

Avoiding Carcinogen Exposure With Intraperitoneal Paclitaxel

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Purpose/Objectives: Diethylhexylphthalate (DEHP) is a lipid-soluble plasticizer commonly used in the manufacture of polyvinyl chloride- (PVC-) based plastics. Previous studies have documented the leaching of DEHP from PVC-based containers and extension sets during the IV administration of paclitaxel.

Design: Study of the leaching of DEHP from infusion bags and peritoneal dialysis solution transfer sets and clinical study of DEHP was proposed.

Setting: The experiments were performed in a laboratory with plastic ware normally used for intraperitoneal chemotherapy delivery.

Sample: Samples were taken from fluids that had been in contact with the plastic ware. Also, blood, peritoneal fluid, and urine were collected from a patient.

Methods: In a controlled laboratory environment, the authors used an established high-performance liquid chromatography assay to determine the rate and extent of DEHP leaching from infusion bags and in the solution transfer set used for early postoperative intraperitoneal chemotherapy (EPIC) administration of paclitaxel. Paclitaxel was tested at a concentration of 40 mg/L to simulate the median dose used for EPIC. In a single patient receiving 34 mg paclitaxel in 1 liter of 1.5% dextrose peritoneal dialysis solution (Dianeal®), the presence and concentration of DEHP in samples of peritoneal fluid and urine were determined during the first 24-hour EPIC administration.

Main Research Variables: DEHP levels in fluids exposed to plastic ware and in the patient's blood, peritoneal fluid, and urine were determined.

Findings: The in vitro studies showed that a solution of 40 mg paclitaxel dissolved in a 1 liter bag of Dianeal resulted in the extraction of approximately 26 mg DEHP over 24 hours. Approximately 2 mg DEHP was leached during the first hour and approximately 1 mg per hour over the following 23 hours. Equivalent results were obtained when 20 mg paclitaxel was dissolved in a 500 ml bag of 6% hetastarch (Hespan®) with a leaching of approximately 13 mg DEHP in 24 hours. Using the same paclitaxel concentration, the chronic ambulatory peritoneal dialysis solution transfer tubing with a total capacity of 10 ml produced approximately 2 mg DEHP over 24 hours, of which approximately 0.5 mg was produced during the first four hours. Samples from a single patient showed that immediately prior to administration, a 1 liter bag of Dianeal containing 34 mg paclitaxel had about 3.3 mg DEHP. Approximately 3% (110 mcg) of unchanged DEHP was recovered from the peritoneal fluid at 24 hours. Total DEHP excreted in urine over the 24-hour period was approximately 900 mcg (27%).

Conclusion: This study showed that the carcinogen DEHP is leached after preparation of paclitaxel from PVC-based containers and DEHP constantly accumulates in the solution transfer tubing.

Implications for Nursing: Unless precautionary steps are taken, DEHP can be transferred to patients receiving intraperitoneal paclitaxel. Steps to minimize patient exposure to DEHP during EPIC with paclitaxel are necessary. In the ideal situation, no DEHP-containing plastic should be used for chemotherapy delivery. If that is not possible, (a) paclitaxel solution should be administered as soon as possible after preparation by the pharmacy, (b) infusion should proceed as rapidly as possible via the Tenckhoff catheter, and (c) the Tenckhoff catheter and extension tubing should be cleared by draining ascites fluid through these tubes prior to subsequent intraperitoneal infusions.

Key Points . . .

- ▶ Diethylhexylphthalate is present in all soft plastic.
- ▶ Polyvinyl chloride in its "soft form" contains diethylhexylphthalate as a softener.
- ▶ This can be leached from the soft plastic with lipid, taxane chemotherapy such as paclitaxel and docetaxel and may transfer the carcinogen to patients unless the appropriate precautions are taken.

Diethylhexylphthalate (DEHP) is a common lipid-soluble plasticizer found in polyvinyl chloride- (PVC-) based plastics. When added to PVC, the plastic product remains soft and pliable, a characteristic that is essential to the function of many plastic items. Animal studies have shown DEHP to be a hepatotoxin, carcinogen, and teratogen (Gray, Beamand, Lake, Foster, & Gangolli, 1982; Keyv & Jacobson, 1982; Singh, Lawrence, & Autian, 1972; Warren, Lalwani, & Ready, 1982). Mono(2-ethylhexyl)phthalate (MEHP), a plasma metabolite of DEHP, has caused hypotension and cardiac arrest in rats (Rock, Labow, Franklin, Burnett, & Tocchi, 1987) and has had cardiotoxic effects on human myocardium (Barry, Labow, Rock, & Keon, 1988).

Paclitaxel is formulated in Cremophor EL® (BASF Corporation, Florham Park, NJ), a vehicle that is an admixture by volume of polyoxyethylated castor oil in 49.7% dehydrated alcohol (Bedford Laboratories, 2001). Previous studies have shown that this admixture caused leaching of DEHP from IV administration bags and extension sets used in IV administration of paclitaxel (Maas, Huber, & Kramer, 1996; Mazzo, Nguyen-Huu, Pagniez, & Denis, 1997; Trissel, Xu, Kwan, & Martinez, 1994; Waugh, Trissel, & Stella, 1991).

The purpose of this study was to determine the rate and extent of DEHP loss from infusion bags and solution transfer

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