PHARMACOSTABILITY OF PLASMA-LYTE 148 AND PLASMA-LYTE 148 + 5% DEXTROSE WITH COMMONLY USED INFUSED THERAPEUTIC AGENTS

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INTRODUCTION
Plasma-Lyte 148 is a balanced, crystalloid intravenous fluid which is calcium-free and isotonic. It has been demonstrated to circumvent hyperchloremic metabolic acidosis and iatrogenic hyponatraemia resulting from use of 0.9% saline and hypotonic solutions respectively. Our aim was to investigate the chemical and physical compatibility of both Plasma-Lyte 148 and Plasma-Lyte 148 + 5% glucose with eight commonly used intravenous drugs in critical care medicine (morphine, midazolam, fentanyl, ketamine, clonidine, aminophylline, salbutamol and furosemide). This will provide vital data to allow the wider use of what appears to be a safer and more economic fluid.

METHODS
Chemical stability was assessed by high performance liquid chromatography (HPLC) using the ‘Hewlett Packard (Agilent) 1100’ HPLC system. A gradient method using 20mM ammonium carbonate (A) and acetonitrile (B) mobile phases and an ‘ACE® Excel 3 SuperC18’ column was used to detect concentration changes in the IV fluid and drug admixtures. The drugs were tested at ‘Y-site’ concentrations observed clinically on the Paediatric Critical Care Unit and a concentration change less than 10% was classed as ‘chemically stable’. The flow rate was set to 0.03 ml/min; column oven temperature to 40°C and injection volume to 5 μl for all drugs admixtures apart from ketamine (4 μl) and furosemide (1 μl). Six repeats of each admixture were assayed at three time points: 0, 2 and 24 hours. Physical stability was assessed by observation of precipitate formation. pH changes were recorded using ‘Fisherbrand Hydrus 300’ pH meter. Normal saline and 5% glucose were used as controls.

RESULTS
All examined therapeutic agents were stable at 2 and 24 hours relative to standard solutions. Relative to starting concentration, all drugs except midazolam were stable (the average percentage drug concentration changes reported were <3% for fentanyl; ≤2% for morphine, ketamine and furosemide; <1% for salbutamol and <0.5% for clonidine and aminophylline. Midazolam had a ~10% increase in concentration at 2 hours, however similar variation was found in all four fluids tested, presumably due to molecular settling. No precipitate formed in any of the samples. All Plasma-Lyte 148 and normal saline combinations remained in a safe, peripheral administration pH range of 5-9, but this was not the case for drugs prepared in 5% glucose. Plasma-Lyte 148 admixtures were found have a pH closest to that of the blood.

CONCLUSION
Compared to standard diluents, the above tested therapeutic agents are chemically and physically stable for 24 hours at the concentrations measured, when diluted with Plasma-Lyte 148 and Plasma-Lyte 148+5% dextrose. pH of all drug-admixtures remained stable for 24 hours.

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