29ème Congrès Aquitain de Médecine d'Urgence

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MODALITES DE PREPARATION ET D'ADMINISTRATION DES AMINES

Kevin FIEVET, IDE, CHIC Marmande-Tonneins

Besoin de protocolisation

- Des médicaments puissants
- Des patients vulnérables
- Une absence de standardisation

JCN Journal of Clinical Nursing
The International Voice of Nursing Research, Theory and Practice

EMPIRICAL RESEARCH QUALITATIVE | Open Access

The influence of intensive care unit culture and environment on nurse decision-making when managing vasoactive medications: A qualitative exploratory study

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Elizabeth Manias BPharm, MPharm, MNursStud, PhD

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Risque d'erreur

Classes of drugs and rates of associated errors

Class	Administrations	No (%*) of errors
Vasopressors and catecholamines	702	57 (8)
Coagulation related	1107	73 (7)
Electrolytes	1450	82 (6)
Antimicrobial	1905	179 (9)
Sedation and analgesia	2136	181 (9)
Others	3668	243 (7)
Total	11 725	857† (7)

*Proportion of administrations that resulted in errors.

Valentin A. Errors in administration of parenteral drugs in intensive care units: multinational prospective study. *BMJ*. 2009.

Risque d'erreur

Table 5 Number o

Agent	
Epinephrine	17/214 (7.9)
Potassium chloride	4/59 (6.8)
Magnesium	6/112 (5.4)
Digoxin	29/496 (5.8)
Lorazepam	26/572 (4.5)
Norepinephrine	9/208 (4.3)
Heparin	20/576 (3.47)
Midazolam	3/92 (3.3)
Dobutamine	11/341 (3.2)
Fentanyl	4/138 (2.9)
Low-molecular-weight heparin	6/225 (2.7)
Other vasoactive agents (e.g., phenylephrine)	9/357 (2.5)
Morphine	8/367 (2.2)
Vecuronium	2/92 (2.2)
Dopamine	14/667 (2.1)

Epinephrine	17/187 (9.0)
Potassium chloride	4/187 (2.1)
Magnesium	6/187 (3.2)
Digoxin	29/187 (15.5)
Lorazepam	26/187 (13.9)
Norepinephrine	9/187 (4.8)
Heparin	20/187 (10.7)
Midazolam	3/187 (1.6)
Dobutamine	11/187 (5.8)
Fentanyl	4/187 (2.1)
Low-molecular-weight heparin	6/187 (3.2)
Other vasoactive agents (e.g., phenylephrine)	9/187 (4.8)
Morphine	8/187 (4.2)
Vecuronium	2/187 (1.0)
Dopamine	14/187 (7.4)

Calabrese A.D. Medication administration errors in adult patients in the ICU. *Intensive Care Medicine*, 2001.

Risque d'erreur

Table 4 Frequency of medication errors in all stages of the medication preparation or administration

Type of error	Number of errors	Percent of total	Factor correction[a]	Corrected percent	Corrected percent of total (%)
Fast bolus administration	189	49.7	524	36.1	43.4
Wrong infusion rate	100	26.3	524	19.1	23.0
Wrong dose or diluent calculation	38	10.0	220	17.3	20.1
Inappropriate diluents	49	12.9	524	9.35	11.2
Inappropriate storage of drug before dilution	2	0.5	220	0.9	1.1
Incompatibility	1	0.3	524	0.2	0.2
Inappropriate storage of diluted drug	1	0.3	524	0.2	0.2
Total	380	100.0	3060	83.2	100.0

[a] Number of observations multiplied by the number of opportunities for errors.

Fahimi F. Errors in preparation and administration of intravenous medications in the intensive care unit of a teaching hospital: An observational study. *Australian Critical Care*. 2008.

Mettons-nous en situation

- Patiente en état de choc malgré remplissage, pour laquelle on a une prescription de Noradrénaline 0.1 µg/kg/min
- La patiente pèse 39kg
- On dispose d'ampoules de 4ml dosées à 2mg/ml et de seringues de tailles variées

  - ➢ Quelle dilution prépare-t-on?
  - ➢ À quelle vitesse l'administre-t-on?

Méthodes de calcul

- Concentration variable :

  Quantité (en mg) de drogue prélevée en fonction du poids:

  poids (kg) x 0,3 + diluant QSP 50ml

  ➔ 0,1 µg/kg/min=1ml/h

Méthodes de calcul

- Concentration fixe :

  La préparation est la même quel que soit le patient

  Ex: 24 mg dans 48ml (0,5mg/ml)
  8 mg dans 40ml (0,2 mg/ml)
  4 mg dans 40ml (0,1mg/ml)
  3 mg dans 50ml ➔ (poids/10)ml/h = 0,1mcg/kg/min
  …

  Le débit est réglé en fonction d'abaques

Taille des seringues

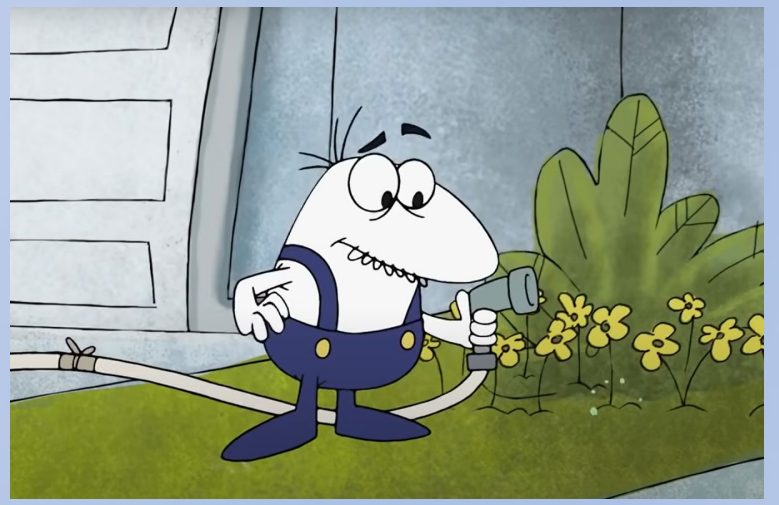
Table 1. Fluid delivery chart showing the effect of start-up times

Time	Distance travelled by plunger driver (mm)	Distance travelled by plunger into barrel (mm)	Volume left in syringe (ml)	Totaliser (recorded from pump) (ml)	Volume actually delivered in preceding hour (ml)
9h00			50.0	0.0	
10h00	0.9	0.0	50.0	0.5	0.0
11h00	1.8	0.0	50.0	1.0	0.0
12h00	2.7	0.7	49.6	1.5	0.4
13h00	3.6	1.6	49.1	2.0	0.5

The two columns showing distance travelled by the plunger indicate how the initial plunger movement is not reflected in a movement of plunger with respect to the barrel. These data would not be charted.

Table 2. Distance of plunger travel per hour to provide a flow rate of 1ml/hr

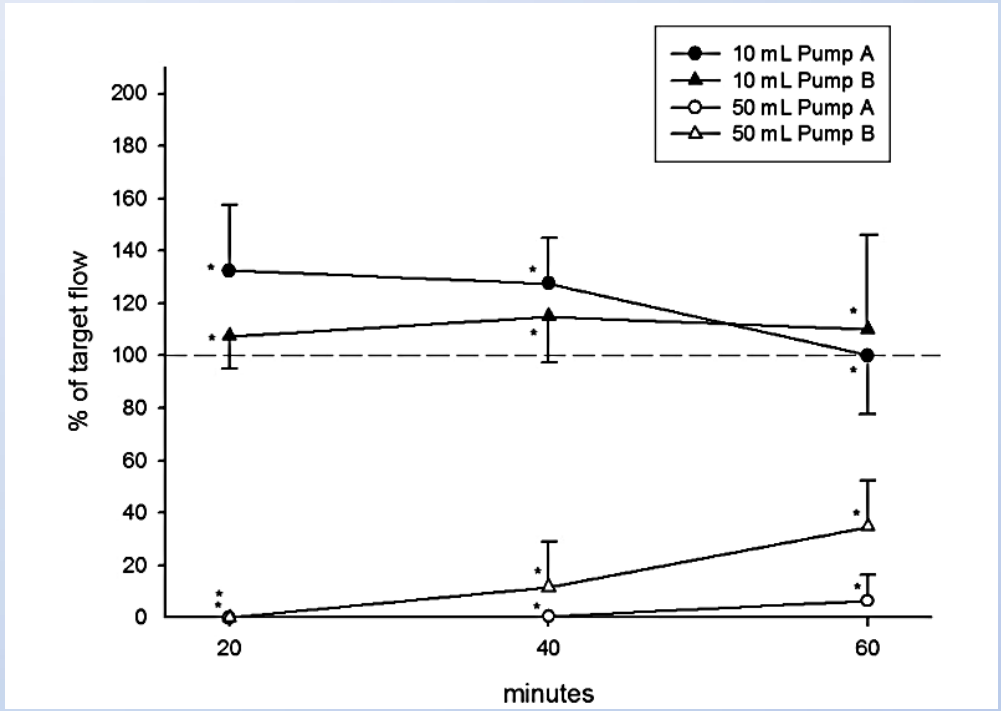
Syringe size	(ml)	2	5	10	20	30	50/60
Distance of plunger travel per hour	(mm)	17.4	8.86	6.15	3.54	2.73	1.81



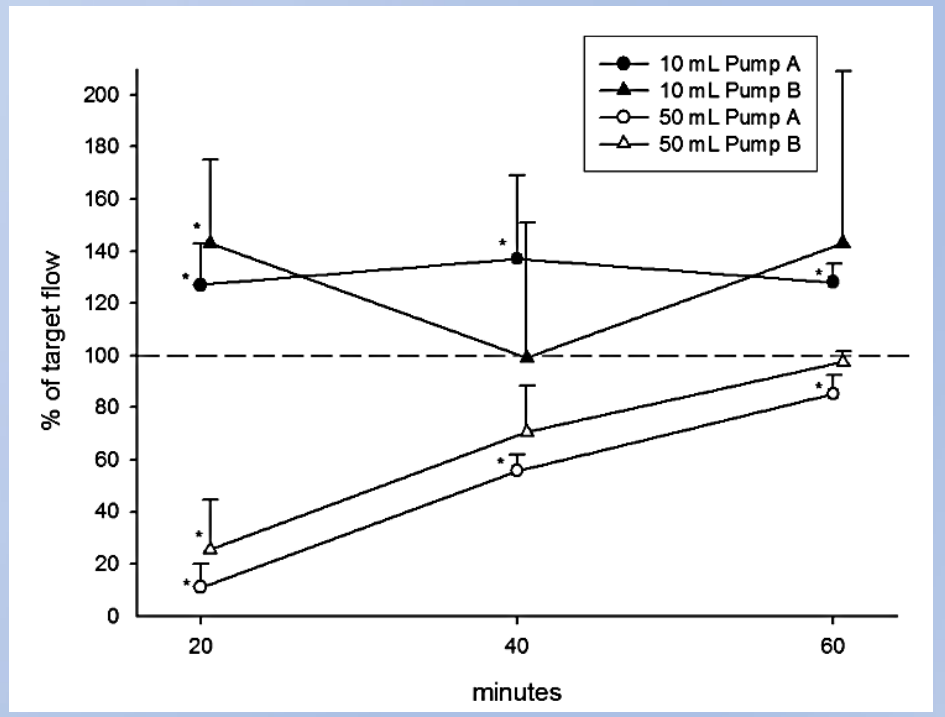
Amoore J. Syringe pumps and start-up time: ensuring safe practice. *Nursing Standard.* 2001.

Taille des seringues

Pourcentage du débit cible atteint en 60 min à 0,4 ml/h selon la taille de la seringue

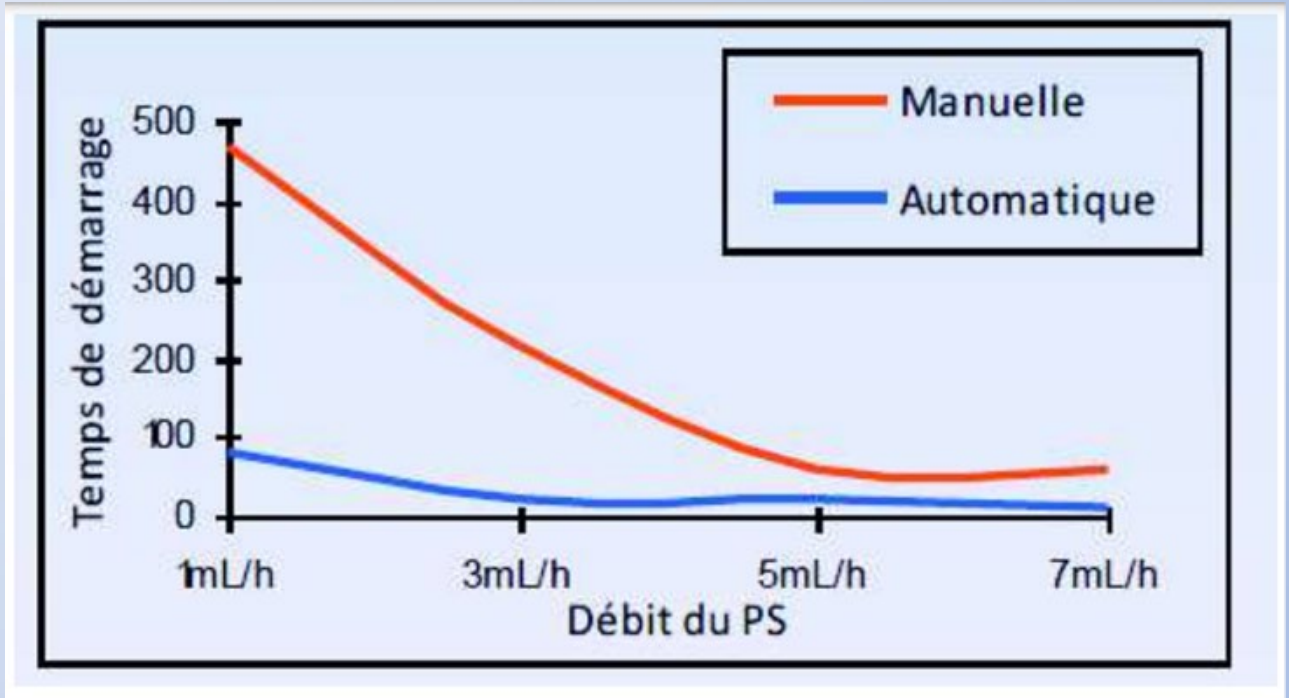


Pourcentage du débit cible atteint en 60 min à 1 ml/h selon la taille de la seringue



Schmidt N. Impact of syringe size on the performance of infusion pumps at low flow rates. *Pediatric Critical Care Medicine.* 2010.

Purge automatique

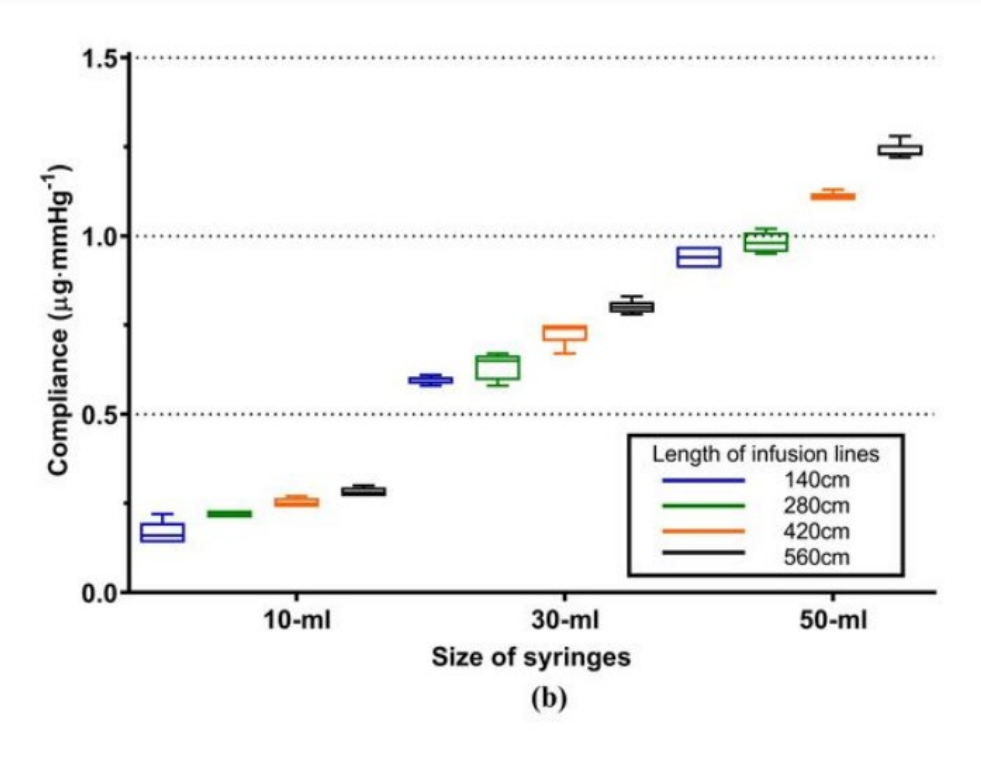


Temps de démarrage du pousse seringue en fonction du débit :
Purge manuelle vs purge automatique

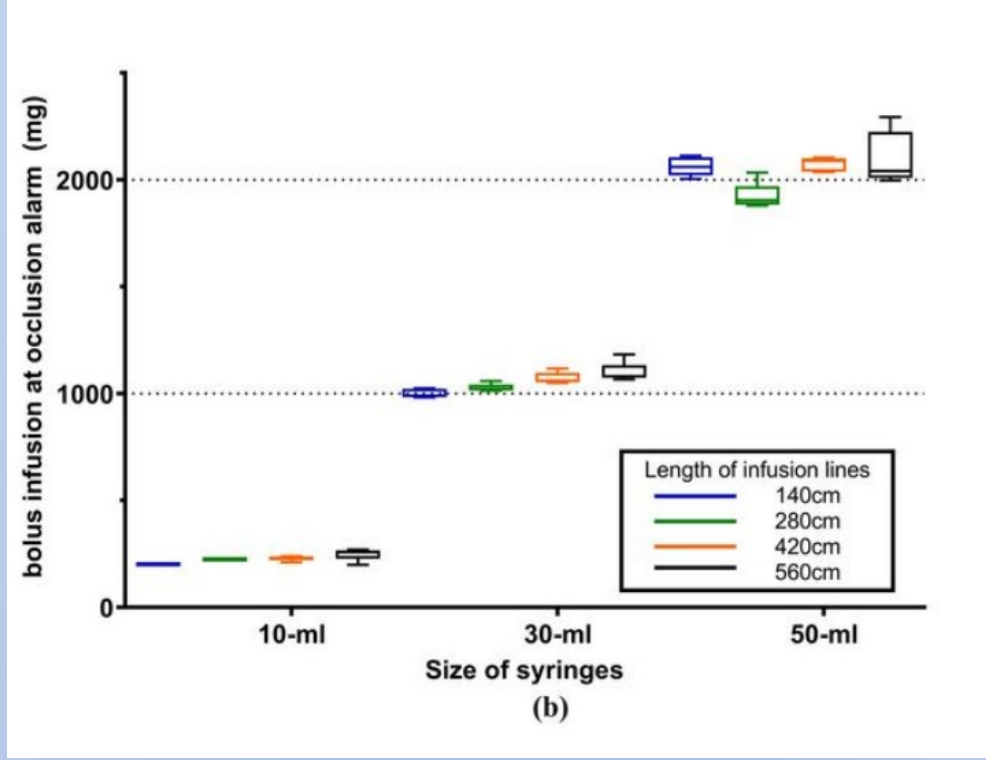
Pinturaud M. Temps de démarrage des pousse-seringues : comparaison de quatre dispositifs dans différentes conditions de débit et d'amorçage. Journées Euro-pharmat, Toulouse. 2010.

Compliance du circuit

Compliance du circuit selon son volume

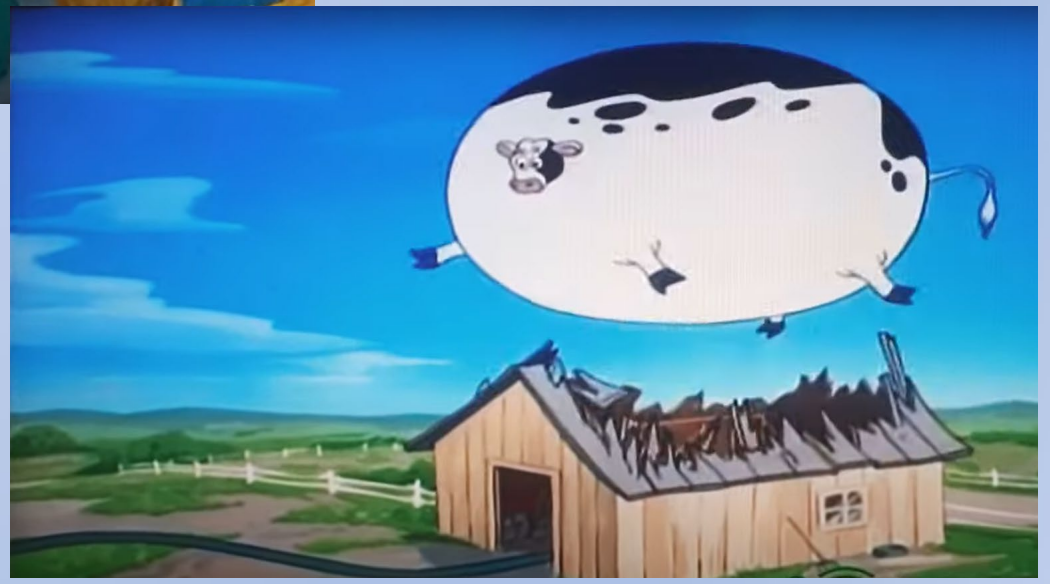


Bolus à la désobstruction selon la compliance du circuit

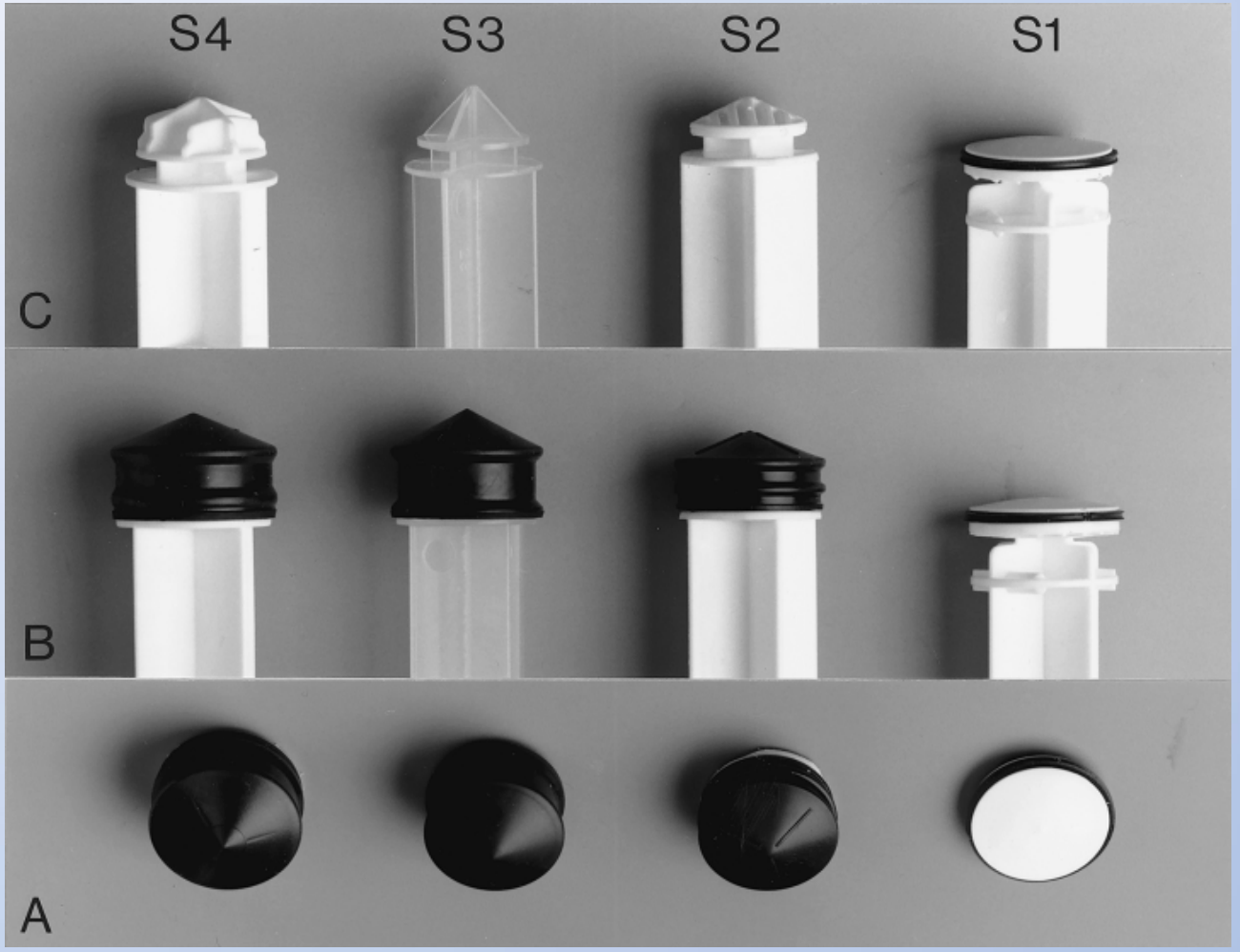


Hong K.Y. Effects of infusion tubing line lengths and syringe sizes on infusion system compliance: an experimental study using a syringe-type infusion pump at low flow rate. *Journal of Clinical Monitoring & Computing*. 2023.

Compliance du circuit



Compliance du circuit



Weiss M. The effects of syringe plunger design on drug delivery during vertical displacement of syringe pumps. *Anaesthesia*. 2000.

Longueur des lignes de perfusions…

Pumps lined up outside patient rooms in a hospital ICU (March 2020).

Institute for Safe Medication Practices. Clinical Experiences Keeping Infusion Pumps Outside the Room for COVID-19 Patients. 2020.

Déplacement verticaux des PSE

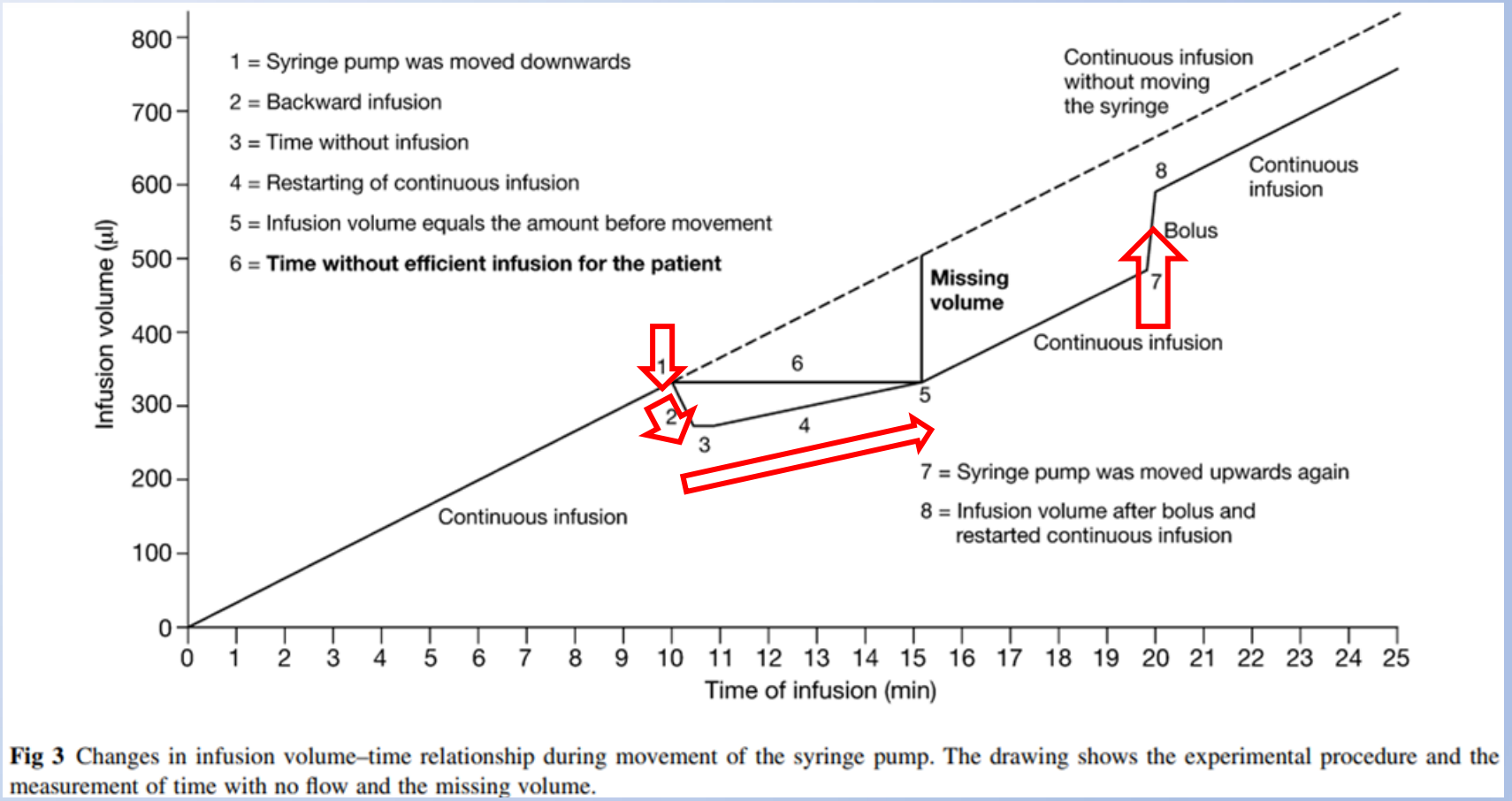


Fig 3 Changes in infusion volume–time relationship during movement of the syringe pump. The drawing shows the experimental procedure and the measurement of time with no flow and the missing volume.

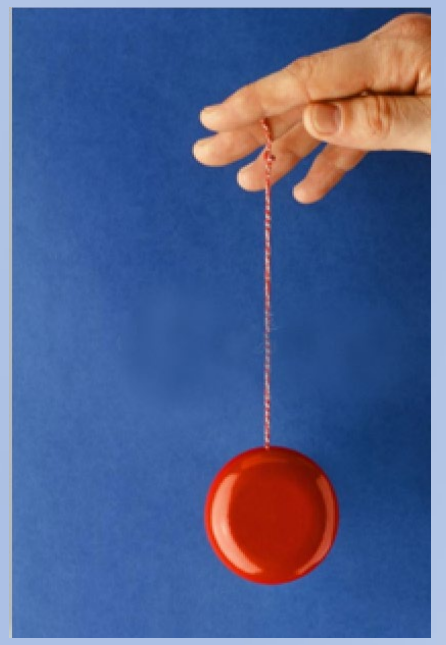
Kern H. Downward movement of syringe pumps reduces syringe output. *BJA: British Journal of Anaesthesia.* 2001.

Déplacement verticaux des PSE

TABLE II Zero drug delivery time (ZDDT) and back flow volume (BFV)

Infusion rate	*1 mL·hr^{-1}*	*3 mL·hr^{-1}*	*10 mL·hr^{-1}*
ZDDT (sec)	217 ± 44.1*	56.8 ± 13.4*	15.3 ± 3.8*
BFV (µL)	12.3 ± 4.1	14.0 ± 3.8	21.1 ± 3.5

Mean ± SD; $n = 17$. *$P < 0.001$ between settings.



Igarashi H. Syringe pump displacement alters line internal pressure and flow. *Canadian Journal of Anesthesia*. 2005.

Homogénéité de la seringue

Écarts de concentrations de catécholamines dans des seringues électriques selon différents modes de préparation

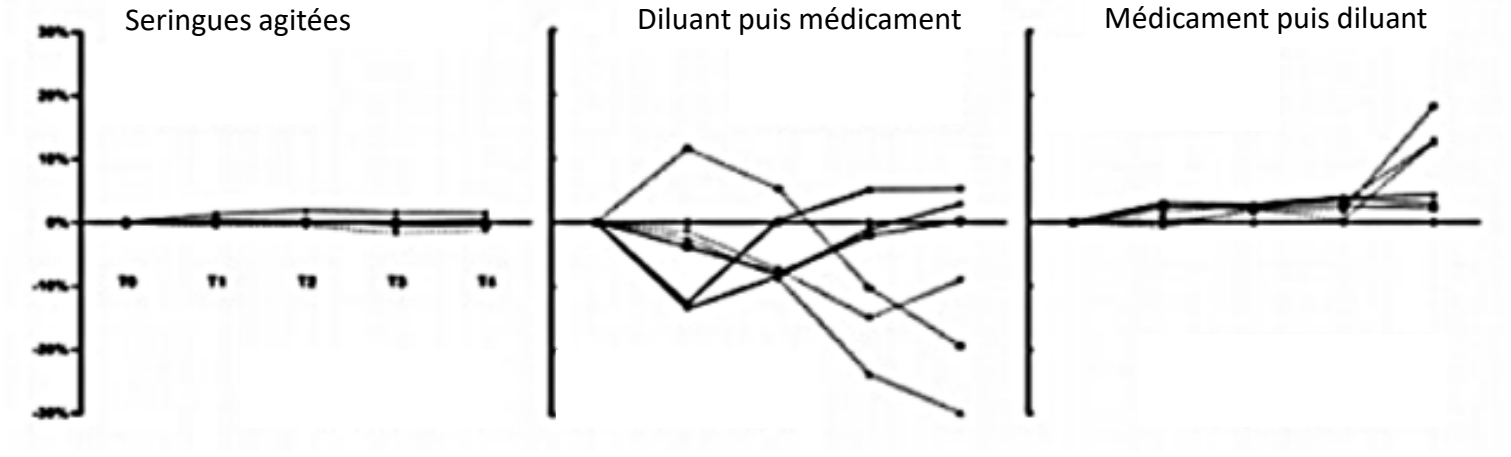


Fig. 1 Dehu Y, CP381 congrès urgences 2010

« Il faut bien secouer, sinon la pulpe elle reste en bas »

Girault F. Doit-on remettre en cause le mode de préparation des seringues électriques (SE) d'adrénaline (Ad) et de noradrénaline (Nad) ? *Réanimation.* 2011.

Homogénéité de la seringue

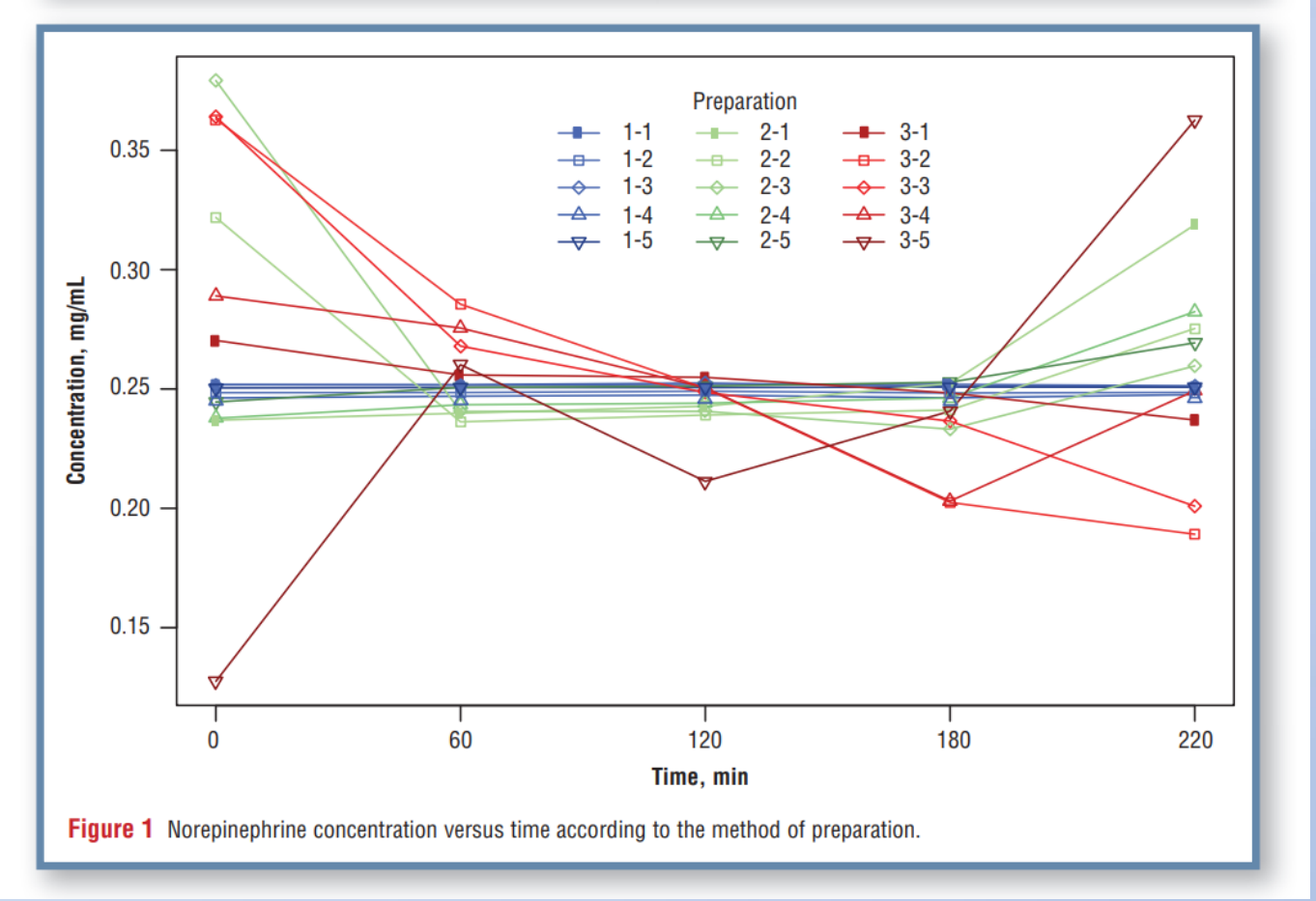
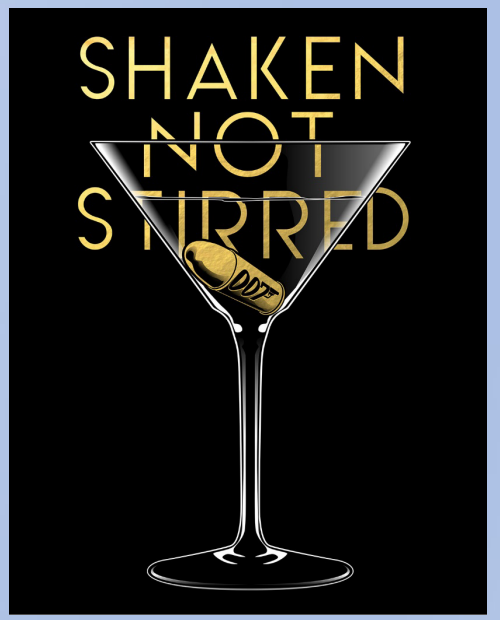


Figure 1 Norepinephrine concentration versus time according to the method of preparation.



1. Agitée
2. NAD puis G5%
3. G5% puis NAD

Garrigue B. Preparing Drugs for Infusion Via Syringe Pump: A Key Step to Ensure Homogeneous Concentration. *Critical Care Nurse.* 2016.

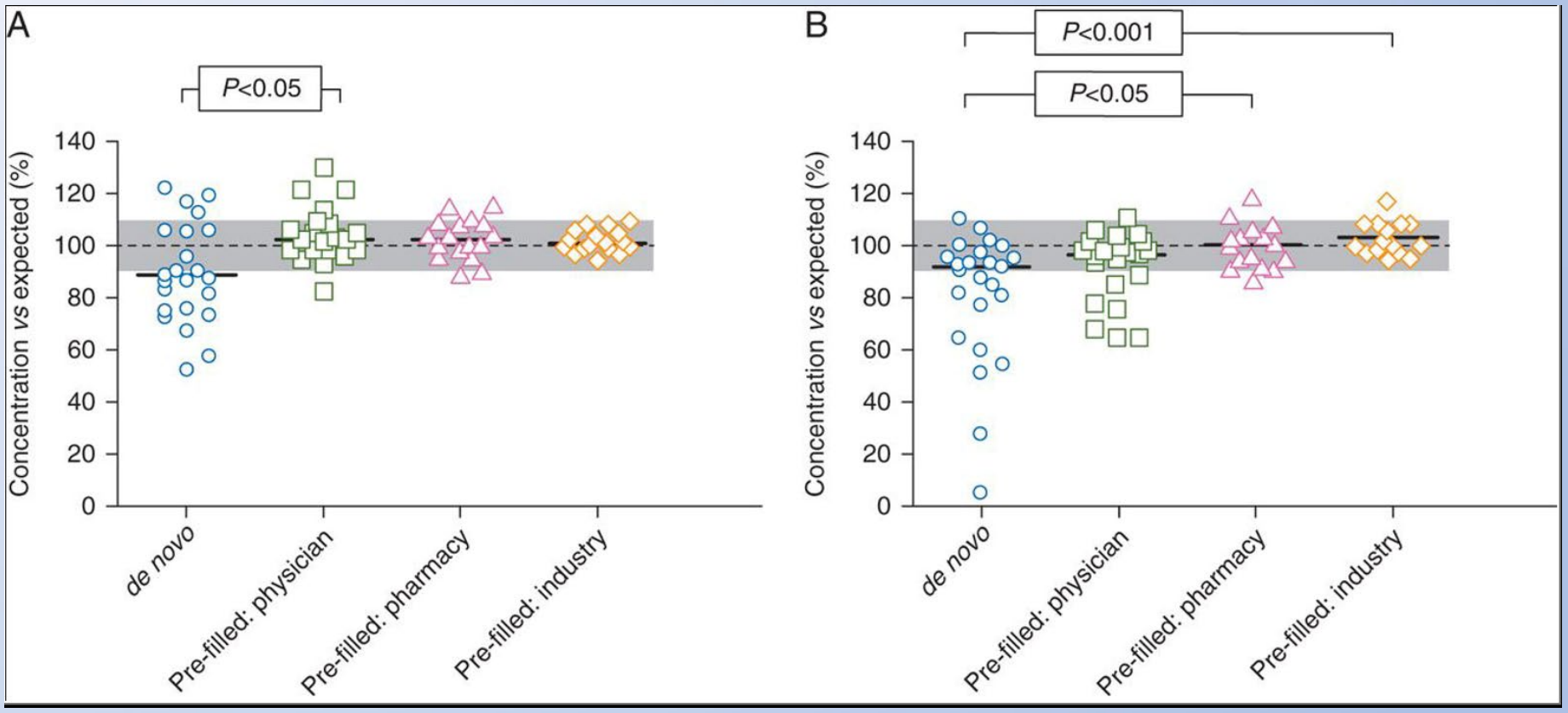
Seringues préremplies ?

Table 1 The influence of infusion preparation technique on time taken to prepare infusions and drug concentration

Syringe type	Time taken from request to administration		Mean concentration of contents as percentage of that prescribed					
	Norepinephrine	Epinephrine	Norepinephrine			Epinephrine		
	Mean time (95% CI) (s)	Mean time (95% CI) (s)	95% CI (%)	sd (95% CI)	Number meeting USP criteria	95% CI (%)	sd (95% CI)	Number meeting USP criteria
Prepared *de novo*	277 (246–308)	274 (242–306)	90.3 (82.3–98.4)	25.6 (19.9–35.9)	7/24 (29.2%)	80.9 (70.0–91.7)	19.0 (14.8–26.7)	12/24 (50.0%)
Pre-filled by physician	146 (129–164)	166 (134–198)	104.5 (99.9–109.1)	13.0 (10.1–18.3)	18/24 (75.0%)	92.2 (86.6–97.7)	10.9 (8.5–15.3)	16/24 (66.7%)
Pre-filled by industry	—	—	102.8 (99.0–106.5)	8.5 (6.3–13.1)	16/16 (100%)	99.8 (95.3–104.3)	7.5 (5.6–11.2)	15/16 (93.8%)
	—	—	102.1 (99.9–104.3)	6.5 (4.8–10.0)		102.9 (99.4–106.3)	4.4 (3.3–6.6)	

Adapa R.M. Errors during the preparation of drug infusions: a randomized controlled trial. *British Journal of Anaesthesia*. 2012.

Seringues préremplies ?



(A) **Concentrations of norepinephrine infusions.** (B) **Concentrations of epinephrine infusions.**

Adapa R.M. Errors during the preparation of drug infusions: a randomized controlled trial. *British Journal of Anaesthesia*. 2012.

Étiquetage

Figure 1 Norepinephrine 5 mg mixed with Ringer's lactate 1000 mL. Note the ballpoint pen marking at the bottom stating '+NOR 5 mg/500 mL'.

Observatoire des Médicaments Dispositifs médicaux Innovations Thérapeutiques

OMéDIT Centre-Val de Loire

FICHE DE BON USAGE

Commission Prescrire

Mise à jour :Avril 2016

Validation Comité stratégique : Juin 2016

RÈGLES POUR L'ÉTIQUETAGE DES PERFUSIONS ET SERINGUES PRÉPARÉES DANS LES UNITÉS DE SOINS

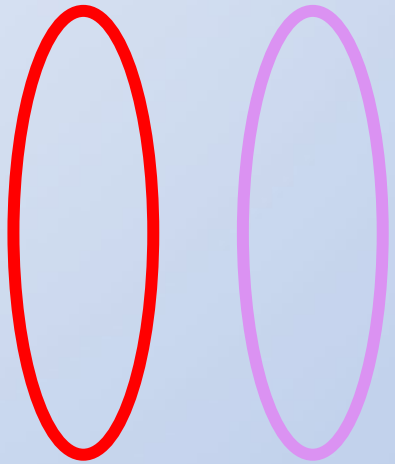
Classe pharmacologique	Exemples	Couleur Pantone*, Trame
Anti - émétiques	Métoclopramide, Ondansétron, Dropéridol	Saumon 156
Hypnotiques	Thiopental, Étomidate, Kétamine, Propofol	Jaune
Benzodiazépines	Diazépam, Midazolam	Orange 151
Antagoniste des benzodiazépines	Flumazénil	Orange 151 et bandes blanches diagonales
Curarisants	Succinylcholine, Atracurium, Cisatracurium, Vécuronium, Rocuronium	Rouge fluorescent 805 ou rouge vif
Antagonistes des curarisants	Néostigmine	Rouge fluorescent 805 ou rouge vif et bandes blanches diagonales
Opioïdes	Morphine, Fentanyl, Sufentanil, Remifentanil, Alfentanil	Bleu 297
Antagonistes des opioïdes	Naloxone	Bleu 297 et bandes blanches diagonales
Sympathomimétiques	Adrénaline, Noradrénaline, Éphédrine, Phényléphrine	Violet 256
Anti - hypertenseurs	Nicardipine, Nitroglycérine, Phentolamine	Violet 256 et bandes blanches diagonales
Anesthésiques locaux	Lidocaïne, Bupivacaïne, Ropivacaïne, Lévobupivacaïne, Mépivacaïne G	Gris 401

Hansel J. Cardiac arrest due to accidental overdose with norepinephrine dissolved in crystalloid. *BMJ Case Rep*. 2020.

Relais des catécholamines

Poiroux L. Minimising haemodynamic lability during changeover of syringes infusing norepinephrine in adult critical care patients: a multicentre randomised controlled trial. *British Journal of Anaesthesia*. 2020.

Relais des catécholamines



Argaud L. Changeovers of vasoactive drug infusion pumps: impact of a quality improvement program. *Critical Care*. 2007.

Take home message

- Augmenter les débits (en diluant plus)
- Minimiser les mouvements verticaux (et la compliance)
- Implémenter des protocoles (avec des indicateurs qualité)
- Ne pas négliger l'impact de la purge automatique
- Etiqueter
- Secouer

BIBLIOGRAPHIE

Baby NAD ?

Baby NAD ?

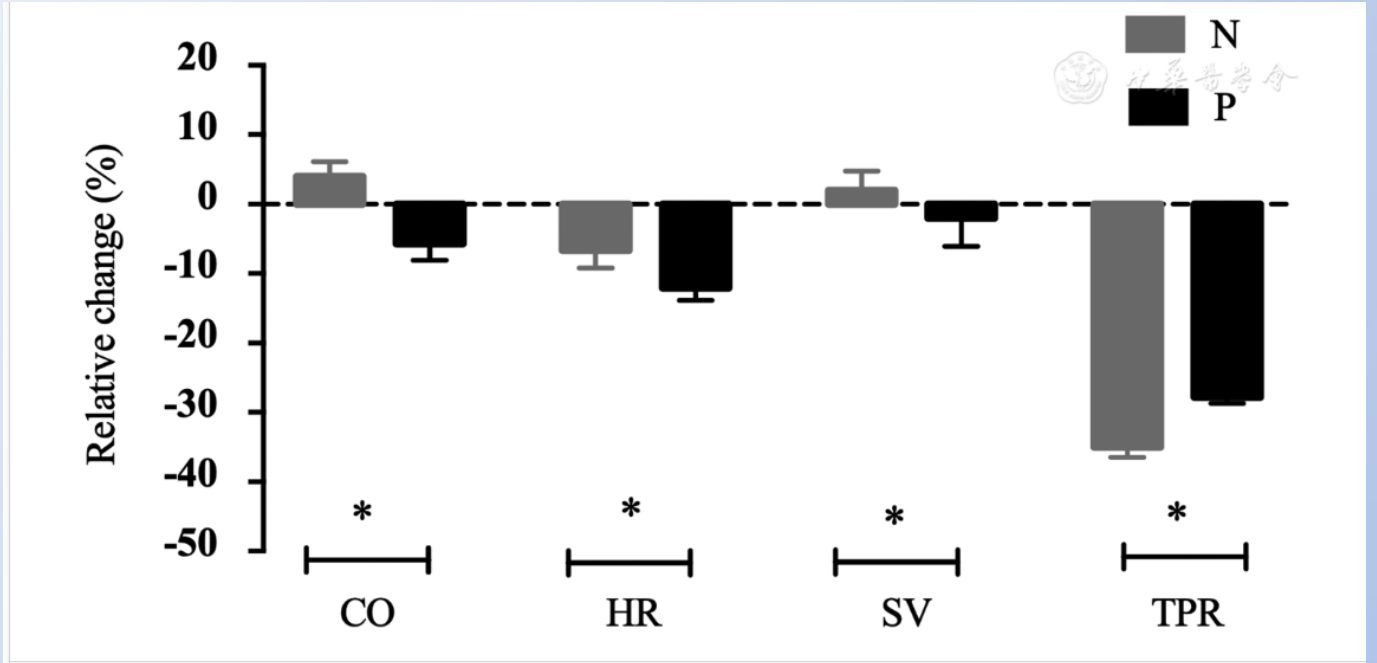


Figure 3: Hemodynamic variables including HR, CO, SV, and TPR at baseline and post-analgesia are presented in parturients receiving norepinephrine (gray) and phenylephrine (black). Norepinephrine treatment is associated with an increase of CO and SV, reduced decrease of HR, and a greater decrease of TPR compared to phenylephrine. Data are shown as mean ± standard error, and intergroup comparison is performed with non-paired *t* test. *$P < 0.05$. CO: Cardiac output; HR: Heart rate; SV: Stroke volume; TPR: Total peripheral resistance.

Wang X. Bolus norepinephrine and phenylephrine for maternal hypotension during elective cesarean section with spinal anesthesia. *Chinese Medical Journal,* 2020.

Baby NAD ?

Table 4
Comparison between bolus mode and continuous infusion : maximal effect for each.

	BOLUS	CONTINUOUS INFUSION	p
MACROCIRCULATION			
MAP (mmHg)	+ 21 (15 ; 30)	+ 16 (9 ;26)	0,07
HR (/min)	− 8 (-12 ; -6)	− 7 (-10 ; -4)	0,2
CO (L/min)	− 1,5 L (-1,1 ; -2,4)	− 0,9 (-1,5 ; -0,2)	< 0,001
SV (mL)	-11 (-8 ; -20)	− 7 (-13 ; -3)	0,009
GALA (°)	+ 12 (6–15)	+ 7 (3–12)	0,04
MICROCIRCULATION			
PHOTOPLETHYSMOGRAPHY			
PI (finger)(%)	-12 (-24 ; 0)	+ 12 (4–20)	0,008
VIDEOCAPILLAROSCOPY			
MFI	-0,1 (-0,24 ; -0,06)	+ 0,3 (0,1 − 0,4)	0,03
TVD (mm2/mm2)	-0,2 (-0,2 − 0,7)	+ 2,3 (1,5 − 3,2)	0,002
PVD (mm2/mm2)	-0,36 (-1,5 ; -0,8)	+ 1,44 (-0,7 ; +3)	0,01

MAP = mean arterial pressure; HR = heart rate; CO = cardiac output; SV = stroke volume; GALA = global afterload angle; TPU = tissue perfusion unit; PI = perfusion index; MFI = microvascular flow index; PPV = percentage of perfused vessels; TVD = total vessel density; PVD = perfused vessel density.

- Bolus de 2 ml (5 mcg/ml)
- Débit continu de 40 ml/h (5 mcg/ml)

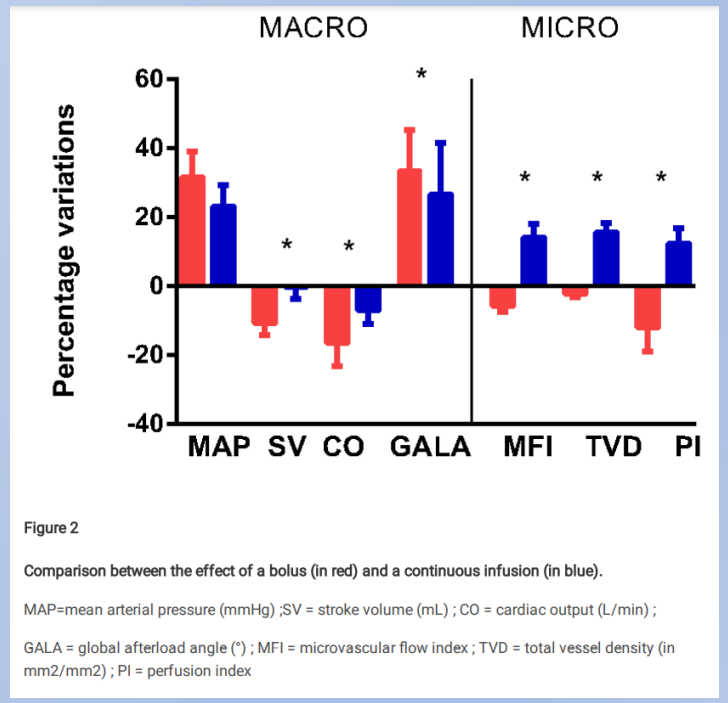


Figure 2

Comparison between the effect of a bolus (in red) and a continuous infusion (in blue).

MAP=mean arterial pressure (mmHg) ;SV = stroke volume (mL) ; CO = cardiac output (L/min) ;

GALA = global afterload angle (°) ; MFI = microvascular flow index ; TVD = total vessel density (in mm2/mm2) ; PI = perfusion index

Kindermans M. Micro- and Macrocirculatory effects of norepinephrine on anaesthesia- induced hypotension: a prospective study. Preprint, 2023.

Noradrénaline périphérique

Table 1. - Studies Evaluating Peripheral Administration of Norepinephrine

Study	Year	Observations	Setting	No. of patients receiving norepinephrine	IV sites evaluated	Total extravasation events	Tissue injuries
Cardenas-Garcia et al	2015	783	ICU	506 (65%)a	Proximal to antecubital fossa	19 (2.4%)	0 (0%)
Lewis et al	2019	202	ICU	146 (72%)	Forearm, antecubital fossa, and hand	8 (4%)	0 (0%)
Medlej et al	2018	55	ED	50 (91%)	Antecubital fossa, forearm, and hand	2 (3.6%)b	0 (0%)
Pancaro et al	2020	14,385	Intraoperative	14,385 (100%)	Not reported outside of extravasation events	5 (0.035%)	0 (0%)

French W. Time to Use Peripheral Norepinephrine in the Operating Room. *Anesthesia & Analgesia.* 2021.

Noradrénaline périphérique

« In the current database analysis, no significant association was found between the use of peripheral intravenous norepinephrine infusions and adverse events. »

Pancaro, C. Risk of Major Complications After Perioperative Norepinephrine Infusion Through Peripheral Intravenous Lines in a Multicenter Study. *Anesthesia & Analgesia*. 2020.

IV should be 18–20 gauge in size
IV location should be proximal to or at the antecubital fossa
Use 4–8 mg in 250-mL concentration
Duration of use should likely not exceed 6–12 h but is based on clinician judgment
Site should be monitored every 2 h during infusion
Have a deescalation plan to wean vasopressor use
Phentolamine or nitroglycerin paste available if extravasation occurs

French W. Time to Use Peripheral Norepinephrine in the Operating Room. *Anesthesia & Analgesia.* 2021.

Quel diluant ?

- La FDA recommande explicitement d'éviter la dilution dans le NaCl seul

- Les monographies divergent selon les labos :
  - G5% uniquement (Renaudin, Viatris, Mylan…)
  - NaCl 0,9% ou G5% (Aguettant…)
  - G5% ou NaCl 0,9% + G5% (Kalceks, Hospira…)

Quel diluant ?

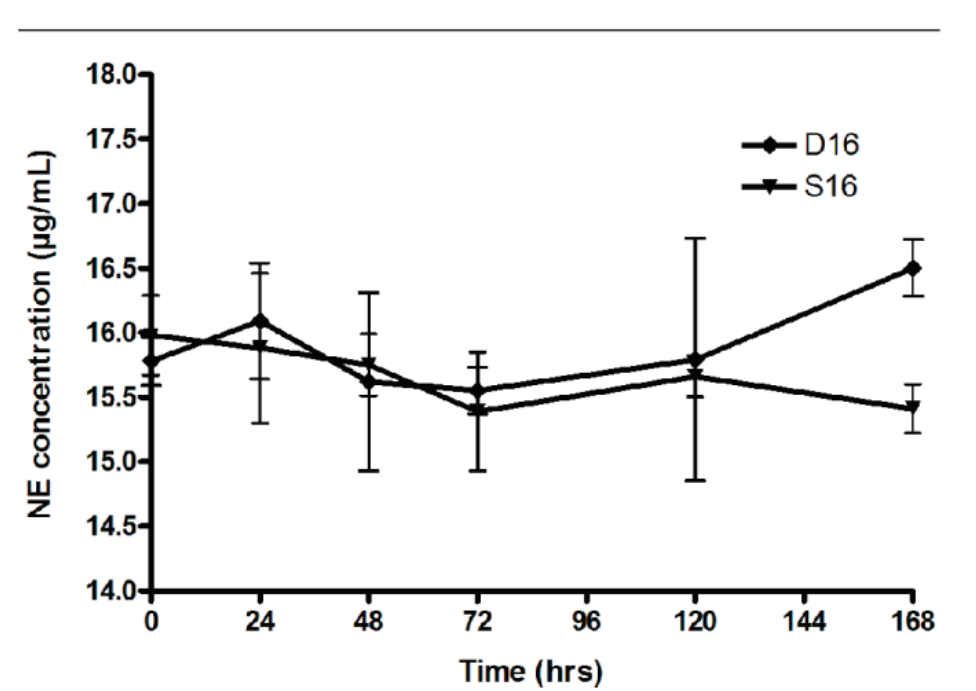
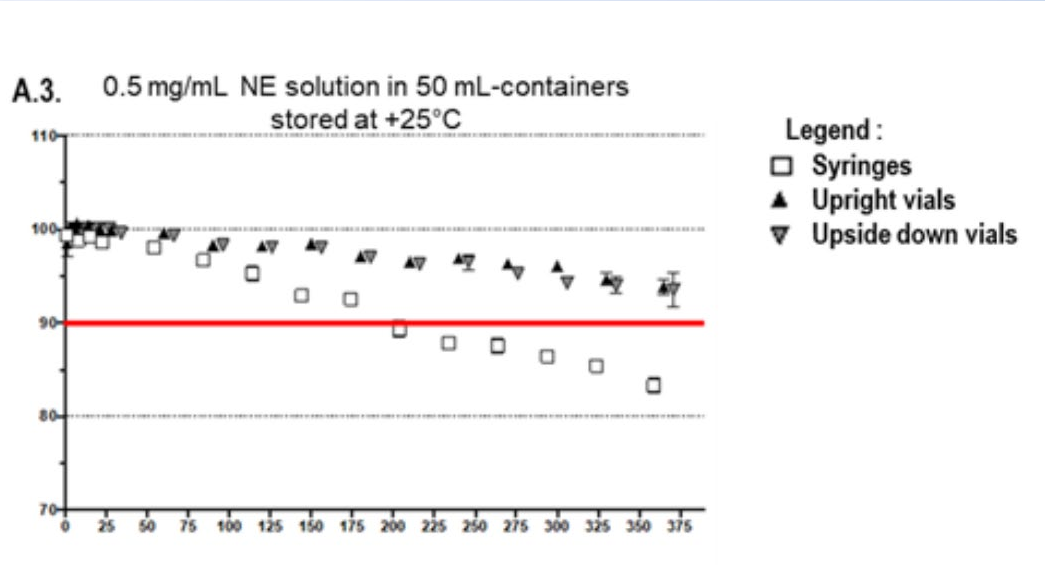


FIGURE 2 Concentrations of norepinephrine (NE) 16 µg·mL^{-1} prepared in dextrose 5% in water or normal saline,

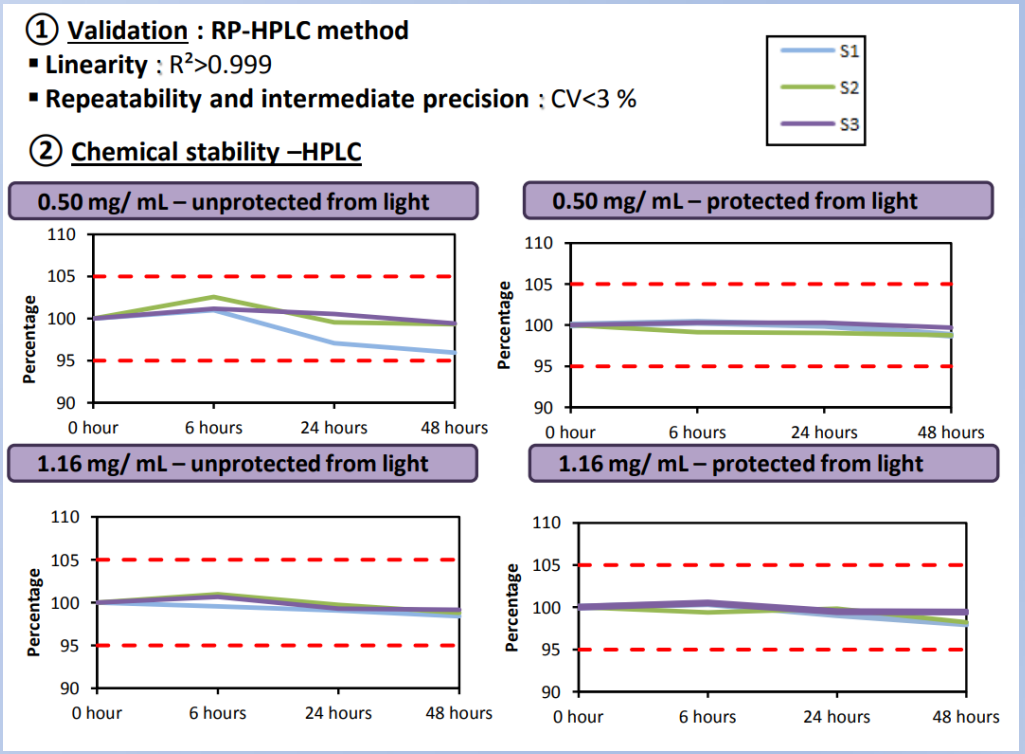
- Stable dans G5% comme dans sérum physiologique à T° ambiante et sans protection de la lumière
- A des concentrations N.A. (4mg/250cc)
- Rôle du pH dans stabilité

Tremblay M. Stability of norepinephrine infusions prepared in dextrose and normal saline solutions. *Canadian Journal of Anesthesia/Journal Canadien D'anesthésie*. 2008.

Quel diluant ?

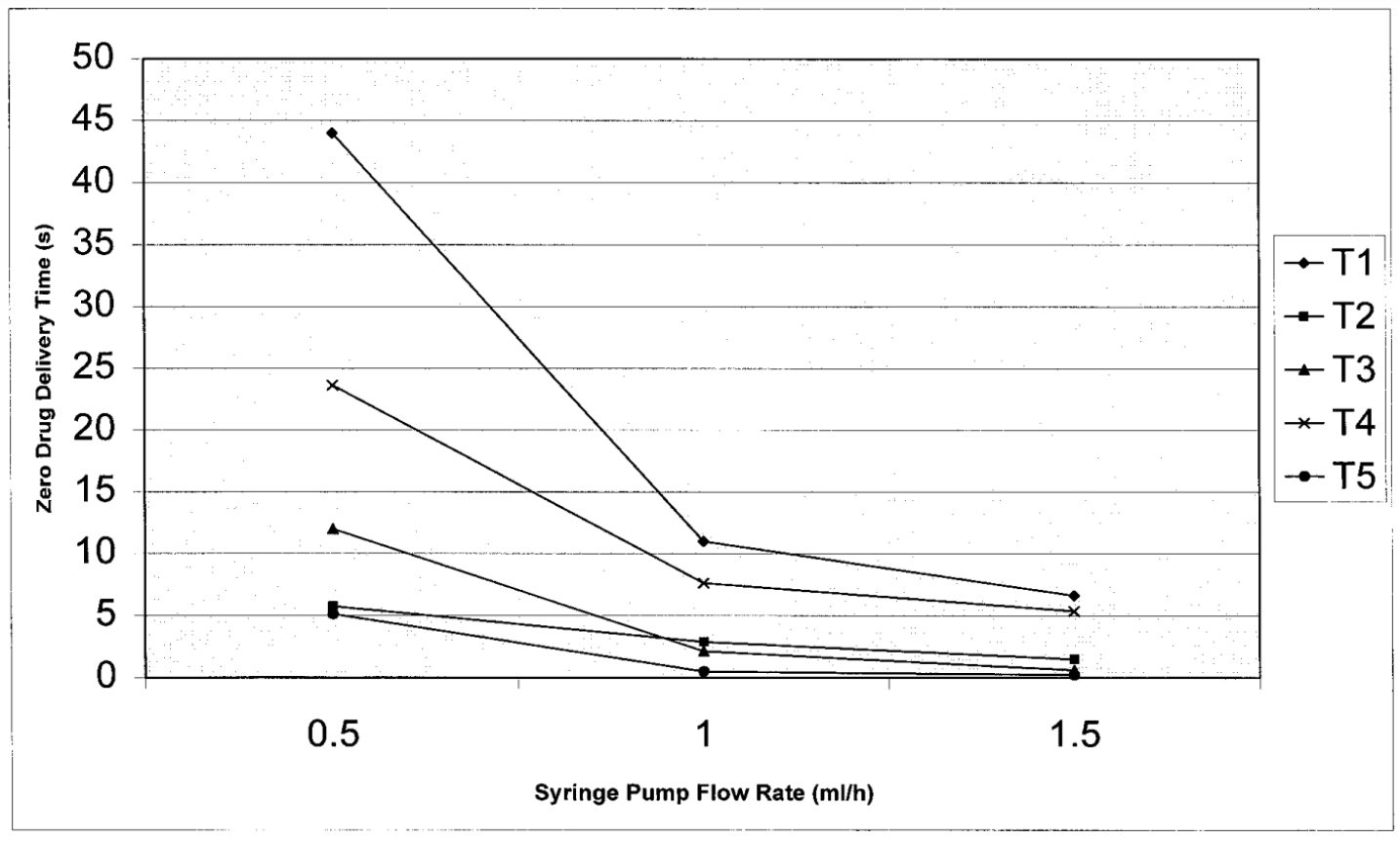


Gilliot S. Long-term stability of ready-to-use norepinephrine solution at 0.2 and 0.5 mg/mL. *European Journal of Hospital Pharmacy.* 2020.



D'Huart E. Physicochemical stability of norepinephrine bitartrate in polypropylene syringes at high concentrations for intensive care units. *Annales Pharmaceutiques Françaises*. 2019.

Compliance du circuit



ZDDT suite à la formation de boucles de 70cm dans des tubulures de différentes compliances

Weiss M. Influence of infusion line compliance on drug delivery rate during acute line loop formation. *Intensive Care Medicine.* 2000.

Seringues préremplies

TABLE 2

Recommendations Regarding the Purchase of Intravenous Push Medications in Ready-to-Administer Forms

Organization	Recommendation
Institute for Safe Medication Practices	• Commercially available, prefilled syringes of medications that are already labeled should be used when possible.[a] • To the greatest extent possible, provide adult IV push medications in a ready-to-administer form (to minimize the need for manipulation outside of the pharmacy sterile compounding area).[a]
The Joint Commission	• Medications in patient care areas are available in the most ready-to-administer forms commercially available or, if feasible, in unit-doses that have been repackaged by the pharmacy or a licensed repackager.[b]
Anesthesia Patient Safety Foundation	• High-alert drugs (such as phenylephrine and epinephrine) should be available in standardized concentrations/diluents prepared by pharmacy in a ready-to-use (bolus or infusion) form that is appropriate for both adult and pediatric patients.[c] • Ready-to-use syringes and infusions should have standardized fully compliant machine-readable labels.[c]
American Society of Health-System Pharmacists	• Whenever possible, medications shall be available for inpatient use in single-unit packages and in a ready-to-administer form. Manipulation of medications before administration (eg, withdrawal of doses from containers, reconstitution of powdered drug products, labeling of containers, and splitting of tablets) by final users should be minimized.[d]

Abbreviation: IV, intravenous.
[a]From Institute for Safe Medication Practices, Safe practice guidelines for adult IV push medications.[9(p8-9)]
[b]From The Joint Commission, Standards BoosterPak for safe medication storage.[12(p10)]
[c]See Eichhorn, APSF hosts medication safety conference.[13(p1)]
[d]See ASHP guidelines: Minimum standards for pharmacies in hospitals.[16(p440)]

Lenz J.R. A Review of Best Practices for Intravenous Push Medication Administration. *Journal of Infusion Nursing*. 2017.

Seringues préremplies

Item	AfC	RtA	Increment
Cost of noradrenaline from concentrate	£2,374,281	£0	– £2,374,281
Cost of ready-to-administer noradrenaline	£0	£5,655,161	£5,655,161
Cost of noradrenaline, any formulation	£2,374,281	£5,655,161	£3,280,881
Cost of dextrose or saline for dilution	£1,222,513	£0	– £1,222,513
Total cost of noradrenaline and dextrose	£8,652,692	£5,655,161	– £2,997,530
Cost of drug preparation tasks	£8,652,692	£1,491,843	– £7,160,848
Cost of pump preparation and reload tasks	£4,893,246	£497,281	– £4,395,965
Total cost of nursing time noradrenaline tasking	£13,545,938	£1,989,124	– £11,556,813
Net monetary benefit, England (per year)			£9,498,445
Net monetary benefit, per 29 bed CCU (per year)			£65,961
Net monetary benefit, per CCU bed (per year)			£2,304

Griffin E. An Economic Analysis of Critical Care Nurse Resourcing Following the Uptake of Ready-to-Administer Noradrenaline for Hypotensive Shock in Adults in England. *Advanced Therapy*. 2022.