Physical compatibility of the propofol emulsion with 33 drugs used in anaesthesiology

Stucki Cyril[1,2], Sautter Anna-Maria PhD[1], Bonnabry Pascal PhD[1,2].

[1] Pharmacy University Hospitals of Geneva, [2] School of pharmaceutical sciences University of Geneva, University of Lausanne Switzerland

BACKGROUND AND OBJECTIVE

The propofol is a lipophilic drug manufactured as a lipid emulsion. The concomitant administration of intravenous drugs induces a risk of emulsion breaking and raises the possibility of infusing large lipid droplets in the patient bloodstream. This situation might lead to fat pulmonary embolism and serious injury for patient health.

The objective of the study was to assess the physical compatibility of propofol emulsion with 33 drugs commonly co-administered in anaesthesiology, in order to give validated recommendations to clinicians.

DESIGN

Drugs frequently used in anaesthesiology and at risk of breaking an emulsion were selected. They were statically mixed in usual concentrations in a **proportion of 1:1** with propofol emulsion (Disoprivan®) during 120 min.

Samples were analyzed at **0, 60, and 120** min. Compatibility evaluation included:
- globule-size analysis with the Master-Sizer S long bed (N=10/drugs)
- zeta potential measurement with the Zetasizer 3000HSa (N=10/drugs)
- pH determination (N=3/drugs)
- visual inspection by microscope (N=3/drugs)

A **scoring system** was developed to classify drugs in 4 grades according to the results in the 4 evaluations:
- compatible
- probably compatible
- probably incompatible
- incompatible
- Each evaluation provides a maximum number of points (10 for globule size/zeta potential and 3 for pH/appearance) related to **their relevance to report the incompatibility ability to break the emulsion**. The number of points correspond to the number of samples in which a change was observed in comparison to propofol alone:
- Size increase (>5um) for the size globule evaluation
- Zeta potential increase (>0) for the zeta potential evaluation
- pH diminution (<3.5) for the pH evaluation
- Globule size visually increasing for the appearance evaluation

A **pH titration curve** was established to determine the propofol emulsion sensitivity to pH variation (Zetasizer nano ZS).

RESULTS

	Appearance	pH	Zeta pot.	Glob. size	Total
Incompatible Drugs					
Amikacine 50mg/ml (Amikin®)	3	0	10	10	20
CaCl2 75mg/ml (CaCl2 HUG®)	3	0	10	10	23
Gentamycin 60mg/1,5ml (Garamycin®)	2	0	10	10	22
HCl 7,25% (Salzsäure 7,25% Braun)	2	3	10	10	25
MgSO4 100mg/ml (Bichsel)	1	0	10	10	21
MgSO4 500mg/ml (Bichsel)	3	0	10	10	23
Vancomycin 50mg/ml (Sandoz)	3	3	10	10	26
Dopamin 25mg/ml (Sintetica)	1	3	0	10	14
Probably Incompatible Drugs					
Adrenalin 1mg/ml (Sintetica)	0	3	0	7	10
Ciprofloxacin 2mg/ml (Ciproxine®)	1	0	0	10	11
Dobutamin 5mg/ml (Fresenius)	1	3	0	7	11
Silicon Oil (Hanseler)	3	0	0	6	9
Lidocain 20mg/ml (Rapidocain®)	1	0	0	6	7
Phenytoin 50mg/ml (Phenydan®)	1	0	0	8	9
Suxametonium 50mg/ml (Lysthenon®)	0	0	8	3	11
Vecuronium 2mg/ml (Norcuron®)	2	0	0	5	7
Ganciclovir 50mg/1ml (Cymevene®)	0	0	0	6	6
Metronidazol 5mg/ml (HUG)	0	0	0	5	5
Midazolam 5mg/5ml (Dormicum®)	0	0	0	5	5
Probably Compatible Drugs					
Atropin 1mg/ml (HUG)	0	0	2	2	4
Ceftriaxon 50mg/ml (Rocephine®)	0	0	0	2	2
Ephedrin HCL 10mg/ml (Bichsel)	0	0	0	1	1
Flucoxacillin (Floxapen®)	0	0	0	1	1
Meropenem 50mg/ml (Meronem®)	0	0	0	1	1
Nitroglycerin 1mg/ml (Perlinganit®)	0	0	0	1	1
Phenylephrin HCL 10mg/ml (Bichsel)	0	0	0	2	2
Thiopental 50mg/ml (Penthotal®)	0	0	0	3	3
Trimetho/sulfamet 400/80mg/5ml (Bactrim®)	0	0	1	0	1
Compatible Drugs					
Amoxicilline/Acid clavulanic 1,2g/20ml (Augmentin®)	0	0	0	0	0
Water for injection (Braun)	0	0	0	0	0
Fentanyl 50ug/ml (Sintenyl®)	0	0	0	0	0
Furosemid 40mg/4ml (Lasix®)	0	0	0	0	0
Noradrenalin 1mg/ml (Sintetica)	0	0	0	0	0

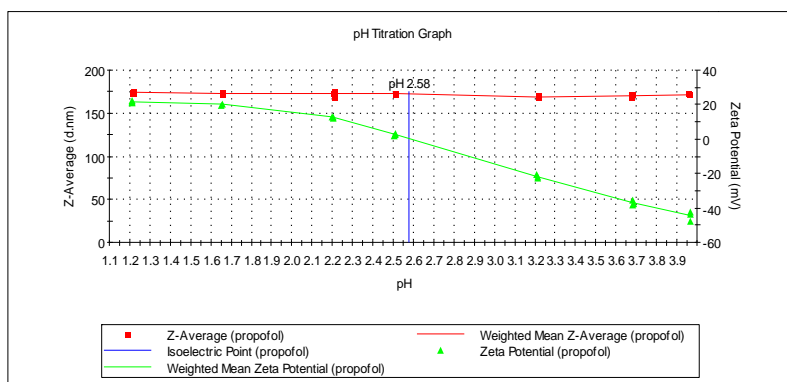Fig 2. Global results with quotation of (in)compatibility with propofol emulsion

Fig 1. pH titration graph and isoeletric point determination

CONCLUSIONS

The risk of emulsion breaking has been confirmed, especially with acidic drugs. Recommendations regarding the possibility to co-administer tested drugs with propofol can be given, and only drugs classified as compatible or probably compatible should be infused on the same administration line.