

Practice Research & Innovation

Quality and safety improvements in the preparation and administration of intravenous cytotoxic therapies with new medical devices

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ABSTRACT

Objective: To find appropriate medical devices that could improve the quality and safety of chemotherapy preparation and administration, for patients, nurses and pharmacists using methods that could be easily transferred to other hospitals.

Methods: The Codan CytoZ system and BD Laboratory saline PosiFlushMC XS syringe were studied in three departments using a customer satisfaction survey along with productivity gains and cost assessments.

Results: Quality assessment of the medical devices was considered very satisfactory (88%). The implementation of medical devices allowed improvements in safety and gains in productivity. The new system enabled the pharmacy department to prepare eight cytotoxic IV bags per hour, per person, on average (while integrating batch code traceability), versus six with the current pump infusion sets but without integrating batch code traceability. However, implementation of the new medical devices increased the cost by 394% compared with standard techniques (assuming one gravity infusion set per bag, and preparation of saline syringes by nurses), but only by 27% when compared with pump technique and pre-filled syringes (one pump-set per bag and two saline PosiFlushMC XS syringes).

Conclusion: As a result of the findings, a multidisciplinary committee in conjunction with the hospital's financial board adopted the medical devices to improve quality and safety during preparation and administration of cytotoxic therapies.

KEYWORDS

Chemotherapy, cytotoxic exposure

INTRODUCTION

Intravenous (IV) therapy is a complex process usually requiring several steps in the preparation of drugs before administration to patients. Several studies have previously identified the frequency of errors that can vary between 13% and 84% in the preparation and administration of IV drugs in most hospitals [1-6]. In the case of anticancer drugs, there is also an additional safety concern about the risk of exposure of nurses and pharmacists to cytotoxic agents. To improve the safety of cytotoxic drugs administration, French legislation has

made it mandatory that the preparation of these drugs must be centralised, computerised and prepared in an isolator or laminar air flow cabinet, under the supervision of a pharmacist [7].

We have previously conducted a survey of chemotherapy processes in our hospital. While containment of exposure during centralised preparation was minimised by using an isolator, the risk of a prick or accidental injection was shown to remain. At the time of the survey, bags for

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IV chemotherapy were delivered to the bedside without priming the infusion set with solvent, making it impossible to rinse the infusion set before disconnection. Nurses were therefore not protected when connecting or disconnecting the infusion sets. In addition, it was shown that patients were not receiving the whole dose because it was not possible to wash out the infusion line and properly administer the dead volume to them. Furthermore, the duration of drug administration could not be monitored by the use of a quality-controlled infusion pump. When specific medical devices (MD) became available in 2006, the hospital's Medicine and Sterile Medical Devices Committee (COMEDIMS) decided to conduct a prospective study allowing a multidisciplinary team to monitor and select the appropriate MD.

The objective of the study described in this paper was to find medical devices that effectively improved the quality and safety of chemotherapy preparation and administration throughout the entire process, for patients, nurses and pharmacists, using methods that could be easily transferred to other hospitals.

MATERIALS AND METHODS

Choice of medical devices

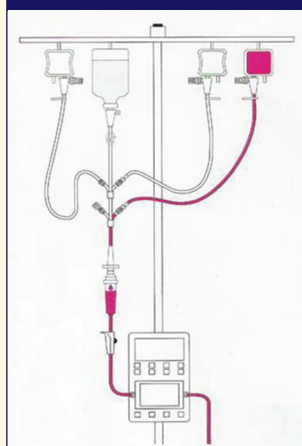
Some medical devices available on the French market for routine hospital use were screened by the pharmacy team. Two medical devices were identified that had potential to match the study objectives: the CytoZ system (Codan Laboratory) and PosiFlushMC XS syringe (BD Laboratory).

The CytoZ system is an infusion set made from PVC, without di(2-ethylhexyl) phthalate (DEHP), consisting of two major elements (see Figure 1a).

ConnectZ is a connection set for preparation of cytotoxic IV solutions. For this study, we selected two versions of ConnectZ, both with a bi-directional (on/off) valve for the injection site, but one with a filter and one without a filter (for the infusion of paclitaxel and cetuximab). The 40 cm tubing (dead volume = 3 mL) was primed with a rinsing solution, and clamped. Injection of the drug into the bag was carried out using a luer-lock valve without a needle, thus eliminating the risk of an accidental prick. ConnectZ was systematically connected to any cytotoxic IV bag delivered by the pharmacy to the wards (see Figure 1b).

The CytoZ Adapter was specially designed to be used with dedicated pump sets, and reconciles the advantages of the CytoZ system with those of precise administration usually provided by the infusion pumps. The adaptors are available with two or four possible connections depending on the

Figure 1a: CytoZ system for administration by pump



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number of cytotoxic agents to be administered to the patient. Interestingly, there is no need to disconnect empty bags. This device was previously shown to improve the safety of cytotoxic drug administration by preventing backward infusion or leakage (non-return valves) (see Figure 1c).

The use of these devices is considered convenient; the nurses simply connect the appropriate dedicated pump-set to the adaptor, according to recommendations made by the pharmacists (standard PVC, PVC without DEHP or opaque). The main fluid channel is primed with a rinsing solution before connecting to the patient's catheter. ConnectZ is then connected to CytoZ Adapter. Administration appears to be facilitated by sliding the clamp on the appropriate solution limiting the risk of exposure. Before administration of subsequent cytotoxic solutions, the main fluid channel could be rinsed in a closed system to prevent mixing several drugs.

The second device, the saline PosiFlushMC XS syringe (Figure 1d), is recommended to rinse implanted central venous access ports, in positive flow, in patients with cancer. These syringes are ready to use, and minimise risks associated with handling.

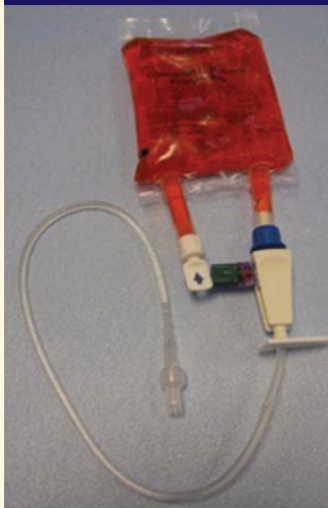
Evaluation of the medical devices

Trials with these two medical devices were performed in the oncology, gastroenterology and pharmacy departments of Beaujon University Hospital for a period of one week. We tested 200 ConnectZ, 80 two-way adaptors, 20 four-way adaptors and 280 pre-filled syringes. Company specialists trained 14 nurses, 10 pharmacists and six pharmacy technicians, and coached them during the trial.

Each medical device was evaluated via a customer satisfaction survey. Three satisfaction forms (one for pharmacy and the others for clinical departments) were used for the follow-up at the end of the first week of use. Each criterion was evaluated on a scale of 1 to 4, with 4 indicating the best score. Analysis of the results was performed by responsible pharmacists and clinical chief nurses.

Productivity gains and cost assessments were also evaluated. An estimate of productivity gains by using syringes

Figure 1b: ConnectZ with a bi-directional (on/off) valve at the injection site



assessed the time required for nurses to collect all items (saline vials, syringes, needles and swabs), fill the syringes and rinse the catheter. The cost assessment was based on a ratio of two syringes per patient. Productivity gains by pharmacy technicians during infusion-bag preparation were estimated by comparing the connection and priming of ConnectZ with a solvent (saline or dextrose) and injection of cytotoxic drugs into the bag by the means of the “on/off” valve without a needle, against the dedicated pump-set with injection by needle directly into the injection site of the bag.

RESULTS

Satisfaction assessment of medical devices showed them to be considered satisfactory (Tables 1-3). Overall, for the CytoZ system, levels of satisfaction were rated as 92%, 76% and 89% by pharmacists, gastroenterology nurses and oncology nurses, respectively. Similarly, the overall level of satisfaction for the saline PosiFlushMC XS syringe was rated as 96% and 87%, by gastroenterology and oncology staff respectively.

Prevention of drug exposure

The study also highlighted several improvements for the safety of nurses, pharmacists, patients and the environment. Firstly, nursing staff were no longer exposed to cytotoxic drugs when connecting or disconnecting cytotoxic IV bags. Moreover, the CytoZ system (primed with dextrose 5% or saline solutions, and rinsed after each drug) generally allows the use of one dedicated pump-set per patient (depending on drug and/or pump). Smaller volumes of residual cytotoxic drugs and medical waste were observed. Three mL of sterile air was injected when completing each preparation. At the end of each infusion, the ConnectZ tube was emptied using sterile air, without any risk of air entering the main fluid channel. The

Figure 1d: Saline XS syringe

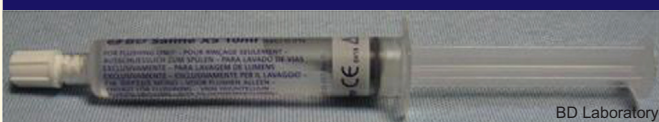
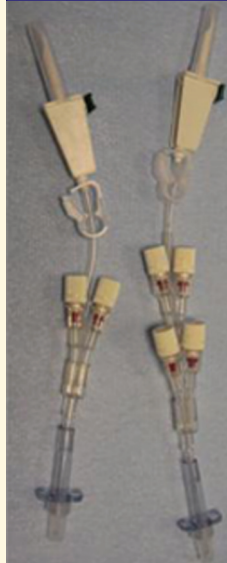


Figure 1c: CytoZ adapters with two or four connections



main fluid channel was then rinsed between each drug, using dextrose or saline.

Improvement in administration practice

Before the study, we noticed that several nurses were not washing out lines between changes of infusion sets. The wash-out may be considered important with pump-sets, because the residual volume can be up to 24-28 mL as compared with 15-17 mL with standard gravity infusion sets. A systematic wash-out between each drug was shown to be facilitated by the CytoZ system, avoiding interaction and potential obstruction of implanted central venous accesses and allowing administration of the full dose to patients.

The CytoZ system allowed easier handling of pumps, facilitating the control of the duration of drug administration and reducing medical waste, because only one pump set per patient was required instead of one pump set per IV bag.

The use of the saline PosiFlushMC XS syringe can also save time for nurses with an estimate of 291 hours/per year for 6,500 syringes, and minimising the risk of accidental injuries using vials and needles.

Moreover, the positive flow of the saline PosiFlushMC XS syringe prevented venous backflow when disconnecting the line, eliminating the risk of overpressure often associated with moving or breakage of implanted central venous catheters.

Improvement in preparation practice

Only two ConnectZ components (with or without filter) were necessary to prepare all cytotoxic IV bags, thus saving space in the isolator.

Priming was quick and easy with ConnectZ, which contains only 3 mL (for a 40 cm line), saving time compared with standard gravity infusion sets or pump sets. This system enabled us to prepare, on average, eight cytotoxic IV bags per hour per person, tracing batch codes on drugs and bags, versus six with pump infusion sets, which did not allow tracing batch codes because of time constraints.

The on/off valve of ConnectZ also allowed pharmacist technicians to extract solvent from the IV bags and inject drugs without needing to use a needle. This avoided several risks including that of pricking for technicians, and risk of leakage from IV bags. As a result, the ConnectZ system allowed us to improve our practices during preparation.

Pharmacoeconomic study

The impact of using the CytoZ system concurrently with one dedicated pump set per patient and two saline PosiFlushMC XS syringes per treatment increased the cost of medical devices by 394% compared with the standard technique (assuming one gravity infusion set per bag and preparation of saline syringes by nurses). The cost of medical devices increased by 115% compared with the pump technique (assuming one pump set per bag, and preparation of saline syringes by nurses), and by 27% compared with the pump plus pre-filled syringe technique (assuming one pump set per bag and two saline PosiFlushMC XS syringes).

DISCUSSION

The use of the CytoZ system, appropriate pump sets and the saline PosiFlushMC XS syringe improves the quality and safety of preparation and administration of cytotoxic medicines for patients and healthcare workers, and can also be considered as a benefit for the environment.

For patients, the administration of cytotoxic drugs can be considered safer. The number of disconnections was minimised, the loss of residual drugs in the dead line-space was reduced, and the duration of administration easier than using infusion pumps. Moreover, patients received the full treatment which is often a concern with cytotoxic agents. Furthermore, ConnectZ may be primed in a sterile

ConnectZ	Pharmacy department
Ease of opening of the packaging	14/16 (87.5%)
Perforation of the vehicle bag	14/16 (87.5%)
Security of the connection to the bag receiving the drug	15/16 (93.8%)
Ease and speed of priming	16/16 (100%)
Withdrawal of drug through the on/off valve	15/16 (93.8%)
Injection through the on/off valve	16/16 (100%)
Space saving	14/16 (87.5%)
Time managing	14/16 (87.5%)
Safety of operator	14/16 (87.5%)

CytoZ adaptor	Gastroenterology department	Oncology department
Ease of opening of the packaging	12/16 (75%)	14/16 (87.5%)
Perforation of the rinsing bag	12/16 (75%)	14/16 (87.5%)
Security of the connection to the rinsing bag	13/16 (81.3%)	14/16 (87.5%)
Ease of priming	12/16 (75%)	12/16 (75%)
ConnectZ		
Satisfaction with pre-primed infusion sets	14/16 (87.5%)	16/16 (100%)
Ease of connecting to the CytoZ adaptor	12/16 (75%)	15/16 (93.8%)
Watertightness of connections	12/16 (75%)	16/16 (100%)
CytoZ system		
Patient safety	12/16 (75%)	15/16 (93.8%)
Quality of treatment	12/16 (75%)	15/16 (93.8%)
Ease of connection	12/16 (75%)	15/16 (93.8%)
Ease of rinsing	13/16 (81.3%)	15/16 (93.8%)
Ease of final disconnection	12/16 (75%)	16/16 (100%)
Convenience	11/16 (68.8%)	14/16 (87.5%)
Time saving	9/16 (56.3%)	7/16 (43.8%)
Health-professional safety	14/16 (87.5%)	16/16 (100%)
Waste control	12/16 (75%)	15/16 (93.8%)

environment using an isolator. The CytoZ system is a closed system, reducing disconnections and hence reducing the risk of microbiological contamination. Use of pre-filled saline PosiFlushMC XS syringes also contributes to a reduction of microbiological and particulate contamination.

For the nursing staff there is a reduced risk of drug exposure because connections are made using ConnectZ, which is primed with dextrose or saline solvent. The only remaining stage when there is a risk of exposure to the cytotoxic drug is after the wash-out of the infusion pump set; the final wash-out of implantable venous accesses is simplified and secured by the pre-filled saline PosiFlushMC XS syringe.

From the pharmacy standpoint, the use of ConnectZ appears to save time during the preparation of cytotoxic IV bags,

Table 3: Results of saline PosiFlushMC XS syringe customer satisfaction survey – clinical departments

Saline PosiFlushMC XS syringe	Gastroenterology department		Oncology department	
Ease of opening of the packaging	16/16 (100%)		11/16 (68.8%)	
Identification of the product	14/16 (87.5%)		14/16 (87.5%)	
Verification of system's integrity (by a click at first plunger handling)	15/16 (93.8%)		11/16 (68.8%)	
Ease of connection	15/16 (93.8%)		15/16 (93.8%)	
Watertightness	16/16 (100%)		15/16 (93.8%)	
Ease of plunger movement	16/16 (100%)		14/16 (87.5%)	
Ease of disconnection	15/16 (93.8%)		15/16 (93.8%)	
Saline PosiFlushMC XS syringe	Yes	No	Yes	No
Time saving	4/4 (100%)	0/4	4/4 (100%)	0/4
Safety for health workers (e.g. less risk of errors, no risk of pricks or cuts, less handling)	4/4 (100%)	0/4	4/4 (100%)	0/4
Hygiene improvement for the patient (less risk of contamination)	4/4 (100%)	0/4	4/4 (100%)	0/4
Does BD syringe improve the rinsing process?	4/4 (100%)	0/4	4/4 (100%)	0/4

enabling better use of human resources while systematically improving preparation practices.

The use of these medical devices also resulted in reduction of cytotoxic drug residues in lines and volume of medical waste (one pump set per patient instead of one per bag).

This trial was also a unique opportunity to re-educate healthcare workers to improve their practice in preparing

[8-9] and administering cytotoxic agents [10].

However, those improvements in safety have a big economical impact. The introduction of these new medical devices in oncology practice was shown to result in an overall annual cost increase of Euros 28,000 in our hospital (1.6% of drug budget for 7,000 anticancer preparations per year). Therefore, to control expenditure, ready-to-use saline PosiFlushMC XS syringes were restricted to the management of implanted venous access ports.

CONCLUSION

The hospital's multidisciplinary COMEDIMS, in agreement with the hospital's financial board, supported the adoption of the devices in departments in which cytotoxic

drugs are given to patients with cancer via an implanted access port. The use of these devices is expected to help standardise good clinical practice and improve quality and safety of cytotoxic drug preparation and administration.

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REFERENCES

- O'Hare MCB, Gallagher T, Shields MD. Errors in the administration of intravenous drugs. *BMJ*. 1995;10:1536-7.
- Hartley GM, Dhillon S. An observational study of the prescribing and administration of intravenous drugs in a general hospital. *Int J Pharm Pract*. 1998;6:38-45.
- Taxis K, Barber N. Ethnographic study of incidence and severity of intravenous drug errors. *BMJ*. 2003;326:684-8.
- Taxis K, Barber N. Causes of intravenous medication errors: an ethnographic study. *Qual Saf Health Care*. 2003;12:343-7.
- Wirtz V, Taxis K, Barber ND. An observational study of intravenous medication errors in the United Kingdom and in Germany. *Pharm World Sci*. 2003;25:104-11.
- Cousins DH, Sabatier B, Begue D, et al. Medication errors in intravenous drug preparation and administration: a multicentre audit in the UK, Germany and France. *Qual Saf Health Care*. 2005;14(3):190-5.
- Légifrance (official website of the Government of France for the publication of legislation, regulation and juridical information) [database on the internet]. Décret n° 2005-1023 du 24 août 2005 relatif au contrat de bon usage des médicaments et des produits et prestations mentionné à l'article L. 162-22-7 du code de la sécurité sociale. [Cited 2008 June 20]. Available from: www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000000631121&dateTexte=
- Ministère de l'emploi et de la solidarité. Arrêté du 22 juin 2001 relatif aux bonnes pratiques de pharmacie hospitalière. [Cited 2008 June 20]. Available from: www.sante.gouv.fr/htm/actu/bpph/rap_bpph.pdf
- Légifrance (official website of the Government of France for the publication of legislation, regulation and juridical information) [database on the internet]. Décision du 5 novembre 2007 relative aux bonnes pratiques de préparation. [Cited 2008 June 30]. Available from: www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000000341518&dateTexte=
- Bard C, Brouard A, Fargeot C, et al. Recommandations AP-HP sur le bon usage des dispositifs médicaux de perfusion. *Rev ADPHSO*. 2007;32(2):21-3.