Original Article

Extended Stability of Intravenous 0.9% Sodium Chloride Solution After Prolonged Heating or Cooling

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Abstract

Purpose: The primary objective of this study was to evaluate the stability and sterility of an intravenous 0.9% sodium chloride solution that had been cooled or heated for an extended period of time.

Methods: Fifteen sterile 1 L bags of 0.9% sodium chloride solution were randomly selected for this experiment. Five bags were refrigerated at an average temperature of 5.2°C, 5 bags were heated at an average temperature of 39.2°C, and 5 bags were stored at an average room temperature of 21.8°C to serve as controls. All samples were protected from light and stored for a period of 199 days prior to being assayed and analyzed for microbial and fungal growth.

Results: There was no clinically significant difference in the mean sodium values between the refrigerated samples, the heated samples, and the control group. There were no signs of microbial or fungal growth for the duration of the study.

Conclusion: A sterile intravenous solution of 0.9% sodium chloride that was heated or cooled remained stable and showed no signs of microbial or fungal growth for a period of 199 days. This finding will allow hospitals and emergency medical technicians to significantly extend the expiration date assigned to these fluids and therefore obviate the need to change out these fluids every 28 days as recommended by the manufacturer.

Key Words—refrigerated fluids, sodium chloride, stability, sterility, warmed fluids

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Intravenous sodium chloride solutions are routinely used in the hospital setting for the treatment of various medical conditions. Some conditions that may warrant the use of intravenous sodium chloride solutions include hypovolemic shock, dehydration, malignant hyperthermia, diabetic ketoacidosis, and hyponatremia.¹⁻⁴ Intravenous sodium chloride solutions are also transported by emergency medical technicians to treat hypothermia and hyperthermia. Recent guidelines for cardiopulmonary resuscitation recommend the use of cold intravenous sodium chloride solution in the treatment of cardiac arrest.⁵ Treatment is carried out by infusing a cooled sodium chloride solution. Similarly, patients presenting with

hypothermia may be treated with an infusion of warmed sodium chloride solution.⁶ In some cases, patients may be given warmed fluids to reduce perioperative hypothermia.⁷

These intravenous solutions are stored in ambulances in portable units that either cool or warm them. Unfortunately, they are being stored for extended periods of time without any knowledge of the effects that extended cooling or heating may have on their stability or sterility. The manufacturer recommends that these fluids be discarded after 28 days.

A review of the published literature failed to show any information on the stability and sterility

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of such solutions when cooled or heated and stored for an extended period of time. In the absence of such information, the use of these fluids represents a potential risk to the patient.

The primary purpose of this study was to determine the stability and sterility of intravenous sodium chloride solutions that had been cooled or heated for an extended period of time. If stability and sterility can be shown for an extended period of time, then the time-consuming and costly process of discarding these fluids after 28 days could be avoided.

METHODS

Fifteen sterile 1 L intravenous bags of 0.9% sodium chloride were randomly chosen for this study. These bags were divided into 3 groups of 5. One group was refrigerated at an average temperature of 5.2°C for 199 days, one group was stored in a warmer at an average temperature of 39.2°C for a period of 199 days, and the control group was stored at an average room temperature of 21.8°C for 199 days. All of the samples were protected from light and stored with the overwrap intact. The sodium concentration was measured using the Synchro LX system chemistry analyzer.⁸ The sodium concentration was determined by indirect potentiometry utilizing 2 glass sodium electrodes, with one acting as a reference electrode. Table 1 provides a summary of the sodium results obtained. Sterility testing was carried out for all the samples that were cooled or heated. The sterility results and characteristics of each media are provided in Tables 2 and 3. The sample volume used to inoculate the samples was 0.1 mL and the incubation temperature was 36°C. The samples were incubated for 72 hours. To supplement the microbial testing, all of the samples that were cooled or heated were also tested for fungal growth. Table 4 provides a summary of the fungal testing results.

Table 1. Sodium concentration (mmol/L)

Refrigerated samples, 5.2°C		Heated samples, 39.2°C		Room temperature samples, 21.8°C	
1	149	6	155	11	152
2	151	7	156	12	151
3	152	8	154	13	151
4	150	9	155	14	151
5	150	10	154	15	152

Table 2. Microbial growth data (refrigerated samples, 5.2°C)

Sample	Blood agar ^a	Chocolate agar ^b	Thioglycollate ^c
1	Negative	Negative	Negative
2	Negative	Negative	Negative
3	Negative	Negative	Negative
4	Negative	Negative	Negative
5	Negative	Negative	Negative

^aBlood agar (TSA with 5% sheep blood): general purpose non-selective, differential media that supports the growth of a wide variety of microbes.

^bChocolate agar with yeast extract: medium for the cultivation of fastidious microorganisms, particularly *Haemophilus spp.* and pathogenic *Neisseria spp.*

^cThioglycollate with dextrose: medium without indicator and Centers for Disease Control and Prevention formulation; general purpose medium for the cultivation of aerobic and anaerobic microorganisms.

Table 3. Microbial growth data (heated samples, 39.2°C)

Sample	Blood agar ^a	Chocolate agar ^b	Thioglycollate ^c
6	Negative	Negative	Negative
7	Negative	Negative	Negative
8	Negative	Negative	Negative
9	Negative	Negative	Negative
10	Negative	Negative	Negative

^aBlood agar (TSA with 5% sheep blood): general purpose non-selective, differential media that supports the growth of a wide variety of microbes.

^bChocolate agar with yeast extract: medium for the cultivation of fastidious microorganisms, particularly *Haemophilus spp.* and pathogenic *Neisseria spp.*

^cThioglycollate with dextrose: medium without indicator and Centers for Disease Control and Prevention formulation; general purpose medium for the cultivation of aerobic and anaerobic microorganisms.

Table 4. Fungal growth data (calcofluor white stain)

Refrigerated samples, 5.2°C		Heated samples, 39.2°C	
1	Negative	6	Negative
2	Negative	7	Negative
3	Negative	8	Negative
4	Negative	9	Negative
5	Negative	10	Negative

Materials

All materials utilized for this study were of analytical grade. The 15 intravenous bags of 0.9% sodium chloride used in this experiment were purchased from B. Braun Medical Inc. (Irvine, CA). The bags utilized for this study were NDC: 0264-7800-00 and lot: J2D408. The samples were cooled using a Gem

Refrigerator (Philadelphia, PA) model TA-0170C. The samples were heated by Olympic Warmette oven (Seattle, WA) model 56910. The temperatures were monitored using a Sanofi Pasteur *Traceable* memory thermometer, model 8585. Sample collection for the microbial testing, fungal testing, and quantitative assay was done in a ISO class 6 room under an ISO class 5 laminar flow hood in accordance with the USP <797> guidelines for compounding sterile components.⁹ The samples were transferred using sterile test tubes (*Vacurette*).

Physical Evaluation

The physical stability of all the samples was carried out by visual inspection. All the samples were evaluated for any visible signs of particulate matter, cloudiness, and color change. Crystallization was absent at the experimental temperatures and for the duration of the study. In addition, the pH of all the samples was measured with the Clinitek Atlas analyzer (Siemens). The Clinitek Atlas utilizes a reflectance spectrophotometer to measure the pH at 630 nm and 550 nm. The acceptable pH range for sodium chloride fluids as stated by the manufacturer is 4.5 to 7.0. The pH results obtained are provided in Table 5. When combined with the ion-selective electrode readings, the pH readings serve as a valuable tool for evaluating stability.

RESULTS

The mean sodium concentration of the refrigerated samples, heated samples, and control samples was 150 mmol/L, 155 mmol/L, and 151 mmol/L, respectively. From a clinical standpoint, these values are considered equal. A Student *t* test analysis was performed to determine whether there was a difference between the mean sodium values of the refrigerated samples and the mean sodium value of the control group. There was no statistical differ-

ence between these 2 groups ($\alpha = 0.05$, $P = .115$). A Student *t* test analysis was also performed to determine whether there was any difference between the mean sodium value of the heated samples and the mean sodium value of the control group. There was a statistical difference between these 2 groups ($\alpha = 0.05$, $P = .0001$). This observed difference was attributed to water loss from the prolonged heating and had no bearing on the intended use of these fluids. The difference was therefore considered to be clinically insignificant. Furthermore, for the refrigerated group and the heated group, a relative error of less than 10% was obtained when compared to the control group.

DISCUSSION

Sterility and stability are major factors in the preparation of pharmaceutical compounds. The importance of such parameters cannot be overstated. The findings of this study have enabled our facility to extend the shelf life of these fluids well beyond the 28 days recommended by the manufacturer. We are a 96-bed hospital that maintains 12 L of refrigerated sodium chloride for use in the event of a malignant hyperthermia emergency. We support 6 ambulances and supply each one with 2 L of sodium chloride that is to be refrigerated and 2 L of sodium chloride that is to be heated. In addition, our emergency department is in the process of changing its policy to begin storing 4 L of refrigerated sodium chloride solutions. This brings the total to 40 L of sodium chloride that would have to be changed out every month and discarded. The direct effect of this study is significant in the amount of time and money that will be saved from eliminating the need to change out these fluids each month. Based on these findings, we will extend the expiration date assigned to these fluids to 90 days. A medication use evaluation was done to compare how many intravenous sodium chloride fluids are being stored by other hospitals and emergency medical service providers. Table 6 provides a comparison of the number of fluids stored by these facilities. It also serves as evidence of the impact that an extended expiration date will have on those facilities that maintain large numbers of heated and cooled fluids.

CONCLUSION

The findings of this study showed that a sterile intravenous solution of 0.9% sodium chloride stored in heated or cooled conditions remained stable and showed no signs of microbial or fungal growth

Table 5. pH readings with Clinitek Atlas Chemistry Analyzer

Refrigerated samples, 5.2°C		Heated samples, 39.2°C		Room temperature samples, 21.8°C	
1	5.5	6	5.5	11	5.5
2	5.5	7	5.5	12	5.5
3	5.5	8	5.0	13	5.5
4	5.5	9	5.5	14	5.5
5	5.5	10	5.5	15	5.5

Table 6. Intravenous sodium chloride utilization

Hospital/ EMS facility	Beds	EMT support	Cooled fluids	Heated fluids	Total fluids
1	460	N/A	30	0	30
2	455	N/A	45	0	45
3	199	No	20	0	20
4	160	Yes	54	0	54
5	96	Yes	28	12	40
6	54	Yes	9	8	17
7	N/A	N/A	60	40	100

Note: EMS = emergency medical service; EMT = emergency medical technician; N/A = not applicable.

for a period of 199 days. The findings of this study will enable hospitals and emergency medical service facilities to significantly extend the expiration date assigned to these fluids and therefore save time and money and decrease the number of fluids that need to be discarded each month.

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