A Systematic Review of Hyaluronidase-Assisted Subcutaneous Fluid Administration in Pediatrics and Geriatrics and Its Potential Application in Low Resource Settings.

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Abstract

The role of enzyme-assisted subcutaneous fluid administration (EASFA) in treating mild to moderate dehydration has been studied in pediatrics, geriatrics, and palliative care. The objective of this systematic review was to evaluate if EASFA is a successful and effective technique to utilize in the treatment of these populations. Outcomes measured in both the intravenous and subcutaneous groups included rate of fluid infusion and number of attempts to successful catheter placement. The authors found that EASFA is a comparable alternative to intravenous fluids in regards to infusion rates in both pediatric and elderly patients with mild to moderate dehydration. Additionally, the higher rate of successful placement of the subcutaneous catheter may prove useful in select populations and low resource settings.

Introduction

Obtaining IV access in a dehydrated pediatric or geriatric patient can be difficult even for the well trained healthcare provider. Subcutaneous fluid administration does not require venous access and has a low risk of infection, but is relatively underutilized in developing countries. Crystalloid fluids are able to be infused into the subcutaneous tissue after administering the hyaluronidase enzyme. This enzyme hydrolyzes the components of the extracellular matrix, increasing tissue permeability and absorption. Hylenex is a relatively new enzyme recombinant of human hyaluronidase that provides fewer side effects than the previous animal derived enzymes. The process involves injecting the enzyme into the desired site, placement of a catheter into the subcutaneous tissue, and infusing the desired fluids.

Figure 1: An example of EASFA using a butterfly catheter in the inferior shoulder area.

Methods

A review of relevant literature from MEDLINE and Cochrane Library from January 1950 to December 2015 was completed. Authors reviewed studies and selected relevant articles based on inclusion criteria

- Evaluation of infusion rates and volume infused OR
- Assessment of successful placement of catheter AND
- Pediatric or elderly population

Statistical analysis was completed using Cohen's D and odds ratios with 95% confidence intervals.

Included Studies

Author	Study Type	Population
Spandorfer	RTC	148 pediatric patients
Kuensting	Retrospective	39 pediatric patients
Allen	Phase IV, single arm study	51 pediatric patients
O'Keeffe	Observational Study	180 geriatric patients
Slesak	Prospective randomized open clinical trial	96 geriatric patients
Dasgupta	Prospective observational study	55 geriatric patients
Noriega	Prospective RCT	67 geriatric patients

Table 1: This table shows the 7 studies that fit our inclusion criteria and were analyzed in the systematic review.

Results

Rate of Infusion: PIV vs. EASFA

Figure 2: This figure shows a Cohen's D of 0.31 indicating a small effect size of IV over EASFA.

Number of attempts to successful catheter placement: PIV vs. EASFA

Figure 3: This figure shows a pooled odds ratio of 7.19 demonstrating ease of placement for the subcutaneous catheter.

Discussion

The first outcome measured was the rate of infusion of IV vs EASFA. Four of the 6 papers that were included exhibited higher rates of infusion within the IV group versus the EASFA group. The overall pooled Cohen's D measure of 0.31 indicates that the IV group contained slightly higher infusion rates compared to the SubQ group. However, this effect size was not significant and considered small. In the studies that showed an IV infusion rate faster than subcutaneous, the average rate was only 7.3 cc/hr faster in IV, which is not clinically significant. No study showed a difference of more than 25 cc/hr faster in the IV group. Interestingly, the Spandorfer RTC trial showed an infusion rate 42.6 cc/hr faster in the subQ group.

Four articles were used to analyze successful catheter placement in the IV and the subcutaneous groups. All of the articles show an increased likelihood of a successful catheter placement using the EASFA method. The overall pooled odds ratio shows a 7 times higher likelihood of successful placement within the SubQ group compared to the IV group. This data seems to fit with what we intuitively know, placing a subcutaneous catheter is achieved with far more success than IV catheter placement.

Conclusions

- EASFA is a comparable alternative to intravenous fluids in regards to infusion rates in both pediatric and elderly patients with mild to moderate dehydration.
- The higher rate of successful placement of the subcutaneous catheter may prove useful in select populations and low resource settings.

Future Applications

Every year, hundreds of thousands of children and adults die from dehydration secondary to diarrheal illnesses around the world. We know that prompt fluid administration is key to saving these lives. The application of this procedure could be revolutionary, especially in low resource settings where there is a lack of trained healthcare personnel to administer intravenous fluids. The ease of catheter placement shows the feasibility to train lay community members to administer fluids when medical care or transport is not readily available. Additionally, this could be considered during a disaster event, cholera epidemic, or anytime patient needs overwhelm the resources of the healthcare system.