TCH-036

RESULTS OF A SYSTEMATIC LONG-TERM STABILITY STUDY FOR READY-TO-USE INJECTABLE DRUGS PRODUCED BY A CENTRALIZED INTRAVENOUS ADMIXTURE SERVICE

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Background

Other injectable preparations than parenteral nutrition admixture and injectable cytotoxic drugs could be prepared by Centralised IntraVenous Admixture Service (CIVAS) if the long-term stability of the drugs is known. However, this information is not always available.

Purpose

To develop a program of chemical drug stability analysis in collaboration between Hospital Pharmacy, Medical Laboratory and Centre of Biostatistics to determine the long-term stability of largely used injectable anti-infectious and non anti-infectious drugs.

Material and Methods

After a setup of the High Performance Liquid Chromatography (HPLC) method,

- 25 drugs (10 antiinfectives, 4 anesthetics, 2 propulsives, 2 detoxifying agents for antineoplastic treatment and 7 with other properties) were reconstituted in laminar air flow hood,
- 15 of them stored directly at 5 ± 3°C and
- 16 stored in the freezer at – 20°C, thawed by microwave following a standardised procedure and stored at 5 ± 3°C before use.

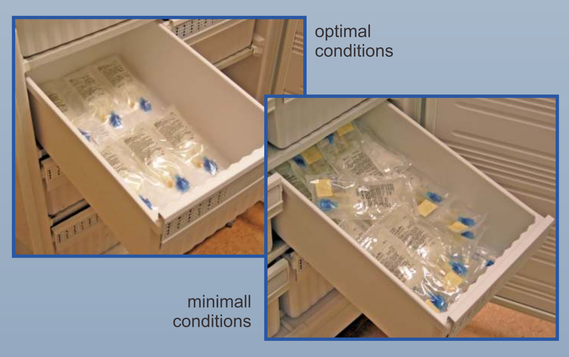
Concentration stability was evaluated by regression analysis..

Results

For each drug, long-term stability has varied from 11 days to 70 days. The freeze-thaw treatment by microwave may enhance the stability (from 30 to 120 days) and allow batch-scale production of intravenous drugs, less expensive in term of manpower and sterile device than a drug reconstitution at the ward. The results were published by 47 posters in international congress and by 34 publications in national and international pharmaceutical journals.

MICROWAVE FREEZE THAW TREATMENT

Drug	Dose/100 ml	Container	Stock - 20°C (days)	Conditions	Cycle	Final Storage at 5 ± 3°C (days)
Cefepime	2 g	pvc	30	Optimales	270 W	11
Ceftriaxone	2 g	polyolefine	98	Optimales	270 W	44
Ceftriaxone	2 g	polyolefine	98	Optimales	800 W	56
Cefuroxime	1.5 g	pvc	90	Optimales	270 W	15
Cefuroxime	1.5 g	polylefine	98	Optimales	800 W	21
Cefuroxime	1.5 g	polyolefine	98	Optimales	270 W	23
Cefuroxime	1.5 g	polyolefine	98	Minimales	270 W	21
Cefuroxime	1.5 g	polyolefine	98	Minimales	800 W	18
Diclofenac	75 mg/100ml + 42mg Bica Sod	polyolefine	60	Optimales	270 W	60
Fluorouracile	800 mg/100 ml NaCl 0,9 %	pvc	79	Optimales	270 W	28
Folinate Sodique	800 mg/250 ml	polyolefine	90	Optimales	270 W	30
Ketorolac	10 mg	polyolefine	15	Optimales	270 W	35
Ketorolac	10 mg	polyolefine	15	Optimales	800 W	35
Ketorolac	20 mg	polyolefine	90	Optimales	270 W	60
Ketorolac	30 mg	polyolefine	15	Optimales	270 W	30
Ketorolac	30 mg	polyolefine	15	Optimales	800 W	35
Levofolinate Calcique	400 mg/250ml	polyolefine	95	Optimales	270 W	30
Piperacilline + Tazobactam	4 g + 0,5 g	pvc	90	Optimales	270 W	35
Temocilline	2 g	polyolefine	30	Optimal	270 W	11
Temocilline	2g/100ml NaCl 0.9%	polyolefine	30	Optimal	270 W	14
Sufentanil + Levobupivacaine	0.6 mg + 625 mg /500 ml NaCl 0.9 %	pvc	120	Optimales	270 W	70
Tramadol	100 mg	pvc	120	Optimales	270 W	60
Vancomycine	500 mg	polyolefine	105	Optimales	270 W	56



CHIMICAL STABILITY AT 5 ± 3°C

Drug	Concentration (mg/ml)	Solution	Container	Time (days)
Cefazoline sodique	10.0	d5	pvc	30
Cefuroxime sodique	15.0	d5	pvc	13
Cefuroxime	15.0	d5	polyolefine	31
Cefuroxime	15.0	d5	polyolefine	31
Doxorubicine	2.0	d5	easy pump (32°C)	11
Fluorouracile + Folinate sodique	24.0 3.2	DC Beads	Syringe	14
Fluorouracile + Folinate sodique	3.2	d5	infusor (32°C)	11
Folinate sodique Procaïne HCl	3.2 0.20	d5 Solution de cardioplégie *	polyolefine pvc	30 60
Sufentanil citrate + Levobupivacaine	0,001 1,250	s	pvc	58
Teicoplanine	4.0	d5	pvc	6
Tramadol + Alizapride	1.0 0.5	d5	polyolefine	30
Tramadol + Dehydrobenzperidol	1.0 0.025	d5	polyolefine	30
Tramadol + Metoclopramide	1.0 0.10	d5	polyolefine	30
Vancomycine HCl	5.0	d5	pvc	58
Vancomycine HCl	10.0	d5	pvc	58
Voriconazole	4.0	d5	pvc	15

* Natrium 6.09 – Natrium lactas 3.19 – Kalium chloride 1.349 – Calcium chloride 2 ag 0.200 q – Magnesium sulfas 7 ag 2.46g aqua ad 1000 ml – Natrium bicarbonate 0.586 g

Conclusions

Our findings contribute to enhance the scale of drugs that may be take on by a CIVAS. This collaboration led to the foundation in 2009 of a drug stability research group included in the University Hospital of Mont-Godinne and already saw itself decreeing 4 prices and nominations.

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Conflict of interest
None