BALANCED ISOTONIC CRYSTALLOID SOLUTIONS *VERSUS*, ISOTONIC CRYSTALLOID SOLUTIONS: A DECISION–MAKING CASE STUDY

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Background and Objective

The European Medicinal Agency has restricted the hydroxyethyl starch's (HES) use for vascular filling since October 2013, due to safety concerns. Following this European decision, the need of crystalloid solutions in the 37 hospitals of the Public Assistance – Hospitals of Paris (AP-HP) had to be reassessed. The use of **balanced** isotonic crystalloid solutions (BICS) *versus* isotonic crystalloid solutions (ICS) was reported to decrease the risk of electrolyte disturbances.
The decision-making process of drugs selection in the AP-HP is based on effectiveness, safety and economics.
The aim of this study was to **assess the interest in using balanced isotonic crystalloid solutions for vascular filling**, in order to list one more or not for the hospital drug formulary (HDF).

Setting and Method

An analysis was conducted by the Therapeutic Evaluation Team (TET) and was submitted to the AP-HP Committee of Medicinal Products (COMED).
This analysis was firstly based on a scientific assessment of ICS (comparison of products' characteristics and French Society of Anesthesia and Intensive Care's (SFAR) opinions review), and secondly on the request of AP-HP Anesthesia and Intensive Care experts' opinions by a questionnaire (each conflict of interest was checked).

Results

Scientific assessment synthesis:

- 3 BICS are marketed in France. Their electrolyte compositions are more or less similar to plasma compsition, which may make them more or less appropriate for vascular filling (especially when large volumes are required).

Crystalloid	**Plasmalyte Viaflo®** (PV)	**Ringer lactate** (RL)	**Isofundine®**	**0,9% sodium chloride** (SC)
Nature	**balanced**	**balanced**	**balanced**	**non balanced**
Characteristics	Sodium 140 mmol/L **Chloride 98 mmol/L** Potassium 5 mmol/L Magnesium 1,5 mmol/L **Acetate* 27 mmol/L** **Gluconate* 23 mmol/L** pH 6,0 – 8,5 **Iso-osmolar** (295 mOsmol/L)	Sodium 131 mmol/L **Chloride 111 mmol/L** Potassium 5 mmol/L **Calcium* 2 mmol/L** **Lactate* 29 mmol/L** pH 5,0 – 7,0 **Hypo-osmolar** (278 mOsmol/L)	Sodium 140 mmol/L **Chloride 127 mmol/L** Potassium 4 mmol/L Magnesium 1 mmol/L **Calcium* 2,5 mmol/L** **Acetate* 24 mmol/L** **Malate* 5 mmol/L** pH 5,0 - 5,9 Hyper-osmolar (309 mOsmol/L)	Sodium 154 mmol/L Chloride 154 mmol/L pH 4,5 – 7,0 Hyper-osmolar (308 mOsmol/L)
Available in the AP-HP	No	**Yes**	No	**Yes**
Proved points	Compatibility with blood (**no calcium)**	Incompatibility with blood (calcium) High risk of **edema** **Lactic acidosis** situations are **contraindicated**	Incompatibility with blood (calcium)	Hyperchloremic acidosis (high **chloride level)**
To be discussed points	More appropriate when large volumes of filling are required (best to maintain electrolyte homeostasis because of its **similarity to plasma composition** and its **physiologic chloride level**)	Higher risk of hyponatremia	**Theoretical concept** (no clinical evidence)	

Table: comparison of crystalloid solutions marketed in France.
*the presence of those ions is responsible of particular precautions for use and drug interactions mentioned in the RCP.

- SFAR's main opinions about balanced solutes:

- It is **not possible to recommend their use for all** acute or perioperative patients (lack of beneficial clinical proof)
- **but they should be preferred** (demonstrated efficacy and safety, link between preventing hyperchloremic acidosis and infusing balanced solutions, deterioration of organ function and mortality increase when unsing non balanced solutions).

AP-HP Anesthesia and Intensive Care experts' opinions:

5 of 17 requested experts responded → **All gave a favorable opinion to Plasmalyte Viaflo®**
3 main directives:

1) **More using crystalloid remains logic due to HES's European restrictions**
2) Hyperchloremic acidosis occurs frequently when infusing large volumes of 0,9% sodium chloride
3) Balanced solutes should be preferred for vascular filling, especially since they have the same efficacy as non-balanced solutes

Moreover, about Plasmalyte Viaflo®:

Strong points	Weak points
• **Low chloride level** and **iso-osmolarity** • Contains **no lactate** is an advantage in case of lactic disturbances • Contains **no calcium** making PV compatible with blood • The risk of hyperchloremic acidosisis is reduced with PV (low chloride level) vs. with SC • PV should replace RL or SC when large volumes of intravenous fluid are required and it may replace RL in almost its all indications	• **Clinical benefit vs. SC must be demonstrated** • Risk of confusion with the look-alike drug named Plasmalyte Viaflo G5® which contains glucose • Plasmalyte Viaflo's price ≈ 5 to 6 times higher than RL's or SC's

Conclusion

Despite of the **interesting concept**, the COMED gave a **temporary unfavorable opinion** to list PV in the AP-HP HDF, due to: i) **insufficient level of scientific evidence**, ii) **risk of confusion**, iii) **too high price**. Moreover, the low rate of experts' response might cause a bias in the assessment. **New strong comparative clinical data (a hospital clinical research project has been submitted) might change the COMED decision.**

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