae and usually death. Lastly, confusion of vincristine with other vinca alkaloids can result in the incorrect drug being administered.

All of these vincristine medication errors are preventable. Increased awareness of the potential severity of these errors, combined with designing systems and using practices to prevent medication errors, has the greatest potential for eradicating vincristine medication errors.

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References

- Alcaraz, A., Rey, C., Concha, A., & Medina, A. (2002). Intrathecal vincristine: Fatal myeloencephalopathy despite cerebrospinal fluid perfusion. *Journal of Toxicology: Clinical Toxicology*, 40, 557-561.
- al Fawaz, I.M. (1992). Fatal myeloencephalopathy due to intrathecal vincristine administration. *Annals of Tropical Paediatrics*, 12, 339-342.
- Al Ferayan, A., Russell, N.A., Al Wohaibi, M., Awada, A., & Scherman, I. (1999). Cerebrospinal fluid lavage in the treatment of inadvertent intrathecal vincristine injection. *Child's Nervous System*, 15, 87-89.
- American Society of Health-System Pharmacists®. (2004a). Hyaluronidase injection. Retrieved March 3, 2004, from <http://www.ashp.org/shortage/hyaluronidase.cfm?cfid=13632878&CFTOKEN=63535491>
- American Society of Health-System Pharmacists®. (2004b). Injectable hyaluronidase approved by FDA. Retrieved July 25, 2004, from <http://www.ashp.org/news/showArticle.cfm?cfid=11005067&CFTOKEN=53865529&id=5514>
- Bain, P.G., Lantos, P.L., Djurovic, V., & West, I. (1991). Intrathecal vincristine: A fatal chemotherapeutic error with devastating central nervous system effects. *Journal of Neurology*, 238, 230-234.
- Berenson, M.P. (1971). Recovery after inadvertent massive overdosage of vincristine (NSC-67574). *Cancer Chemotherapy Reports*, 55, 525-526.
- Berwick, D.M. (2001). Not again! Preventing errors lies in redesign—not exhortation. *BMJ*, 322, 247-248.
- Bleck, T.P., & Jacobsen, J. (1991). Prolonged survival following the inadvertent intrathecal administration of vincristine: Clinical and electrophysiologic analyses. *Clinical Neuropharmacology*, 14, 457-462.
- Boyle, D.A., Schulmeister, L., Lajeunesse, J.D., & Anderson, R.W. (2002). Medication misadventure in cancer care. *Seminars in Oncology Nursing*, 18, 109-120.
- Brown, K.A., Esper, P., Kelleher, L.O., O'Neill, J.E.B., Polovich, M., & White, J.M. (2001). *Chemotherapy and biotherapy guidelines and recommendations for practice*. Pittsburgh, PA: Oncology Nursing Society.
- Casteels-Vann Daele, M., Beirinckx, J., & Baines, P. (1977). Overdosage with vincristine. *Journal of Pediatrics*, 90, 1042-1043.

- Chae, L., Moon, H.S., & Kim, S.C. (1998). Overdose of vincristine: Experience with a patient. *Journal of Korean Medical Sciences*, 13, 334–338.
- Clark, B.S., Gallegos, E., & Bleyer, W.A. (1997). Accidental intramuscular vincristine: Lack of untoward effects and recommendations for management. *Medical and Pediatric Oncology*, 28, 314–315.
- Department of Health. (2003). National guidance on the safe administration of intrathecal chemotherapy. Retrieved March 4, 2004, from http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/ClinicalGovernance/ClinicalGovernanceGeneralInformation/ClinicalGovernanceGeneralArticle/fs/en?CONTENT_ID=4031335&chk=FihnsD
- Dettmeyer, R., Driever, F., Becker, A., Wiestler, O.D., & Madea, B. (2001). Fatal myeloencephalopathy due to accidental intrathecal vincristine administration: A report of two cases. *Forensic Science International*, 122, 60–64.
- Dorr, R.T., & Alberts, D.S. (1985). Vinca alkaloid skin toxicity: Antidote and drug disposition studies in the mouse. *Journal of the National Cancer Institute*, 74, 113–120.
- Dyer, C. (2001). Doctors suspended after injecting wrong drug into spine. *BMJ*, 322, 257.
- Facts and Comparisons. (2004). *Drug facts and comparisons* (57th ed.). St. Louis, MO: Author.
- Fernandez, C.V., Esau, R., Hamilton, D., Fitzsimmons, B., & Pritchard, S. (1998). Intrathecal vincristine: An analysis of reasons for recurrent fatal chemotherapy error with recommendations for prevention. *Journal of Pediatric Hematology/Oncology*, 20, 587–590.
- Ferner, R.E. (2000). Medication errors that have led to manslaughter charges. *BMJ*, 321, 1212–1216.
- Gaidys, W.G., Dickerman, J.D., Walters, C.L., & Young, P.C. (1983). Intrathecal vincristine. Report of a fatal case despite CNS washout. *Cancer*, 52, 799–801.
- Gensia Sicor Pharmaceuticals, Inc. (1999). Vincristine sulfate injection [Package insert]. Irvine, CA: Author.
- Greuter, W., McNeill, J., Barrie, F.R., Burdet, H.M., Demoulin, V., Filgueiras, T.S., et al. (Eds.). (1999). International code of botanical nomenclature. Retrieved March 5, 2004, from <http://www.bgbm.org/iapt/nomenclature/code/SaintLouis/0000St.Luistitle.htm>
- Grush, O.C., & Morgan, S.K. (1979). Folinic acid rescue for vincristine toxicity. *Clinical Toxicology*, 14, 71–78.
- Hoffman, J.M., & Proulx, S.M. (2003). Medication errors caused by confusion of drug names. *Drug Safety*, 26, 445–452.
- Institute for Safe Medication Practices. (1998, September 23). Accidental administration of IV meds intrathecally. *ISMP Medication Safety Alert*, 3(19), 1.
- Institute for Safe Medication Practices. (2000, April 5). Pain, paralysis, and knowledge of impending death from intrathecal vincristine. *ISMP Medication Safety Alert*, 5(7), 1–2.
- Institute for Safe Medication Practices. (2003, April 8). Fatal reports of intrathecal vincristine continue. *ISMP Medication Safety Alert*, 8(7), 4.
- Iqbal, Y., Abdullah, M.F., Tuner, C., & Al-Sudairy, R. (2002). Intrathecal vincristine: Long-term survivor of potentially fatal chemotherapy error. *Annals of Saudi Medicine*, 22, 108–109.
- Jochimsen, P.R. (1982). Subacute vincristine toxicity following five consecutive daily doses. *American Journal of Clinical Oncology*, 5, 437–441.
- Kaufman, I.A., Kung, F.H., Koenig, H.M., & Giammona, S.T. (1976). Overdosage with vincristine. *Journal of Pediatrics*, 89, 671–674.
- Kosmidis, H.V., Bouhoutsou, D.O., Varvoutsis, M.C., Papadatos, J., Stefanidis, C.G., Vlachos, P., et al. (1991). Vincristine overdose: Experience with 3 patients. *Pediatric Hematology and Oncology*, 8, 171–178.
- Kwack, E.K., Kim, D.J., Park, T.I., Cho, K.R., Kwon, I.H., & Sohn, Y.K. (1999). Neural toxicity induced by accidental intrathecal vincristine administration. *Journal of Korean Medical Sciences*, 14, 688–692.
- Lau, G. (1996). Accidental intraventricular vincristine administration: An avoidable iatrogenic death. *Medical Science and Law*, 36, 263–265.
- Laws, D. (2001). The time has come for non-interchangeability of spinal and epidural equipment with intravascular access ports [Letter to the editor]. *British Journal of Anaesthesiology*, 86, 903.
- Maeda, K., Ueda, M., Ohtaka, H., Koyama, Y., Ohgami, M., & Miyazak, H. (1987). A massive dose of vincristine. *Japanese Journal of Clinical Oncology*, 17, 247–253.
- Manelis, J., Freundlich, E., Ezekiel, E., & Doron, J. (1982). Accidental intrathecal vincristine administration. Report of a case. *Journal of Neurology*, 228, 209–213.
- Mayne Pharma (USA Inc.). (2004). Vincristine sulfate injection [Package insert]. Paramus, NJ: Author.
- Meggs, W.J., & Hoffman, R.S. (1998). Fatality resulting from intraventricular vincristine administration. *Journal of Toxicology: Clinical Toxicology*, 36, 243–246.
- Menzel, E.Z., & Farr, C. (1998). Hyaluronidase and its substrate hyaluronan: Biochemistry, biological activities and therapeutic uses. *Cancer Letters*, 131(1), 3–11.
- Olçay, L., & Safak, T. (2003). Inadvertent intramuscular administration of vincristine: Lack of untoward effects without any treatment except administration of hot compresses. *Pediatric Hematology and Oncology*, 20, 427–428.
- Root, T., & the British Oncology Pharmacy Association. (2001). Medical errors. Appropriate training should avoid accidental intrathecal injection of vincristine [Letter to the editor]. *BMJ*, 322, 1423.
- Rowinsky, E.K., & Donehower, R.C. (2001). Antimicrotubule agents. In B.A. Chabner & D.L. Longo (Eds.), *Cancer chemotherapy and biotherapy: Principles and practice* (3rd ed., pp. 329–372). Philadelphia: Lippincott Williams and Wilkins.
- Schochet, S.S., Lampert, P.W., & Earle, K.M. (1968). Neuronal changes induced by intrathecal vincristine sulfate. *Journal of Neuropathology and Experimental Neurology*, 27, 645–658.
- Schulmeister, L. (1999). Chemotherapy medication errors: Descriptions, severity, and contributing factors. *Oncology Nursing Forum*, 26, 1033–1042.
- Shepherd, D.A., Steuber, C.P., Starling, K.A., & Fernbach, D.J. (1978). Accidental intrathecal administration of vincristine. *Medical and Pediatric Oncology*, 5, 85–88.
- Slyter, H., Liwnicz, B., Herrick, M.K., & Mason, R. (1980). Fatal myeloencephalopathy caused by intrathecal vincristine. *Neurology*, 30, 867–871.
- Stefanou, A., & Dooley, M. (2003). Simple method to eliminate the risk of inadvertent intrathecal vincristine administration [Letter to the editor]. *Journal of Clinical Oncology*, 21, 2044.
- Stones, D.K. (1998). Vincristine overdosage in paediatric patients [Letter to the editor]. *Medical and Pediatric Oncology*, 30, 193.
- Thomas, L.L., Braat, P.C., Somers, R., & Goudsmit, R. (1982). Massive vincristine overdose: Failure of leucovorin to reduce toxicity. *Cancer Treatment Reports*, 66, 1967–1969.
- U.S. Food and Drug Administration. (2004). Listing of approved oncology drugs with approved indications. Retrieved March 5, 2004, from <http://www.fda.gov/cder/cancer/druglistframe.htm>
- Wakem, C.J., & Bennett, J.M. (1975). Inappropriate ADH secretion associated with massive vincristine overdosage. *Australian and New Zealand Journal of Medicine*, 5, 266–269.
- Williams, M.E., Walker, A.N., Bracikowski, J.P., Garner, L., Wilson, K.D., & Carpenter, J.T. (1983). Ascending myeloencephalopathy due to intrathecal vincristine sulfate. A fatal chemotherapeutic error. *Cancer*, 51, 2041–2047.
- Williams, R.L. (2002). Reducing medical errors: A review of innovative strategies to improve patient care. Retrieved March 5, 2004, from <http://www.usp.org/patientSafety/briefsArticlesReports/testimony/rwlTestimony2003-05-08.html>
- Womer, R.B., & Bickert, B. (2003). In reply: Simple method to eliminate the risk of inadvertent intrathecal vincristine administration [Letter to the editor]. *Journal of Clinical Oncology*, 21, 2044.
- Woods, K. (2001). *The prevention of intrathecal medication errors. A report to the chief medical officer*. London: Department of Health.
- Zaragoza, M.R., Ritchey, M.L., & Walter, A. (1995). Neurologic consequences of accidental intrathecal vincristine: A case report. *Medical and Pediatric Oncology*, 24, 61–62.