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Assessment Intermittent Dosing of Antibiotics: IV Infusion or IV Push? The Impact of Administration Technique on Dose Delivered, Nursing Practice and Hospital Budget

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SUMMARY

Purpose: Hospitalised patients are often treated with Intravenous (IV) antibiotics due to their critical illnes or inability to swallow oral medication. Intravenous therapy can be achieved by intermittent IV infusion, IV push administration or continuous infusion regimens. Tubing residuals impact the administration of adequate drug doses. We evaluated whether IV push injection is superior to intermittent IV infusion for antibiotics in a theoretical model. Based on these findings we describe the implementation of this administration protocol in a large size non-university hospital (1.403 beds) in Belgium, with its benefits and disadvantages.

Methods: All Antibiotics on the formulary of the hospital were evaluated for their aptness to be administered by slow IV push injection. The nursing practice of the two administration techniques was analysed on a pilot ward. The financial impact was also briefly considered, with emphasis on the materials used.

Results: For the intermittent infusion technique the tubing residual was 12 mL, resulting in a net loss of 24% per dose. For the IV push technique, there was no residual volume as the syringe is connected directly the injection site of the patient. Practice on the pilot ward showed that less intervention were needed with IV push administration as compared to intermittent infusion, resulting in time saving for the nurse.

Conclusions: The IV push administration is the technique of choice, is time-saving and results in cost reduction. The implementation of this protocol has to be well prepared, supervised and guided but is relatively easy.

Keywords: Intravenous; Antibiotics; IV push administration; Hospital; Antibiotic stewardship; Dead volume

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INTRODUCTION

Administration of a correct dose of antibiotics is pivotal in the adequate treatment of life-threatening infections [1]. Depending on the antibiotic class, both the time above the minimal inhibitory concentration of the antibiotic (MIC) or the peak concentration of the antibiotic, can be influenced by the posology of the prescribed antibiotic treatment [2]. Thus inadequate dosing can lead to treatment failure or unwanted toxicity, and on a community level to selection of resistant strains [3]. Hospitalized patients are often treated with Intravenous (IV) antibiotics, because of their critical illness or the inability to swallow oral medication. Intravenous therapy can be achieved by intermittent IV infusion, IV push administration or continuous infusion regimens [4]. It has been demonstrated that tubing residuals impact the administration of adequate drug doses [5]. We evaluated whether slow IV push injection is superior to intermittent IV infusion for antibiotics in a theoretical model. Based on these findings we describe the implementation process of this administration protocol in a large size non-university hospital (1.403 beds) in Belgium, with its benefits and disadvantages.

MATERIALS AND METHODS

The intermittent infusion system for antibiotics used in our hospital (AZ Delta hospital, Roeselare, Belgium) consists of a side infusion with the antibiotic agent to be administered dissolved in 50 mL of fluid (preferably saline 0.9%), connected to the main infusion system with an Intrafix® SafeSet (B.Braun, Melsungen, Germany). Baxter (Braine l'Alleud, Germany) viaflo 50 mL saline 0.9% is preferably used to dilute the antibiotic agent (commonly manufactured as freeze-dried powder vial) for intermittent infusion. For IV push injection, the antibiotics are dissolved in the smallest amount of aqua for injection (10 or 20 mL) and administered in a syringe, directly connected to a side port of the main infusion system. This side port is flushed with saline 0.9% (10 mL) before and after bolus injection.For time-controlled infusion, a syringe with the drug solution is placed in an automated infusion pump and connected to the main infusion system using a 1 × 3 mm, LL M/F 200 cm infusion pump extension (Dialex Biomedica, Bilzen, Belgium).All Antibiotics on the formulary of the hospital were evaluated for their aptness (based on the

package leaflet or clinical expertise) to be administered by slow IV push injection. The following antibiotics can be administered in IV push injection in our hospital: amoxicillin, amoxicillin/clavulanic acid, aztreonam, cephazoline, cefepim, ceftazidim, ceftriaxon, flucloxacillin, meropenem, penicillin G and temocillin. Piperacillin-tazobactam, vancomycin, clarithromycin, clindamycin, cotrimoxazole, aminoglycosides and quinolones were excluded from this technique.An analysis of the nursing practice was performed per administration moment for the two techniques under examination. Furthermore the financial impact of this was also briefly considered, with emphasis on the materials used.

RESULTS

Residual volume calculation and impact on net dose administered

For the intermittent infusion system the total residual solution present in the infusion system was 20 mL in a clinical setting [6] (air chamber, tubing and flask); after forced evacuation of the air chamber (actually not safe in a clinical setting but frequently used practice) this still was 12 mL. This was measured in an in vitro test environment. For the slow IV push technique, there was no residual volume as the syringe is connected directly to the 3-way tap of the infusion system, after injection de side port is flushed by saline 0.9% (10 mL). For time-controlled infusion system the residual volume was 1.25 mL. Table 1 summarizes some standard treatment regimens and the impact of the administration system on the actual dose administered.

Changes to the work flow

Based on the theoretical calculations of net dose loss of the antibiotics considered, a change in practice was made with the emphasis on IV push injection. The nephrology ward was selected as pilot ward, based experience with vascular access. Clear instructions were developed by the hospital clinical pharmacists and the vascular access nurse for the slow IV push administration: A video with the procedure was developed and made accessible through YouTube [7] and summary of the technique on a poster with listing of the different antibiotics, do's and don'ts. Practice in this ward showed that, although a 3 minute presence bedside was required to perform, less interventions were needed as compared to the intermittent infusion technique (installing side infusion, stopping side infusion) resulting in time saving for the nurse. In our hospital, the material cost saving for slow bolus administration versus intermittent infusion was calculated at 105.928 EUR per year.

DISCUSSION

With As could be demonstrated the standard side infusion technique for intermittent infusion (common practice in most hospitals) resulted in a minimum loss of net daily dose administered of 24% (for meropenem there is a minimum loss of 12% due to the bigger solution fluid). This can have a considerable impact on the peak levels of the antibiotics, as well as on the time above MIC-depending on the antibiotic class the surrogate for efficacy. Plagge et al. [7] found similar results for the percentage of medication loss and adapted the protocol for infusion at the University Hospital of Basel by increasing the volume of solution (100 mL), thus diluting the injected fluid and decreasing the loss. However, some restrictions apply: if medication has to be administered several times a day, this can generate a strongly positive fluid balance, which may not be desired. It can be applicable for dosing regimens of once daily administrations.In line with these findings, Cooper et al. [8] advocated the flushing of intravenous lines, rather than diluting the solution to tackle this dose loss. This however is not without risk for the patient, as more manipulations are necessary.

Another possibility is the administration of the antibiotic using time-guided infusion pumps. The dead space in this system is considerable lower (1.25 mL in a 2 m tubing), and can be still reduced using shorter tubing. However, the cost of infusion pumps for a hospital wide implementation is high, and not applicable in each hospital. We advocate the use of slow IV push technique, where the antibiotic is diluted in a syringe with 10 or 20 mL aqua for injection and administered as a slow bolus over 3-5 minutes bedside by the nurse. There are several advantages to this administration technique: cost-effectiveness as expensive side bags and connectors are no longer needed and there is no need for expensive infusion pumps, 100% bioavailability of the dose prescribed as this system has no dead space, and local reactions can be monitored directly. Is also helps to improve the nurse-patient interaction

Tab. 1. Data on net medication loss of selected antibiotics based on in the *vitro* test procedure.

Antibiotic	Dose (mg)	Volume for Infusion (mL)	Frequency (times/day)	Concentration (mg/ml)	Minimum Residual dose (ml)	Net Dose Administered	Net Daily Dose (mg)	Theoretical Daily Dose (mg)	Minimum Loss (%)
Amoxicillin	1000	50	4	20	12	760	3040	4000	24
Amoxicillin/ Clavulanic acid	1000	50	4	20	12	760	3040	4000	24
Cefepim	1000	50	4	20	12	760	3040	4000	24
Ceftriaxon	2000	50	1	40	12	1520	1520	2000	24
Ceftazidim	2000	50	3	40	12	1520	3040	4000	24
Flucloxacillin	1000	50	6	20	12	760	4560	6000	24
Meropenem	2000	100	3	20	12	1760	5280	6000	12
Penicillin G	1000	50	6	20	12	760	4560	6000	24
Temocillin	2000	50	2	40	12	1520	3040	4000	24

during the 5 minute administration.The slow infusion technique is not to be used if it is not compatible with the manufacturer's instructions: this is the case for vancomycin (red man syndrome), co-trimoxazol, piperacillin-tazobactam, clarithromycin and clindamycin. Quinolones, aminoglycosides and linezolid are not manufactured as freeze-dried powders but in solutions of +100 mL in Belgium, thus not compatible for IV push administration. In AZ Delta, this technique was implemented on the nephrology ward for 3 months in a test phase: local reactions were uncommon (2 cases on flucloxacillin) and were not severe; nurses reported more ease of use than the intermittent infusion technique. After this test period the IV push injection protocol was implemented hospital-wide, supported by teaching protocols for the nurses provided by our clinical pharmacist and nurse specialist for vascular access. The prescription module in the electronic patient file was adapted to this new administration mode. The whole transition process was finalized in 9 months.The IV push administration technique for selected antibiotics is the technique of choice as it delivers the dose of antibiotics as prescribed, is time-saving for the nurse and results in considerable cost reduction for materials used (more than 100.000 EUR per year in our 1.403 bed Hospital). The implementation of this protocol has to be well prepared, guided and supervised but is relatively easy.

CONCLUSION

Compared with the 2D, the 3D laparoscopic system can significantly reduce the operative time, errors and increase the operating comfort of the surgeon in performing laparoscopic surgery. However, more literature with larger data sample sizes is required to better assess the advantages of 3D vision in laparoscopic.

CONFLICTS OF INTEREST

The authors declare no competing interests.

All authors declare that the material has not been published elsewhere, or has not been submitted to another publisher.

DATA AVAILABILITY

Authors declare that all related data are available concerning researchers by the corresponding author's email.

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DECLARATIONS

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- Ethics approval was not applicable in this project.

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