Survey of medication protocols

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1 Introduction

Medication protocols allow clinicians to administer the correct amount of medication to the patient. Medication protocols may include any procedure necessary to accomplish this goal safely, i.e. to prevent medical/medication errors.

In cooperation with the JRP partners The UMC Utrecht has compiled and disseminated a survey about medication protocols among European hospitals. In order to reach an international target population, a digital survey was developed. The survey was uploaded to the drugmetrology.com website and was made publically available. In the process we contacted several clinicians in order to discuss the questions and the results and to further substantiate some of the common answers.

The aim was to acquire the most relevant medication protocols with an emphasis on preventing adverse drug events (ADE's) as a result of using infusion technology. Special attention was given to multi-infusion and the flow-rate variation. The analysis will be used to establish the necessary accuracy of the flow rate set point in order to be able to control the patient's infusion treatment [REG].

2 Results and discussion

The survey was filled in by 10 different clinical experts from different European countries.

2.1 Protocols

One of the most interesting findings was that infusion system assembling protocols generally existed but were rarely strictly followed in practice. Consequently, clinicians were not commonly familiar with such protocols but nevertheless followed rules by experience.

Medication concentrations and flow rates were well established in protocols. However, clinicians mentioned that medication is highly dependent on application, patient and department. No clear-cut answer could be given. In short, a 'typical' flow rate for a defined application does not exist. We have, however, acquired some values, which will be presented. In order to find the right flow rate set point it is recommended to compare the answers with written protocols that should exist within hospitals.

2.2 Population description

Hospitals / institute

6 of the participants were affiliated with university medical centres, 1 in both peripheral and university medical centres and 3 were unknown/anonymous or unclear. Table 1 shows an overview of the institute types we received.

Institute	Number*
Peripheral/Generalhospital	1
University medical center	6
Commercial / Profit	1
Unknown	3

Table 1. Number of participants by affiliation

*Multiple affiliations possible, n = 10.

Profession

6 Nurses responded, all nursing experts or head nurses, except one who just stated 'nurse'. One respondent was also active as an infusion pump expert consultant besides a nursing expert. 4 doctors responded of which two were specialized anaesthesiologists, one was a neonatologist and one was an unspecified physician. Table 2 shows an overview of the professions of the participants.

Profession	Number*
Nurse	6
Neonatologist	1
Anesthesiologist	2
Infusion consultant	1
Unspecified physician	1

Table 2. Profession

*Multiple professionspossible

Department

Especially in larger hospitals, departments can be part of a larger organizational body. From the answers it could be concluded that the definition of a department varied somewhat in detail among the respondents. Therefore a list will be presented of all the given answers.

- Surgery
- Neonatology
- Intensive care unit
- Healthcare
- Internal medicine
- Vital medicine[1]
- Neurology

It has been found that there is a connection between department and flow-rate difficulties, this will be discussed.

2.3 Infusion process

Number of infusion pumps

From the survey it became clear that the number of pumps and were highly dependent on the department and the patient. Although the modus was 1 pump, 5 pumps were a common average of pumps in departments where multi-infusion was likely to be used.

In neonatology the average estimated number of pumps was found to be around 5, single pump setups were virtually non-existent, the minimal number of pumps in neonatology was about 4. On other departments treatment using just 1 pump occurred more often, although one respondent from surgery stated that all patients were treated with multi-infusion. The highest value we received was 15 pumps, the average overall value was 4with a standard deviation of 4.24. Figure 1 shows the normal (Gaussian) distribution.

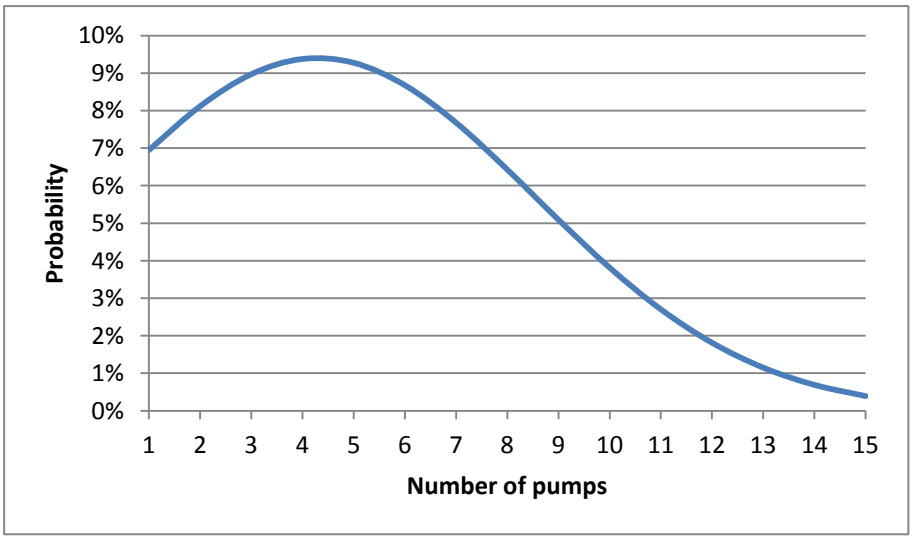

Figure 1. Normal distribution of the number of pumps.

[1]Organizational entity consisting of departments of OR centre, ICU and emergency department.

Protocols for assembly of an infusion setup

To the question what elements a protocol for assembling the infusion setup contained the answers varied. After discussing the matter in person it was found that strict protocols were generally not known by hearth of the clinician. Table 3 shows an overview. Notice that the percentages in the multiple-choice answers reflect the ratio of the total population that picked the answers. Figure 2 shows an overview of all the multiple-choice answers.

Protocol element	Number	Percentage
Placement of pumps	3	30%
Characterization of disposables	4	40%
Sequence of connection /solutions	3	30%
Use of multi-lumen catheters	5	50%

Table 3. Elements of assembly protocol

From the answers it appears that a protocols usually contains all the listed items. Although the use of multi-lumen appear more often, no conclusions can be drawn with this relatively small certainty (± 1.58, 95% CI). Also no relation between the protocol elements and de clinician's background was found.

Clinical effects of flow variation

Inotropic agents and vasopressors were mentioned as critical drugs sensitive to flow rate variation. Many drugs are both inotropic and vasopressors. Cardio-active drugs were also stated of influence. Especially in neonatal care flow rate variation was found to exert clinical effects because of under- or over-dosing. Narrow therapeutic ranges are closely related to adverse effects. From neonatal care the height of the pump was told to be of influence on the flow rate by one nursing specialist. 4 respondents, active mainly in adult health care did not observe or know about such effects. It should be noted that many of these respondent were not working in an ICU either.

Patient characteristics

Adults were the most common patient group, this was consistent with the background of the participants. Table 4 shows an overview.

Patientgroup	Number	Percentage
Adults	7	70%
Children	2	20%
Neonatalpatient	3	30%
Otherspecificpatientgroup	3	30%

Table 4. Patient groups

ADE's as a result of using multi-infusion

ADE's (adverse drug events) and other medical errors are a sensitive subject. Therefore it could be expected not all clinicians answer such questions freely.

The use of a protocol to and the use of multi-lumen to prevent mixtures were given as answers to prevent ADE's. Still, unexpected clinical interventions such as a kink in the infusion line could disrupt the flow rate and cause ADE's, one participant in neonatal care stated. Also the absence of line markings was given as a cause of ADE's with the use of multi-infusion in general. One participant in anaesthesiology stated that flow rate variations cause adverse events weekly/monthly, often as a result of inappropriate use. In neonates the therapeutic ranges of infused drugs were stated to be particularly narrow. The anaesthesiologists mainly stated changing hemodynamic parameters as a result flow rate variation. Again, the inotropic agents and vasopressors were illustrated as critical drugs in relation to ADE's. Most ADE's were caused by inappropriate use. Clinicians were not able to tell whether mutual influence of infusion lines were responsible for flow rate variation but most did not dismiss that possibility.

Medication types used by the clinician

A tendency towards the use inotropic agents was found. Most treatment procedures needed some kind of muscle regulator. The use of a certain type of medicine is related to the speciality of the clinician. Anaesthesiologists obviously used analgesia but this was also common in other department including neonatology. In neonatal care the inotrope dobutamine is common. Antibiotics and anti-epileptics were also used in neonatology, this caused clinical effect as a result of flow rate variation as well. A narrow therapeutic range was stated as an indication for profound side-effects. In neonatal care parental fluid is also common but also in adult critical health care such oral intake of nutrition is often not possible. Other medications that were mentioned were: anti-emetica, KCl and TPA.

Pharmaceutical	Number	Percentage
Analgesia	4	40%
Cytostatics	4	40%
Cardio-active	4	40%
Inotropic-agents	7	70%
Others	3	30%

Table 5. Used pharmaceuticals

Number of patientbeing treated with multi-infusion

In general/peripheral hospitals the number of pumps is generally lower than in university hospitals. The reason is that in University hospitals complex cases are treated that typically require multiple medications. One nursing experts estimated that 50% of the patients were treated with multi-infusion in a peripheral hospital, whereas 70% of the patients were treated with multi-infusion in university hospitals. Respondents from surgery stated that all patients were treated with multi-infusion. In neurology an estimate of 20% was given. Other university hospital personnel answered "all" or "most".

Common pathologies

Many respondents did not provide the specific pathologies of their patients. However, the pathologies should be consistent with the clinical specialities of the respondents. The pathologies that were provided included prematurity, birth defects, low birth weight and oxygen shortage in neonates but also sepsis. Other pathologies were: cancer in oncology, neurological suffering and everything related to the head in neurology.

Flow rates and concentrations

A typical flow rate that was given is 1 ml / h. Drug concentrations differed and were highly dependent on the type of drug and the patient. The patient weight is an important factor. Consequently neonates are usually infused with small concentrations. The flow rate is dependent on the therapeutic range and the half-life of the pharmaceutical. In general in surgery and neonatal care low concentrations and flow rates are often used. Participants used different units, not always including the patient weight as a factor. In neonatal care 5 µg / kg / min was used for inotropic agents, 1 mg / kg / day for analgesia and 1 mg / kg / h for anti-epileptics.

From one anaesthesiologist the following answer was received: Norepinephrine 0.02 mg/ml or 0.1 mg/ml titrated to effect. Vasopressor-dependency (high doses of norepinephrine) means a higher probability of hemodynamic instability with flow-rate variations. Analgesia, inotropic agents and cardio-active agents were commonly specified on flow rate or concentration by the respondents, table 6 shows an overview.

Clinicians stated that dosage and flow rate can generally be found in protocols.

Department	Mass flow rate
Surgery	0.02 – 0.1 mg / ml* cardio-active
	0.5 – 1 ml / h several
Neonatology	5 - 15 µg / kg / min† inotrope
	1 mg / kg / day analgesia

Table 6. Explicitly stated mass flow rates

* Concentration only.

†Concentration per kg of patient weight but not the concentration of the solvent.

Technical details of the infusion setup

The technical details of the infusion setup used varied among the respondents. Most respondents used some kind of check valves. In anaesthesia there was experience in the use of PCA (patient controlled analgesia) pumps. Filters were used in neonatal care, but were stated not to have a regular place in practice by one of the respondents. Smart sites were mentioned in neonatal care to prevent the medical solvent to contact with the outside air. Syringe and volumetric pumps were both used, also in combination. One respondent had experience with the use of pumps at the patient's residence. Aside from the use of filters in neonatal care no relation between the setup and other answers could be found.

Infusion treatment process

The phases of the infusion treatment process can usually be found in protocols. In anaesthesiology/surgery tubing was never changed during the operation. Changing of the syringe depended on flow rate. One respondent from surgery stated that a protocol was used in the post-operative phase where replacement of the material should be exercised every 96 hours. In neonatal care infusion was also renewed every 96 hour and the bags used in volumetric pumps every 24 hour. One respondent informed us about the guidelines which stated that renewal every 9 hours was recommended for parenteral infusion and for blood transfusion every 24 hours renewal should be performed. The entire infusion process can be described as follows (stated by a neonatologist): a doctor prescribes the medication. The pharmacy prepares the medication at the prescribed concentration, pharmacy also prepares the infusion tubing. Nurses eventually administer the infusion to the patient by connecting the medication and infusion lines to the infusion pumps which are already available at the department.

Patient response to multi-infusion treatment

With the use of multi-infusion the patient response was in many cases different from what the clinician expected. Anaesthesiologists reported patient response was in some cases the opposite of what was expected and in some other cases the patient did not respond at all, although this might have been a result of mixing up the medicine and not a flow rate difference. In neonatal care a different patient response was not described as common, although blood pressure difference as a result of flow rate change did occur often. However, this is expected when, for example, the pump height is altered. One respondent doubted whether flow rate changes as a result of multi-infusion were more significant than the differences in the patient physiology and the severity of the pathology of the patient. However, many clinicians acknowledged that mutual influence of infusion lines could be a cause of flow rate variation on top of the existing physiological variation between different patients.

Physical properties of influence in infusion treatment

External physical properties of influence in infusion treatment were known by some of the respondents. Light was stated several times as a cause for the reduction of pharmacological potency. Chemical stability and interaction with other medication was also stated. Some of the participants were aware of the influence of viscosity, pressure and ambient temperature but no hierarchy of these effects was provided.

Prevention of medication errors

A number of preventive measures were given by the participants. Driving flow behind critical medications, using multi-lumen and using low concentrations and high flows were answers given by ananaesthesiologist. Another anaesthesiologist recommended to use continuous flow of saline on the "inotropic lines", not using drips in order to keep flow rates constant. Also not using the IV dedicated for volume therapy in concomitant inotropic support was recommended. In neonatology it was suggested that following the protocols that did exist would improve overall safety. Protocols were not always followed at this point. One respondent recommended to use more markings, coloration and other information on the pumps and the lines that helps clinicians performing the infusion process in the correct manner. Also a nurse suggested that a pharmacist should perpetrate the medication instead of the nurse. Smart pumps were also mentioned. However, it was stated that in some departments, especially outside intensive care smart pump might only complicate the infusion process. Finally, good education aimed at the proper use of infusion pumps was given as a suggestion.

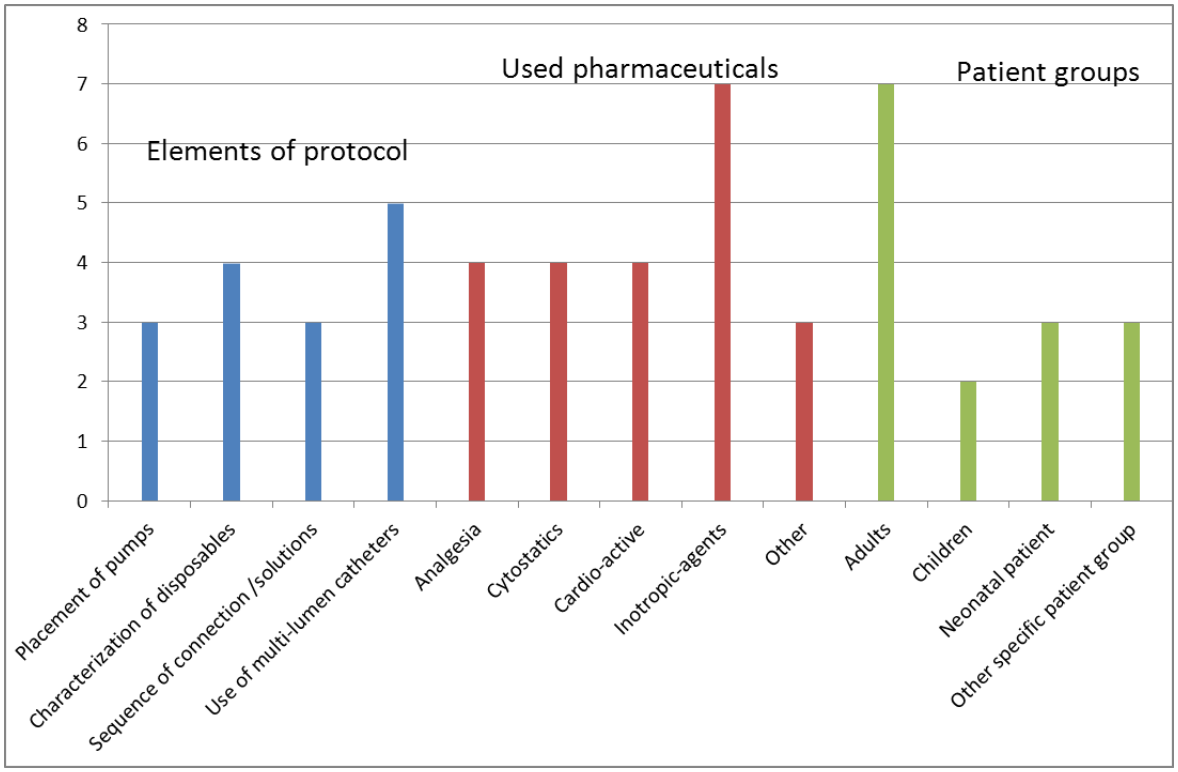

Figure 2. Overview of multiple choice answers

3 Conclusion

Medical errors do occur, usually as a result of human error. It is also common that a patient does not respond to medication as expected, even when medication errors are not the cause. Most respondents were aware of flow rate differences that in several cases resulted in clinical effects. However, they found it hard to determine whether this was the result of mutual influences between the infusion lines. Nevertheless many clinical professionals found that assumption plausible.

Overall, responses on pharmaceuticals such as inotropic agents, vasopressors and cardio-active were often stated to be sensitive to flow rate changes. ADE's were rare in relation to flow rate differences, but the use of multi-infusion in general probably resulted in some known ADE's as stated by the participants.

Flow rates were generally low, related to the therapeutic range of the medication. Flow rates were found to be in the area of millilitres per hour. Concentration varied a lot with the used pharmaceuticals. Neonatology came forward of as the most prone to flow rate errors. Neonatal personnel were especially aware of the adverse effects of flow rate in combination with multi-infusion. Again, inotropes were among the most critical pharmaceuticals to result in adverse effects when flow rate is altered.

4 Optimization

Some clinicians experienced trouble understanding the question. We have interviewed clinicians and discussed the survey with some clinicians active in the UMC Utrecht and received valuable feedback. Some points for future improvement:

- It was not particularly clear what kind of pumps were discussed. Especially those who worked with a lot of different pumps mentioned large differences between the types of pumps and the location where pumps were applied.
- Number of patient treated with multi-infusion was interpreted as an absolute number in some cases.
- Flow rates and concentrations were usually too diverse to answers. The question could be inquired for particular common pharmaceuticals with pre-defined units.

Appendix I: Overview of survey questions

- 1. How many infusion pumps do you use in general on one catheter for infusion treatment of your patients? How many do you maximally put on one catheter?

- 2. Do you use a protocol for assembling the infusion system? If so, which elements does it contain?
    - Placement of pumps
    - Characterization of disposables that are used (syringes, infusion lines etc.)
    - Sequence of connection of solutions / medications
    - Use of multi-lumen catheters

- 3. Have you ever encountered clinically relevant effects of flow rate variations? If so, during which treatment was did this occur? If not, during which treatment do you expect these to take place?

- 4. In your experience, have you encountered adverse drug events (ADE) caused by the use of multi-infusion?
  - Why does this occur?
  - How often does it occur?

- 5. Could you share with us some details about the situation/setting in which an ADE or clinically relevant flow rate variation could occurs? Please consider the following sub questions:

- 5a. Medication type, consider also a combination of medications
    - Analgesia
    - Cytostatics
    - Cardio-active
    - Inotropic-agents
    - Other
- 5b. Patient characteristics
    - Adults
    - Children
    - Neonatal patients
    - Other specific patient group with specific pathology
- … 5b. How many patients are being treated using multi-infusion?

- 5c. What is the most common and/or critical pathology of the patient in relation to clinically relevant flow rate fluctuations or ADE's?

- 5d. Could you disclose, in relation to the previous questions, the drug concentrations in which ADE's occur?

- 5e. Could you disclose, in relation to the previous questions, the flow rates of the pumps in which ADE's occur?

- 5f. What are the technical details of the infusion setup used in your department? Which configurations and which sequence do you use for which application and which of the following elements:
  - pumps
  - lines
  - syringes
  - check valves

- filters
- other

- 6. Could you explain something about the different phases of the treatment of a patient?
  - In which phase are you using what materials? (e.g. filters, check valves, infusion lines, syringes)
  - What in general is the frequency of your material replacement (e.g. infusion line, syringe replacement)?
  - In which phase undertaking what procedure will an ADE most likely occur?

- 7. Using multi-infusion, has it ever occurred that you wanted to alter a medication rate but the patient response to the medication was different from what you expected (considering this is not related to the state of the patient)?
  - Was it ever the opposite of your expectation?
  - Did it ever occur that the patient completely failed to respond to the medication or responded too late?

- 8. Have you ever considered that external physical properties and physical properties of the medication may influence drug delivery? If so, what are these properties?

- 9. Are there any procedures to prevent ADE's that you take or could think of?

- 10. Are you familiar with earlier research carried out with relation to the performance (accuracy) of infusion devices? If so, did you take the outcomes into account when using these devices?

- 11. Is there anything else you would like to inform us about in relation to the subject?

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