Measuring the Performance of Multi-Pump Infusion Systems with Spectrophotometry

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Background: Infused drugs are often delivered to a patient via an infusion system consisting of a pump, tubing, and the intravascular catheter. For some patients receiving multiple infusions, the output of 2 or more pumps merge at a junction point or manifold, often with a carrier, then flow together through one catheter lumen. The rate at which a pump delivers fluid, even at a static setting, changes over time with cycles ranging in length from seconds to minutes because of the way the pumps are designed and manufactured. The composition of the combined pump output at the point where it meets the patient's bloodstream is affected by the changing rates of the multiple pumps and by fluid dynamics, particularly mixing that occurs in the infusion system dead volume. For many drugs, the rate variations are small enough to not be clinically relevant. However, short term variations in drug concentration may be clinically relevant when fast-acting drugs with a short half-life are given at high concentrations and low flow rates. These conditions are encountered when treating patients limited in the total amount of fluids they can receive, such as in pediatric populations. To understand the performance of multi-drug infusion systems, we need to determine the overall system flow rate and the composition of the combined infusion.

Methods: We have developed a technique to continuously measure the composition of a fluid containing multiple drugs flowing together. We combine this composition measurement with gravimetric measurement of total fluid flow to determine the overall rate of delivery. This is an improvement over previous methods which used a mechanical fraction collector to integrate the delivered fluid over one-minute intervals and required manual processing before measurement. This approach is similar to (Snijder et al, 2016) which used continuous spectrophotometry to measure the composition of fluid flowing through a flow cell. Flow cells add considerable dead volume, increasing mixing of the fluids being measured. Our approach is to use a multi-lumen catheter inserted into a piece of clear tubing. The tubing is inserted into a carrier plate which holds it in the light path immediately distal to the end of the catheter. This allows measuring the fluid composition precisely where it would reach a patient's bloodstream. In previous work, we use dyes such as methylene blue and tartrazine yellow as model drugs (Tsao 2013, Parker 2017). We use a narrow band light sources selected to be at the spectral absorbance peaks of the model drugs (e.g., ThorLabs M660L4 for methylene blue) and measure the amount of transmitted light at each band simultaneously using a spectrophotometer (Ocean Optic USB2000). We calibrate the system using known concentrations of the model drug across the concentration range of interest, producing a series of light measurements at various concentrations, and build a linear regression model to interpolate measurements between these points. By using narrow band light sources that are chosen to match non-overlapping absorbance peaks of the model drugs, we can independently measure the concentration of several model drugs without interaction.

Results: We have collected preliminary data comparing the new measurement system to the previous techniques. We are finding that we get data more often (10 to 300 measurements/second vs 1 measurement/minute), with minimal manual intervention, and with comparable spectral and amplitude resolution.

Conclusion: Precise measurement of the performance of multi-drug infusion systems is necessary to better understand the limitations of these systems, particularly when high

concentration, fast-acting drugs with short half-lives are given at low flow rates. Understanding the system's current performance is essential for devising improvements, both to individual infusion pumps and to the whole multi-pump system.

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