Therapeutic monoclonal antibodies (mAbs) are commonly administered to patients through intravenous (IV) infusion, which involves diluting the medication into an infusion solution (e.g., saline and 5% dextrose). Using the wrong diluent can cause product aggregation, which may compromise patient safety” Luo et al (2020).

Abstract:

Therapeutic monoclonal antibodies (mAbs) are commonly administered to patients through intravenous (IV) infusion, which involves diluting the medication into an infusion solution (e.g., saline and 5% dextrose). Using the wrong diluent can cause product aggregation, which may compromise patient safety. We and others have shown that Herceptin® (trastuzumab) and Avastin® (bevacizumab) undergo rapid aggregation upon mixing with dextrose and human plasma in vitro. In this study, we evaluated the compatibility of a panel of 11 therapeutic mAbs with dextrose or saline and human serum. These mAbs were randomly selected for their distinct formulations and IgG isotypes (IgG1, IgG2, IgG4, and Fc-fusion protein). All the mAbs appeared to be compatible with saline and human serum. However, mAbs that were formulated at acidic pH (≤ 6.5) exclusively formed insoluble aggregates upon mixing with dextrose and serum. Such aggregation was not detected for the mAbs that are at neutral pH (7.2-7.5) or in buffers containing sodium chloride. Mass spectrometric analysis revealed that the insoluble aggregates were composed of mAb molecules and
several serum proteins (e.g., complement proteins, apolipoprotein, fibronectin) that are characterized by an isoelectric point of pH 5.4-6.7. At proximate pH to the isoelectric point values, those abundant serum proteins appeared to undergo isoelectric precipitation with mAb molecules. Our observations highlight a potential risk of protein aggregation at the blood-IV interface if a diluent is incompatible with a specific mAb formulation. This information has implications in guiding the design of product formulations and the selection of the right diluent for intravenous infusion of therapeutic mAbs. Abbreviations: ADC: antibody-drug conjugate; D5W: 5% dextrose in water; IM: intramuscular; IV: intravenous; LC-MS/MS: liquid chromatography-tandem mass spectrometry; mAb: monoclonal antibody; SC: subcutaneous; pI: isoelectric point.

You may also be interested in...

- MRSA sepsis following clandestine intravenous infusion
- Principles of intravenous drug infusion in anaesthesia
- Hypersensitivity and infusion-site adverse events with intravenous fosaprepitant

Reference: