LIDOCAINE POISONING RESULTING FROM MEDICATION DOSING ERROR IN OUTPATIENT CLINIC

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BACKGROUND

The Los Angeles County (LAC) Department of Public Health (DPH), Acute Communicable Disease Control Program (ACDC) was notified by an emergency department (ED) physician at a local hospital of a cluster of two patients seen at two EDs on the same day, within a relatively short time frame. Each patient was transported to the ED after developing generalized tonic-clonic convulsions soon after conscious sedation and local anesthesia was administered for a therapeutic abortion (TAB) procedure at a local outpatient clinic. ACDC, LAC Health Facilities (HF) Inspection Division, and the U.S. Food and Drug Administration (FDA), conducted a joint site visit to the clinic the day following the incident. A meeting was held with the clinic medical director, physician, and administrative staff to determine the sequence of events leading to the patients' convulsions, assess patient charts, review policies and procedures, observe medication preparation practices, and to recommend control and prevention measures. Subsequent site visits were made by ACDC and LAC DPH Toxics Epidemiology Program nurses to observe the medication preparation procedure for TAB and to conduct chart reviews of all patients who underwent TAB procedure on the same day as the incident.

This report describes the collaborative investigation and the efforts of multidisciplinary agencies to identify the etiology of generalized convulsions occurring to patients undergoing local anesthesia at a local clinic, and to ensure that safety practices and procedures are implemented to prevent further incidents.

METHODS

ACDC conducted a joint site visit to the clinic with an evaluator from the HF Inspection Division and an inspector from the FDA. Interviews were completed with the clinic medical director, clinic physician, and clinic manager to assess procedures performed in the clinic and to elicit the sequence of events leading to the patients' (Patient 1 and 2) convulsions. Patient 1 and 2's charts were reviewed. The investigative team toured the clinic to view TAB preparation/procedure rooms. The team inspected the medication storage and preparation rooms, as well as the locked controlled medication area and medication inventory records. Policies and procedures for TAB were reviewed, including those for surgical abortion, analgesia, and sedation services; standards of care for local anesthesia; emergency procedures; medication error management; pharmaceutical services; controlled substances; and scope of practice for nurse practitioner and nurse midwife. Open vials and unused pre-filled syringes with medications prepared for anesthesia administration left over that day were retrieved and collected for testing by the FDA. Interview of clinician and observation of practice for lidocaine preparation for TAB was observed. A line list was obtained of the 20 patients who underwent TAB on the same day and their medical records were reviewed. HF Inspection Division made several follow-up visits, including one with the State Pharmacy Consultant, to review medication policies and procedures, give recommendations, and enforce corrective actions as deemed necessary for continued surgical procedures. A blood sample from Patient 1 was analyzed for lidocaine.

RESULTS

During site visit #1, ACDC conducted a chart review of the two patients who developed convulsions shortly after receiving local anesthesia and conscious sedation. Patient 1 received intravenous bolus injections of fentanyl and propofol and four paracervical injections of lidocaine (40 mLs total) with vasopressin. These medications were in compliance with the clinic's standard protocol for conscious sedation and local anesthesia for patients undergoing TAB procedure. Approximately one hour and fifteen minutes later, Patient 2 received similar injections of fentanyl and propofol, and lidocaine paracervical injections without vasopressin. Almost immediately after receiving the paracervical injections, each

patient developed nystagmus for less than five seconds, followed by generalized tonic-clonic convulsion and hypoxemia. Clinic medical staff provided Patients 1 and 2 with oxygen, respiratory support, and intravenous midazolam with resolution of convulsions, and each patient was transported to local EDs by emergency medical services for further evaluation. Both patients recovered with observation in the ED and did not require hospital admission. After Patient 2 was transported to the ED, the clinic staff discovered an opened vial of lidocaine 2% in the medication preparation area. The clinic staff concluded that Patients 1 and 2 most likely received 2% lidocaine inadvertently instead of the 0.5% concentration, exceeding the recommended dose. According to the clinic's Standards of Care for Local Anesthesia, the lidocaine dose for local anesthesia is not to exceed 2 mg per pound or 4.5 mg/kg, with a maximum dose per hour of 550 mg. For most patients, this is achieved with 20-40 mLs of 0.5% lidocaine. If Patients 1 and 2 had received 40 mLs of lidocaine 2%, their doses were 800 mg (250 mg above the maximum recommended dose) or 14.5 mg/kg for Patient 1 and 9.2 mg/kg for Patient 2.

ACDC contacted both local EDs to inquire about stored blood samples. Blood for Patient 1 was sent to a private laboratory and revealed a lidocaine level of 4.2 mcg/mL, drawn 88 minutes after the lidocaine injections. Based on a half-life of 1.5-2 hours and a volume of distribution of 1.1 L/kg for lidocaine[1], pharmacological extrapolation corresponded to an estimated peak lidocaine level of 8-12 mcg/mL for Patient 1[1]. The therapeutic peak range for lidocaine is 1.5-5.0 mcg/mL. Signs of toxicity for lidocaine may be seen with serum levels of 7.3-12.0 mcg/mL[1]. Stored blood samples were not available for Patient 2. The FDA confirmed 1.98-2.03% lidocaine concentrations in syringe residuals retrieved on the day after the incident, exceeding the expected concentration of 0.5%.

The staffing pattern for the TAB on the day of the incident included one certified registered nurse practitioner (CRNP) who performed pre-operation assessments; one CRNP who prepared the lidocaine syringes in the morning for the procedures and also monitored the post-operation and recovery room; one certified registered nurse anesthetist (CRNA) who prepared and administered anesthesia; one physician who administered paracervical lidocaine injections (prepared by the CRNP at the beginning of the day) and performed the procedures; and one reproductive health assistant (RHA) who prepared the patients for TAB and assisted the physician and nurses.

Remaining scheduled TAB procedures for that day were immediately cancelled in the clinic after Patient 2 exhibited the same reaction as Patient 1. All medications utilized to administer local anesthesia for TAB and all leftover medications pre-drawn into syringes for subsequent procedures were sequestered by the clinic. The sequestered medications included an empty 50 mL vial of lidocaine 0.5%, a few mLs in a 50 mL vial of lidocaine 2%, three 50 mL bottles of propofol 1% with approximately 5-30 mL of medication left in the bottles, three 2 mL syringes of fentanyl, an empty 1 mL vial of vasopressin, and five unlabelled syringes filled with a white substance (ranging from 2 to 12 mLs). There were some syringes filled with lidocaine, labeled "20cc lidocaine (0.5%)," and some labeled "20cc lidocaine (0.5%) w. 4U Vasopressin." The FDA took samples of the medications listed above for analysis.

The clinic kept the controlled substances (narcotics) in a locked cabinet with entry by authorized licensed staff only, and maintained inventory records for each drug count and use. Lidocaine was kept inside the laboratory in a locked cabinet without documentation or records. The clinic's formulary did not include lidocaine 2%. The clinic's inventory order sheet indicated that 25 vials of 50 mL lidocaine 2% were ordered, and the clinic's inventory control data sheet indicated that 22 vials of 50 mL lidocaine 2% were in the clinic. During site visit #1, the clinic reported having returned the stock of lidocaine 2% to central supply; however, administration was unable to produce the tracking invoices to confirm such a transaction.

ACDC and Toxics Epidemiology nurses reviewed the medical records of all patients who underwent TAB procedure with local anesthesia on the day of the incident. Twenty charts were reviewed for demographic information, medical history, treatments and medications administered, and vital signs. There were no specific risk factors identified that were unique to Patients 1 and 2 that may have contributed to the onset of tonic-clonic convulsions.

During site visit #2 to the clinic, an ACDC nurse met with the CRNP to review their routine practice of local anesthesia preparation of lidocaine for TAB procedures. The CRNP typically prepares the medications alone over a one hour time span just prior to the clinic services opening. The CRNP regularly prepares four 12 mL syringes of lidocaine for each scheduled TAB procedure. The CRNP reported that on the day of the incident, a combined total of ninety-six 12 mL syringes of lidocaine and lidocaine with vasopressin were pre-filled and prepared using sterile technique in the morning. Ninety-six syringes are usually prepared on the days TABs are performed: 40 syringes of lidocaine only and 56 syringes of lidocaine with vasopressin. The 12 mL syringes are filled between 11–12 mL to allow for waste by the physician prior to direct insertion into the patient. The CRNP obtains twenty-four 50 mL vials of lidocaine from a locked cabinet and five 1 mL vials of vasopressin (20 U/mL). Ninety-six syringes are placed onto a sterile field. The CRNP adds 0.5 mL of vasopressin into a 50 mL vial of lidocaine to obtain a reconstitution of 10 units vasopressin in 50 mL of lidocaine. This procedure is repeated for ten vials of lidocaine mixed with vasopressin. Each 50 mL vial of lidocaine combined with vasopressin is marked with a "V" prior to withdrawing medication into the syringes to distinguish from the vials with lidocaine only. Forty syringes with combined lidocaine/vasopressin are prepared first. Each syringe is identified with a blue and white label reading "20cc lidocaine (0.5%) w. 4U Vasopressin." The remaining 56 syringes are filled with lidocaine only and identified with a white label reading "20cc lidocaine (0.5%)." After preparing the 96 syringes, they are separated, wrapped in a towel, and kept in two separate metal trays. Each tray is identified for type of medication utilizing the same labels placed on the syringes. The CRNP provides the metal trays to the RHA to keep in a centralized location (portable table in the hallway) for use during the day of TAB procedures. The RHA removes the appropriate syringes of lidocaine from the metal trays and sets them inside the procedure room on a sterile field for the physician to administer to the patients.

During site visit #2, the RHA reported finding 22 empty vials of lidocaine by the trashcans just outside the facility. Of those 22 empty vials, 19 were lidocaine 2% and the other three were lidocaine 0.5%. Eight of the lidocaine 2% vials found were marked with a "V" on the bottle. According to the inventory control data sheet, the clinic had received 22 vials of 50 mL lidocaine 2%. The lidocaine 2% vials were stored next to the lidocaine 0.5% on the same shelf in the medication preparation room. Both concentrations of lidocaine are prepared by the same manufacturer and have a very similar appearance, including the same vial size, label markings, and blue-colored vial caps.

Several clinical practices were of concern and several problems were identified during the medication preparation demonstration.

- Storage of lidocaine 2% (which is neither part of the clinic formulary nor regularly stocked) together with regularly-stocked lidocaine 0.5%.
- Improper storage of medications. Medications with similar appearance should be stored in different locations to prevent potential error, provided they are part of the formulary.
- Lack of documentation and record keeping of lot numbers of lidocaine and vasopressin administered.
- Inadequate labeling of pre-filled syringes with lidocaine used for TAB procedures. Although the concentration printed on the labels for each syringe was correct, each label should read exactly what each syringe contains, i.e., 10 mL lidocaine (0.5%) with 2U vasopressin or 10 mL lidocaine (0.5%).
- No verification of concentration of drugs used. The CRNP who prepared the lidocaine did not notice using lidocaine 2% verses lidocaine 0.5% during the medication preparation process.
- Lack of a written procedure for pre-filling lidocaine syringes for TAB procedures.
- Placement of pre-filled lidocaine syringes in an open, unsecured area.
- Lack of record-keeping of number of unused lidocaine syringes discarded at the end of the day.

In addition, during site visit #1, the CRNA who prepared the propofol on the day of the incident reported that the medication was prepared by pre-filling syringes for all patients scheduled for TAB at the beginning of the day; however, the syringes prepared for that day were neither labeled nor dated. The CRNA stated that sometimes the pre-filled propofol syringes are labeled and timed for two to three patients prior to surgery. It was discovered that after filling the syringes, the CRNA kept them in a lab coat pocket for storage for an undetermined length of time prior to administration. This practice allows for a

breach in aseptic technique, and is not supported by the clinic's General Anesthesia and Deep Sedation Protocol.

ACDC notified HF Inspection Division, Toxics Epidemiology, and the FDA of the retrieved empty vials of 2% lidocaine. Toxics Epidemiology and ACDC recommended that HF Inspection Division carefully review medication procedures and practices of the clinic (storage, preparation, and administration) and requested that a California State certified pharmacy consultant conduct a comprehensive assessment and recommend measures and practices to prevent medication errors.

On the day following the incident, HF Inspection Division ceased operations of anesthesia-related procedures at the clinic until the completion of an audit of pharmacy practices and corrective actions were instituted.

CONCLUSION

Past case reports of fatal overdoses occurred in the 1970s, with hematomas noted at the paracervical injection sites, resulting in communication with the vascular system [2]. Patients 1 and 2 in this investigation likely experienced a similar reaction.

ACDC, HF Inspection Division, Toxics Epidemiology, and the FDA collaborated in the investigation of a cluster of two patients who developed tonic-clonic convulsions and hypoxemia shortly after administration of conscious sedation and paracervical local anesthesia for TAB procedure. The investigation included chart review, staff interviews, medication preparation observation, review of policies and procedures, and laboratory analysis. The investigation strongly suggested a medication dosing error evidenced by discovery of 19 empty 2% lidocaine vials, above expected lidocaine concentration levels in syringe residuals, and an elevated blood lidocaine level in Patient 1.

Several contributing factors in the clinic processes which may have increased the risk of medication error were identified during this investigation. These included failure to return medication to the manufacturer which is not part of the clinic formulary, stocking the same medication of different concentration and similar appearance next to each other, non-adherence to all of the "Six Basic Rights of Medication Safety Practices" (drug, dose, patient, time, route, and documentation) during medication preparation, inappropriate labeling of medications, and finally, lack of written protocol and procedures for the verification of medication dosage prepared by one staff and administered by another, and the safe storage of medications prepared in advance for procedures.

This case illustrates the risk of medication error in local facilities which lack formal protocols for anesthesia. This investigation also served to identify several practices throughout the clinic which may have contributed to the medication errors. This case demonstrates the benefit of multi-agency collaboration to investigate, identify and correct problems.

REFERENCES

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