NOREPINEPHRINE SYRINGES IN THE OPERATING ROOM : PRECISION OF PREPARATION AND PHARMACY'S CONTRIBUTION

COM20-77159

Margaux DELAMOTTE[1], Lucie SERREAU[2], Nicolas GILLIER[2], Guillaume BINSON[1], Antoine DUPUIS[1]

[1]CHU Poitiers, Service de Pharmacie, Poitiers, France - [2]CHU Poitiers, Service Anesthésie – Réanimation, Poitiers, France

INTRODUCTION

Norepinephrine (NE) is used to manage anesthesia-induced arterial hypotension (intermittent IV bolus or continuous infusion), defined as a mean arterial pressure lower than 65 mmHg (threshold below which the risk of complications increases).

Objective : investigate the reliability of NE syringe reconstituted (by dilution at 1:400) at the operating room and assess the feasibility to prepare ready to use 5 µg/mL NE syringes at the pharmacy unit using the development of a HPLC-DAD stability indicating method.

MATERIALS & METHODS

Chromatographic conditions

- Injection volume: 50 µL, flow rate: 1 mL/min, λ: 278 nm,
- Mobile phase : acetonitrile/water (5/95; v/v) with 0.1% acetic acid
- Column : Purospher®STAR 150mm x 4.6mm RP-18 endcapped 5µm

- Analysis of syringes reconstituted in the operating room : Z-test (α = 5%)
- Analysis of syringes prepared at the pharmacy unit : Student's T-test (α = 5%)

RESULTS

RESULTS OF METHOD VALIDATION

r^2	≥ 0.9998
Residuals values (%)	≤ 4.86
RSD (%)	≤ 5.54
Percent recovery (%)	≤ 106.25
LOQ (µg/mL)	2.5

r^2: correlation coefficient ; RSD : relative standard deviation ; LOQ : Limit of quantification

RESULTS OF DOSAGES OF SYRINGES

	Syringes reconstituted in the operating	**Syringes prepared at the pharmacy unit**
Quantity (n)	50	9
Mean concentration (µg/mL [CI 95%])	5.81 [5.11 – 6.50]	5.01 [4.85 – 5.16]
Median (µg/mL)	5.09	5.09
p- value	0.022	0.98
Values outside bias (± 10%) (%)	68	0

CI : confidence interval

RESULTS OF STABILITY STUDY

	Concentration (µg/mL) **± bias compared to day 0**
D1	5.11 (+ 2 %)
D3	4.88 (-2.6%)
D7	4.80 (- 4.2%)
D14	4.77 (– 4.8%)
D28	4.78 (- 4.6%)

DISCUSSION

- An HPLC-DAD method was developed and validated, and can be routinely used to perform a batch release of such preparations,
- Reconstitution practices in the operating room show a very high variability, providing large error in the administered dose and leading to potential serious clinical consequences,
- The preparation at the pharmacy unit of ready-to-use syringes at 5 µg /mL showed better results (100% of concentrations ranging from 4.5 - 5.5 µg/mL),
- During 28 days, no significant variation of the NE concentration was observed in the syringes (≥ 90 % of the initial concentration), storage in a fridge was proposed for better microbiological stability,
- Our results are in accordance with previous studies reporting NE stability data, but it is the first to describe at least 28-day stability of NE in 5 µg/mL ready-to-use syringes.

CONCLUSION

- To manage anesthesia-induced arterial hypotension, the preparation of ready-to-use 5 µg/mL NE syringes bolus should be prepared at the pharmacy unit,
- It will be possible to manufacture these preparations in advance, to control them and to stock them in the anesthesia departments (allowing easy and quick access to the preparation),
- Further experiments are required in order to assess microbiological stability of syringes.