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SPECIAL

Review of evidence on handling hazardous drugs and Products in Urology Services; consensus document between the Spanish Urology Association and the Spanish Society of Health-System Pharmacists

Revisión de la evidencia sobre el manejo de medicamentos y productos peligrosos en los servicios de Urología; documento de consenso entre la Asociación Española de Urología y la Sociedad Española de Farmacia Hospitalaria

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Abstract

Objective: The intravesical administration of hazardous drug products is a standard practice in the urology setting, which potentially exposing medical personnel to these drug products. It was deemed necessary to have a consensus document among the scientific societies involved (the Spanish Urological Association and the Spanish Society of Hospital Pharmacy) that collects the best available evidence on the safest handling possible of dangerous drug products in the setting of urology departments.

Method: We reviewed the legislation and recommendations on the handling of dangerous drug products, both at the national and international level.

Results: There is national legislation and regulations for protecting workers who handle dangerous drugs and products, as well as recommendations for handling to protect both the product and workers.

Discussion: Following the strategic lines of the European Parliament for 2014-2020 in the chapter on occupational safety and health, the Spanish Urological Association and the Spanish Society of Hospital Pharmacy proposed a series of actions that decrease the risks of exposure for practitioners and caregivers involved in the handling of these products.

Conclusions: After this review, 19 recommendations were established for handling dangerous drug products, which can be summarised as the need to train all individuals

involved (from management teams to patients and caregivers), adopt systems that prevent contaminating leaks, implement exposure surveillance programmes and optimise available resources.

KEYWORDS: Occupational exposure++ Hazardous drugs++ Closed system transfer device++ Intravesical instillation++ BCG++ Mitomycin C.

Resumen

Objetivo: La administración intravesical de medicamentos peligrosos es una práctica habitual en el ámbito de la urología, con posible exposición del personal sanitario a dichos medicamentos. Se considera necesario disponer de un documento de consenso entre las sociedades científicas implicadas -Asociación Española de Urología y Sociedad Española de Farmacia Hospitalaria- que recoja la mejor evidencia disponible para el manejo, de la forma más segura posible, de medicamentos peligrosos en el ámbito de los servicios de Urología.

Método: Se ha realizado una revisión de la legislación y de las recomendaciones sobre el manejo de medicamentos peligrosos tanto a nivel estatal como internacional.

Resultados: Se dispone de legislación nacional y de normativas para la protección de los trabajadores que manipulen medicamentos y productos peligrosos, así como recomendaciones de manipulación para la protección tanto del producto, como de los trabajadores.

Discusión: Siguiendo las líneas estratégicas del Parlamento Europeo para el período 2014-2020 en el capítulo de seguridad y salud laboral, la Asociación Española de Urología y la Sociedad Española de Farmacia Hospitalaria proponen una serie de actuaciones que hagan disminuir los riesgos de exposición de los profesionales y cuidadores implicados en su manejo.

Conclusiones: Tras esta revisión se establecen 19 recomendaciones para el manejo de medicamentos peligrosos que pueden resumirse en la necesidad de formación de todas las personas implicadas (desde los equipos directivos hasta los pacientes y cuidadores), la adopción de sistemas que no permitan fugas contaminantes, programas de vigilancia de las exposiciones y optimización de los recursos disponibles.

PALABRAS CLAVE: Exposición ocupacional, Drogas peligrosas, Sistemas cerrados, Instilación vesical, BCG, Mitomicina C.

Introduction

The term "Hazardous drugs" was introduced for the first time by the American Society of Health-System Pharmacists (ASHP) in 1990[1] and later adopted by the Occupational Safety and Health Administration (OSHA), designated for the first time by the National Institute for Occupational Safety and Health (NIOSH) in 2004[2]. The hazardous nature of these medicines lies in the chemical risk, related to carcinogenic, teratogenic, genotoxic and toxic activity on the reproductive process or on a specific organ in low doses, or because this is a new drug similar to others with this type of risk.

El United States NIOSH lists potentially hazardous treatments to be chemotherapy, antivirals, hormones, and others, mentioning endovesical instillations for chemotherapy and BCG in patients with non muscular invasive bladder cancer as a source of potential contamination involving hazardous substances[3].

The Spanish Urology Association (AEU) ensures that the standard referring to this speciality is disseminated and applied, and the Spanish Society of Health-System Pharmacists (SEFH) ensures appropriate, safe and effective use of the drugs and healthcare products.

The Technical Document for the National Institute of Occupational Health and Safety (INSHT) on preparation and administration of hazardous drugs[4] recommends a consensus document between the two societies compiling recommendations for handling hazardous drugs in the field of Urology Services.

Exposure to hazardous drugs in the workplace and health risks for healthcare personnel have been documented over the last four decades[2]. The number of health workers exposed to these substances has risen due to greater use, new drugs and longer use as life expectancy has risen, representing a challenge for healthcare centres[5] that have to adapt their procedures to handling these drugs[6].

The European Union has acknowledged this concern through the European Union Occupational Safety and Health Agency (EUOSHA)[7], raising the alarm on lack of legislation harmonisation on risk prevention for healthcare workers.

The aim of this document is inform healthcare professionals about the best possible evidence to safely handle Hazardous Drugs in the field of Urology.

Methods

The legislation and scientific literature was reviewed on 3 November 2016 by consulting the Medline and The Cochrane Library Plus electronic databases. The following search terms were used: occupational exposure, hazardous drugs, closed system transfer device, intravesical instillation. The most relevant complete text articles and works from the last 5 years on this topic were selected. Finally, an additional manual search was performed among the selected article references.

Results

There is no clear evidence of the impact of these hazardous drugs on the healthcare population. However, some information might draw our attention to this potential risk. Several studies have demonstrated greater exposure to these products among this group of workers. There is epidemiological data supporting the fact that exposure to these drugs has an effect on embryo development and on reproductive functions[8], although the methodology in these studies has been questioned[9] and it has not been possible to confirm that this cancer risk is higher than among the rest of the population, so it is essential to take measures that help reduce this exposure, where preventive activity is the most appropriate[10,11].

Exposure could take place by inhaling and cutaneous contact/absorption; ingestion or injection, are much less frequent. Environmental contamination, including air, gloves, clothing, work surfaces, floors, etc. can have different origins, from original contamination of the container or drips, to spills and splashes when handling them.

The probability that a worker will experience adverse effects due to a hazardous drug increases with the quantity and the frequency of exposure, affecting nurses, pharmacists and technicians but also nursing assistants or non healthcare staff such as cleaners, porters, laundry staff[12-14]. It is important to clean and decontaminate the place where work has involved hazardous substances.

One cause of contamination is using needles and conventional transfer systems that allow aerosol formation, vapour release or dripping medicines. In intravesical administration, the contamination risk is greater than in other clinical fields, as drug concentrations are greater than when administering intravenously. There are guides for handling hazardous drugs, including some for staff who carry out endovesical instillations with BCG and chemotherapy, adapted to the latest recommendations from the NIOSH[15] or the SEFH[16].

In 2004, Directive 2004/37/EC set a hierarchy of protection measures and the use of closed systems[17]. In 2007, the ISOPP (International Society of Oncology Pharmacy Practitioners) set level 1 for elimination, substitution or replacement of the product for a less toxic one (rarely possible in the healthcare field); level 2 with use of closed systems for complete isolation; level 3 with suitable control and ventilation systems and reduction of time and workers being exposed, and level 4, with Personal Protection Equipment (PPE) (lab coat, gloves, eye protection, breathing protection...) and staff training[18].

The NTP 1051, uses the name Closed System Drug Transfer Devices (CSTD) to refer to devices to transfer drugs that prevent contaminants from entering and stops the release of the drug being handled, avoiding aerosols and vapours by equalling out the pressure inside and outside the vial. In Spain, these devices are considered to be healthcare products. In the United States, the FDA (Food and Drug Administration) has established the ONB product code for CSTD devices, thereby defining the quality of the systems, although they do not substitute work in the Biosafety Cabinets.

The choice of a CSTD should consider sterility of the prepared solution, safety for use (easy to transport, handle and transfer liquids), total transfer of the solutions, avoiding product losses, universal use (suitable for connections, sealing)[19]. The cost estimation is relevant (having published that CSTD systems can be cost-effective, even at times and in places with limited resources[20,21].

In 2013, the European Commission published the Prevention and Best Practice Guide specifying that a risk should be avoided rather than reduced, or the drug should be replaced with another less hazardous substance[22]. Preventive measures should follow an order: starting with technical solutions, then organisational and, finally, personal/individual.

The United States Pharmacopoeia (USP) on handling hazardous drugs (USP 800) from 2016 indicates that contamination should be controlled to a limit that is "As Low As Reasonably Achievable" (ALARA), forcing

the use of closed systems in preparation and administration of hazardous drugs although it does not recommend which to use[23].

In Spain, protection for workers against risks of exposure to carcinogenic agents or mutagens is legislated by RD 665/1997[24] and modified by RD 1124/2000[25], and the INSHT has published Technical Prevention Notes NTP 740[26] and NTP 1051[27], and the Technical Document on hazardous drugs justifying this consensus document[4].

With regard to the most used medication in vesical instillations, Table 1 shows the most used hazardous drugs in this field and Table 2 summarises the INSHT recommendations.

Table 1

Some of the most usual hazardous drugs in the field of Urology

MEDICINE	CLASSIFICATION	DESCRIPTION
Adriamycin/ Doxorubicin	2A (IARC)	Probably carcinogenic for humans
Mitomycin C	2B (IARC)	Possibly carcinogenic for humans
BCG	Biological risk	
Epirubicin	D (FDA)	Clear evidence of a teratogenic risk

IARC:International Agency for Research on Cancer; FDA: Food and Drug Administration.

Table 2

INSHT recommendations for handling the most usual hazardous drugs in urology

Medicine, Pharmaceutical form (*Specialities*)	Presentation	Preparation recommendations	Administration recommendations	FDA RE; IARC category	NIOSH list / Reason
Bacillus Calmette Guerin (BCG) powder for intravesical suspension (*OncoTICE®*) powder and solvent for intravesical solution (*Vejicur®*)	Vial	Prepare in CSB II or AE, with double thickness gloves and lab coat and mask. Use CSDT. Do not prepare in areas where parenteral medicines are being prepared to avoid cross contamination, or perform terminal cleaning afterwards.	Administer wearing double gloves, lab coat, eye and breathing protection.	FDA RE C	1
Mitomycin powder for injectable solution	Vial	Prepare in CSB IIb or AE, with double gloves, lab coat and mask. Use CSDT.	Administer wearing double gloves and lab coat; use eye protection when there is a risk of splashing and breathing protection if there is a chance of inhaling it.	IARC 2B; FDA RE D	1

AE: negative pressure sterile insulator; CSB IIb: class IIb biosafety cabinet; FDA RE: pregnancy risk category from the Food and Drug Administration; IARC: carcinogenic risk for humans classification according to the International Agency for Research on Cancer; CSDT: closed system drug transfer.

Taking into account the aforementioned aspects and following the strategic lines from the European Parliament for the 2014-2020 period in the chapter on occupational health and safety, the AEU and the SEFH propose a series of actions that lower the risks of exposure for professionals and carers involved in handling these drugs.

- Health authorities and management teams should be aware of the danger to which healthcare staff are exposed.

- Training should be provided for healthcare professionals who work in any of the phases of handling hazardous drugs (from transport and storage to preparation and administration), regarding inherent risks for handling these drugs and possible protection measures.

- Contamination levels due to hazardous drugs should be monitored periodically in the preparation and administration areas.

- Surveillance programmes should be set up on occupational health for healthcare professionals involved in handling hazardous drugs.

- Information should be provided to patients and family members on how to prevent exposure to hazardous drugs.

- Management and occupational health teams at hospitals should promote basic standards for preparing hazardous drugs, laid down in the Medicine Preparation Best Practice Guide[21].

- Hospitals should promote effective use of Personal Protection Equipment (PPE) and closed systems for preparation and administration of hazardous drugs.

- Sterile hazardous drugs should be prepared in Class IIb or higher biosafety cabinets.

- A system should be arranged that does not produce contamination during the entire process, preparation, transport and vesical instillation.

- Transport should be easy and safe, in sealed containers. Packaging should be labelled clearly, legibly and contain safety warnings.

- Only a small number of staff should transport hazardous drugs who are properly trained on how to handle them.

- Double gloves should be worn or gloves for handling cytostatics, waterproof lab coat plus breathing protection measures (FFP3 type mask) and eye protection.

- Rigorous cleaning and decontamination should be performed in the place where the vesical instillation takes place according to the procedure approved in each centre by the Occupational Risk Prevention and/or Preventive Medicine Service. These procedures should have clear and specific instructions to be applied after using BCG.

- A system should be arranged that can transfer the entire prepared solution to reduce any loss of efficacy resulting from incomplete transfer, particularly with BCG. A three-way valve might be considered to do this, washing the probe with a small amount of saline solution, without having to disconnect the hazardous medicine packaging.

- The system being used should be compatible with the material used to carry out the vesical instillation, thereby lowering exposure risks.

- The vesical probe should be the finest possible calibre, mainly latex-free and water-repellent to avoid urethral trauma.

- To reduce exposure to the drug, the system used to administer the medication and the system used to wash the probe should be joined throughout the process, even when the vesical probe is being removed.

- Collection and elimination of residue should be labelled properly and have safety warnings.

- Patients will be trained on how to deal with their excretions, adding bleach to the toilet in an approximately equal volume to their urination,

and letting it act for 15 minutes before flushing the chain, and they will be informed of the importance of hand-washing hygiene.

The review of the available evidence made it possible to make 19 recommendations for handling hazardous medicines that can be summarised by the need to train the people involved (from management teams to patients and carers), adopting systems guarantee no contaminating leaks, surveillance programmes on exposure and optimisation of available resources.

Bibliography

ASHP technical assistance bulletin on handling cytotoxic and hazardous drugs (review). Am J Hosp Pharm. 1990;47(5):1033-49.

Preventing occupational exposure to antineoplastic and other hazardous drugs in health care settings. National Institute for Occupational Safety and Health (NIOSH). Department of Health and Human Services. 2004;165.

Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP, Cincinnati, OH. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH). 2016;161.

Medicamentos peligrosos. Medidas de prevención para su preparación y administración. Barcelona. Instituto Nacional de Seguridad e Higiene en el Trabajo (INSHT); 2016.

Valero García S, López Briz E, Vila Clérigues N, Poveda Andrés JL. Hazardous drugs: new challenges, new opportunities. Farm Hosp. 2016;40(2):124-7.

García-Alcántara BG, Perelló Alomar C, Moreno Centeno E, Modamio P, Mariño EL, Delgado Sánchez O. Impact of the new handling recommendations for hazardous drugs in a hospital pharmacy service. Farm Hosp. 2017;41(2):257-69.

Occupational health and safety risks in the healthcare sector. Guide to prevention and good practice. European Commission Directorate-General for Employment, Social Affairs, 2011.

Rekhadevi PV, Sailaja N, Chandrasekhar M, Mahboob M, Rahman MF, Grover P. Genotoxicity assessment in oncology nurses handling anti-neoplastic drugs. Mutagenesis. 2007;22(6):395-401.

Exposición a los carcinógenos y cáncer relacionado con el trabajo: una revisión de los métodos de evaluación. Observatorio Europeo de Riesgos. Agencia Europea para la Seguridad y la Salud en el Trabajo; 2014.

Meier K, Griffith N, Chen B, Chuk K, Daouphars M, Doreau C, et al. Safe handling of oral chemotherapeutic agents: An European perspective. European Journal of Oncology Pharmacy 2011;5:4-10.

Fransman W, Peelen S, Hilhorst S, Roeleveld N, Heederik D, Kromhout H. A pooled analysis to study trends in exposure to antineoplastic drugs among nurses. Ann Occup Hyg. 2007;51:231-9.

Hedmer M, Tinnerberg H, Axmon A, Joensson BAG. Environmental and biological monitoring of antineoplastic drugs in four workplaces in a Swedish hospital. Int Arch Occup Environ Health. 2008;81:899-911.

Constantinidis TC, Vagka E, Dallidou P, Basta P, Drakopoulos V, Kakolyris S, et al. Occupational health and safety of personnel handling chemotherapeutic agents in Greek hospitals. Eur J Cancer Care (Engl). 2011;20:123-31.

Connor TH, Anderson RW, Sessink PJM, Broadfield L, Power LA. Surface contamination with antineoplastic agents in six cancer treatment centers in Canada and the United States. Am J Health-Syst Pharm. 1999;56(14):1427-32.

Personal Protective Equipment for Health Care Workers Who Work with Hazardous Drugs. National Institute for Occupational Safety and Health (NIOSH). Department of Health and Human Services. 2009;106.

Alonso Herreros JM, Cercós Lletí AC, Gaspar Carreño ML, González-Haba Peña E, Márquez Peiró J, Pernía López MS. Estructura para la manipulación segura de Medicamentos Peligrosos: recomendaciones sobre instalaciones, sistemas cerrados y equipos de protección individual. En: Medicamentos Peligrosos. Monografías de Farmacia Hospitalaria y Atención Primaria. Sociedad Española de Farmacia Hospitalaria. 2016.

Directiva 2004/37/CE del Parlamento Europeo y del Consejo, de 29 de abril de 2004, relativa a la protección de los trabajadores contra los riesgos relacionados con la exposición a agentes carcinógenos o mutágenos durante el trabajo (Sexta Directiva específica con arreglo al apartado 1 del artículo 16 de la Directiva 89/391/CEE del Consejo). Diario Oficial de la Unión Europea (30 de abril de 2004).

International Society of Oncology Pharmacy Practitioners. ISOPP Standards of Practice. Safe Handling of Cytotoxics. J Oncol Pharm Pract. 2007;13 Suppl:1-81.

Guía de Buenas Prácticas de Preparación de Medicamentos en Servicios de Farmacia Hospitalaria. Dirección General de cartera básica de servicios del SNS y Farmacia. Ministerio de Sanidad, Servicios Sociales e Igualdad. Junio 2014.

Sánchez-Rubio J, Lozano MC, Iglesias I, Sánchez-Rubio L, Rodríguez B, Moreno R. Use of a Closed-system Drug Transfer Device (PhaSeal) and Impact on Preparation Time. Int J Pharm Compd. 2012;16(5):431-3.

Edwards MS, Solimando DA, Grollman FR, Pang JL, Chasick AH, Hightman CM, et al. Cost savings realized by use of the PhaSeal® closed-system transfer device for preparation of antineoplastic agents. J Oncol Pharm Pract. 2013;19:338-47.

Riesgos para la salud y la seguridad en el sector sanitario. Guía de prevención y buenas prácticas. Comisión Europea. Dirección General de Empleo, Asuntos sociales e Inclusión. Unión Europea; 2013.

Hazardous Drugs. Handling in Healthcare Settings. USP 39-NF 34. USP General Chapter 800. Section 5.2 (Supplement) Feb. 2016.

Real Decreto 665/1997, de 12 de mayo, sobre la protección de los trabajadores contra los riesgos relacionados con la exposición a agentes cancerígenos durante el trabajo. BOE 124, 24 de mayo de 1997, p. 16111-5.

Real Decreto 1124/2000, de 16 de junio, por el que se modifica el Real Decreto 665/1997, de 12 de mayo, sobre la protección de los trabajadores contra los riesgos relacionados con la exposición a agentes cancerígenos durante el trabajo. BOE 145, 17 de junio de 2000, pp. 21443-4.

Guardino Solá X, Rosell Farrás MG, Galisteo Manzanares M. NTP 740: Exposición laboral a citostáticos en el ámbito sanitario. Instituto Nacional de Higiene y Seguridad en el Trabajo; 2006.

Guardino Solá, X. NTP 1051 Exposición laboral a compuestos citostáticos: sistemas seguros para su preparación. Instituto Nacional de Higiene y Seguridad en el Trabajo; 2015.

Author notes

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