

Proceedings Paper

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Fifth DSRG symposium at CHU UCL Namur, 18/10/2019. “Centralization of injectables and robotization”

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Abstract: The physico-chemical stability of an injectable preparation (IV) is conditioned by different parameters. A collaboration between the pharmacy, the chemistry laboratory and the statisticians of the scientific support unit was established in 1996, in order to carry out long-term chemical stability studies of commonly used IVs and to be able to take charge of their preparation in pharmacy. In 24 years of activity, the Drug Stability Research Group (DSRG) tested 39 IV at different concentration and temperature of storage. The DSRG has organized an annual symposium since 2015. The theme of the 2019 edition was devoted to the robotization of injectable reconstitution operations, focused on their impact on the workplace and the existing equipment.

Keywords: automatic compounding; injectable drugs; physico-chemical stability; robotization.

Introduction

The administration of intravenous drug therapy is a common practice in hospital [1]. From the 1970s, hospital pharmacists gradually took charge of the production and/or reconstitution of parenteral nutrition mixtures, chemotherapy cures and other injectable drugs (IVD) [2, 3]. Production units have gradually been set up in hospitals [4].

Although American and European bibliographic sources provide information on the long-term stability of reconstituted IVD, some data are missing [5–7] or conflicting [8].

A collaboration between the pharmacy, the chemistry laboratory and the statisticians of the scientific support unit was established in 1996, in order to carry out long-term chemical stability studies of commonly used IVD and to be able to take charge of their preparation in hospital pharmacy [9]. In 24 years of activity, 39 drugs have been reconstituted in a sterile environment and stored at different temperatures: 32, 17–25, 5 ± 3 , -20°C . The stability of the concentration was evaluated by regression analysis. The results were disseminated in 62 publications and 91 posters.

The molecules and dosages studied corresponded to the practice in the field of the CHU.

At the same time, with the development of stability studies, the production unit expanded and relaunched microwave freeze-thaw treatment stability studies [10] to evaluate the long-term stability of the most widely used IVD.

The increase in reconstituted doses led to mechanization and then automation of compounding [11].

A first symposium devoted to “Towards an increased centralization of the preparation of injectable drugs” was organized in 2015. This symposium was then repeated each year [12–14].

The 5th edition was held on 18/10/2019, again at the CHU UCL Namur, in Yvoir. One hundred eighty people gathered in Heremans’s auditorium to witness the day theme: “Centralization of injectable drugs and robotization”.

Several speakers had agreed to take the floor, including, of course, hospital pharmacists who came to explain their experience with different types of compounding equipment, but also actors in robotization in the broad sense of the term and its influence in the short, medium and long term in the workplace.

A summary of their presentation is available below.

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Part I. Robotics and impact on the workplace

Being human in a robot world.

Prof. R. Ronsse, UCLouvain, Belgium

A paralyzed patient can now walk on both legs using a robotic exoskeleton. This brings a radical upheaval for patients with neurological damage, leading to therapeutic and psychological benefits. In addition, robots can help rehabilitate patients who have suffered brain damage, such as after a stroke, as well as replace the missing limb of an amputee. The presentation presents the technical, scientific and ethical challenges associated with this robotics of assistance and rehabilitation. Attention is focused on engineering issues, for example concerning the mechanical structure or programming of these devices, and medical issues, such as the efficiency and learning capacities of this “increased” user. Finally, how similar technology can be used to design human or animal artefacts using robots, again through the challenges linked to the interactions between these devices and their environment was discussed [15, 16].

Impact of technology on the workplace: evolution or revolution.

Th. Dermine, Catch Charleroi, Belgium

For several centuries, the link between technological progress and employment has raised questions. While it is clear that technological change is changing the nature of employment and the tasks performed by humans, it also gives rise to fears that employment will become scarce. The copyist monks already asked this question in the 15th century when the first printing machines appeared. Today, there are entire categories of workers who fear for the sustainability of their jobs in the face of the threat of digitalization. Through a series of analyzes, the presentation aims to deconstruct certain myths and assess the impact of recent changes on the world of work [17].

Centralization of the production of chemotherapy at three sites: establishment of an organization with two production units.

Dr. S. Coulon, GHEF, France

The Grand Hôpital de L'Est Francilien (GHEF) is the result of the merger of three hospitals (Meaux, Marne-la Vallée and Coulommiers) in 2017. In this context, the unique Indoor Pharmacy (IP.) has created a pool of pharmacotechnology. For this, it has gradually centralized its three Cytotoxic Preparation Units (CPU) on a single site (n° 1). The site 1 CPU (7,500 preparations per year) has resumed the activity of site 2 (2,500 preparations per year). To absorb the preparations of site n° 3 (9,000 preparations per year), it was decided to open in 2018 a new CPU on site n° 1, independent in terms of Air Treatment Center (ATC) and insulators (two per CPU). The presentation makes a review at one year of the start of the second CPU, on this organization compared to the previous organization. This organization has been compared with that of centralization on a single unit. The evaluation criteria chosen being: technical and human resources, practices used, quality assurance, logistics and IT. During the development of the project, several scenarios had been mentioned, including the extension of the existing CPU. The option of having two separate units was chosen so that the Health Facility, which now produces 18,000 preparations per year, is fully responsible for its production, which is the case. The six months of hindsight have highlighted constraints, particularly in terms of inventory management, which however can be controlled with the evolution of software. The operation of a pharmacotechnical pool with two separate units remains comfortable because it allows us to be the back-up of other establishments and calmly consider an increase in activity [18].

Part II. Production robots

Compounding material review.

Prof. J.-D. Hecq, CHU UCL Namur, Belgium

Automated preparation systems have appeared on the market over the past 15 years as an alternative to manual IV

preparation. A literature review was carried out on the reconstitution of IVs. The following methods have been identified: manual, semi-automatic and automatic. A classification was made into three categories: automatic syringes, peristaltic pumps and reconstitution of mixtures by automatic machines. The number of compounding robots is increasing. The different characteristics of each device are described. Ampoules cannot be manipulated by these robots. High dose vials improve reconstitution time compared to current dosage vials. The advantages of automated preparation are: greater consistency of processes and products, greater product precision, integrated digital processing, precise and complete documentation, reduced wrist effort and injuries, reduced personnel requirements, increased worker satisfaction. The disadvantages of automated preparation are as follows: risk of breakdown/downtime, dependence on power supply, software (updates), high investment costs/high maintenance costs, specialized personnel with additional training, reduced worker satisfaction, complexity when products are switched or added, new errors appear. This review allows the potential user to know the current availability on the market [19].

Management of parenteral nutrition production machines: example of the Baxa EM 2400 machine.

Dr. T. Quessada, Hospices Civils de Lyon, France

Over the years, aseptic filling machines have gradually established themselves for the production of parenteral nutrition bags (NP). The current models of PLCs are mainly offered by the following manufacturers: Baxter, BBraun, Impromediform and Hemedis. Sometimes using a peristaltic pump, sometimes syringe pumps as a filling system, they have slightly different metrological characteristics. But other differences must be investigated to control pharmaceutical production in a controlled atmosphere zone. To this end, a recent thesis proposed “guidelines for the management of automatic production in parenteral nutrition”. The main points to check and the tests to consider are illustrated. The advantages and disadvantages of automated production are then recalled in comparison with manual production previously used. Automated compounders are generally used according to manufacturers’ recommendations. However, these reflect a general mode of use and can restrict the activity desired by the pharmaceutical user. Through two studies, a use outside the manufacturer’s recommendation is presented in order to extend the possibilities of preparation, always

under pharmaceutical responsibility and in a secure manner for the patient. This consists of keeping a weekly assembly of the configuration of the automated compounder under laminar air flow, in class A. The exchange of information between the various actors of the automated production of NP (industrialists, pharmacists, regulatory authorities) are the best way to develop the production of NP bags to meet the demands of clinicians for the benefit of patients [20, 21].

Diana Onco +.

D. Devolder, UZ Leuven, Belgium

As preparation practices are a fundamental part of the daily routine of hospital pharmacists, the move towards a well-managed production process opens up new horizons with automation in mind. This technology allows you to work more precisely, improve production capacity, minimize drug waste and much more. But it also introduces new challenges on the standardization of the list of drugs, the possibility of batch production and interfacing with current systems. To navigate in calm and placid waters, user experiences are a reliable source of knowledge to answer the question of whether Diana ONCO + fits into your chemotherapy preparation unit.

Multi – syringes and dose banding.

J. Ramaut, UZ Gent, Belgium

The presentation describes the path taken by the UZ Gent pharmacy over the past five or six years to automate the process of preparing cytotoxic substances. The experiences with the different devices, their faults and the obstacles overcome and those being resolved are detailed.

Pharma Help isolator.

Dr. C. Cros, Institut Curie, Paris, France

The objective of this communication is to present the steps that led to the choice of automation, to describe the automated process and to provide feedback on automation. In a context of growing activity, our unit has chosen automation in order to secure its production. The manufacturing of standard dose bags is carried out by an automated process (PharmahelpV1) controlled by gravimetry coupled with

bottle recognition by digital camera. Manufacturing data (productivity, quality, maintenance, resources) and evaluation of chemical contamination were collected over a period of seven years. Between 2011 and 2017, 73,373 preparations were made (10,481/year), representing an average of 21% of total production. Average productivity increased from 52 (2011) to 68 (2017) preparations/day/operator. Ten drug molecules and 23 products have been developed. Out-of-specification preparations (deviation > 5%) represented on average 0.6% of production over this period (0.9% in 2011 vs. 0.2% in 2017). The anomalies causing these non-conformities were technical and human: 90 and 17% in 2011 vs. 43 and 57% in 2017. Automated production requires human intervention representing 1 FTE preparer/day and 0.5 pharmacist FTE/day. The level of chemical contamination is very high on the surfaces of the bags produced by an automated system and identical to those produced manually. In addition to the protection of personnel, the production of insulators allows us today to guarantee aseptic preparation and work facilitated on a daily basis. The use of an isolator, however, adds ergonomic constraints which have been optimized during development. Automation should always be an institutional project. It is a strategy that has guaranteed stable productivity, taking care of the additional activity with a constant workforce, to achieve a high level of quality with a positive impact on the activity of ambulatory services.

Robotization, example of the KIRO[®] Robot.

Prof. S. Crauste-Manciet, – Université de Bordeaux, France

Hospital Robotics has recently appeared as a possible alternative to the manual production of injectable drugs in hospital pharmacies. Through an example, the Kiro[®] robot from Grifols, the objective of the presentation is to focus on the development of a specific simulation program for the qualification of robots. The presentation highlights the interest of qualifying the robot with representative compositions of drugs on the market, the importance of qualifying each specialty in order to be able to exclude active principles and formulations not suitable for robotization. The contribution of robotics with regard to quality control and the prevention of microbiological and chemical risks is also discussed. Finally, the evaluation of productivity is studied as a criterion to integrate into robotics qualification in order to be able to position these new technologies in the global context of aseptic hospital preparation [22, 23].

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