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Hydrogen-ion potential of dobutamine hydrochloride solutions exposed to environmental conditions of neonatal intensive care units

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Abstract

Objective: To verify the hydrogen-ion potential (pH) of dobutamine hydrochloride solutions under environmental conditions similar to those of neonatal intensive care units.

Methods: We analyzed the pH of the drug diluted in 5% dextrose in water or 0.9% NaCl under different conditions of temperature (22 and 37 ºC) and light (dark, fluorescent light bulbs, and phototherapy equipment), using colorless and amber intravenous sets at time intervals of 0, 1, 24, 48, 72, and 96 hours.

Results: The pH values of the marketed form of the drug and the diluted drug were similar. The pH means were 3.45±0.19 at 22 °C and 3.55±0.20 at 37 °C. The average of the pH according to light conditions were as follows: in the dark = 3.62±0.09, under room light = 3.63±0.07, and exposed to phototherapy = 3.31±0.16. Solutions stored in colorless intravenous sets had a lower mean (3.41±0.24) than those kept in amber intravenous sets (3.52±0.15). We found lower pH values in the solutions exposed to phototherapy using colorless intravenous sets (3.17±0.03) than in those using amber intravenous sets (3.55±0.03).

Conclusion: There was higher variation in the pH of the solutions exposed to phototherapy, and the use of amber intravenous sets reduced such effect.

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Introduction

Drugs and solutions are considered to be stable when they keep up to 90% of their chemical activity and physical properties unchanged. Temperature has an influence on the rate of chemical reactions because it promotes higher kinetic energy than the activation energy, and light energy may cause molecular decomposition with binding breakdown or rearrangement produced by photolysis.[1,2]

One of the indicators of the chemical behavior is the hydrogen-ion potential (pH) value. Drug stability is inversely proportional to the difference from the optimal pH value.[1,2]

Concern has been raised in the clinical practice regarding the influence of the environmental characteristics of neonatal intensive care units (NICUs), such as the action of heat and light originated by the use of incubators and phototherapy equipment, respectively, on drug stability.

Dobutamine hydrochloride is widely used at NICUs and its pH value may range between 2.5 and 5.5.[3] However,

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we could not find in the literature studies on the stability of this drug at temperatures higher than 25 ºC or exposed to irradiance and light intensity comparable to those produced by phototherapy equipment.[4-10]

Since drug administration under preestablished environmental conditions is essential for the maintenance of drug stability and, as a consequence, for providing adequate treatment, promoting patient's safety, and supporting the clinical practice of the nursing team responsible for administrating the solutions,[11] the objective of the present study was to verify the pH of dobutamine hydrochloride solutions throughout time under varied temperatures, light conditions, and using different intravenous administration systems (IAS) simulating the clinical practice of nursing teams at NICUs.

Method

This experimental study was approved by the Research Ethics Committee, and data collection was conducted at a laboratory environment between May and July 2007.

The sample comprised 180 pH values of dobutamine hydrochloride and 5% dextrose in water (DW5) and 0.9% NaCl (NS) diluents in its marketed form and solutions composed of these elements at a concentration of 7 mg/mL according to the study conditions and at predefined periods of time.

Solutions were stored in IAS using a graduated glass tube (burette). For explanatory purposes, the extension of the intravenous set used previously to the installation of the infusion pump was defined as proximal portion, and the extension used after installation of the infusion bomb was of distal portion.

We used conventional phototherapy equipment, featuring fluorescent light bulbs, with a constant mean distance of 48 cm between the device and the distal portion of the intravenous set. Irradiance was measured using a radiometer located at a distance of 48 cm.

A luxmeter was used to measure the light intensity of the fluorescent light bulbs falling upon the burette (mean of 430 lx) and upon the distal portion of the intravenous set (mean of 230 lx). We also measured the illumination at 48 cm from the phototherapy equipment (mean of 9,000 lx). Wrappers used to keep the IAS in the dark allowed light incidence of at most 2 lx.

pH measurement was carried out using ExStik pH Waterproof Meters, model PH100, Extech® (Waltham, Massachusetts, USA). The pH values were determined immediately after the electrode is placed in the samples of solutions kept in glass beakers.

After measuring the pH of drugs and diluents in their marketed form, the admixtures were placed in burettes constituting the study solutions, and pH values were measured again. After filling up the intravenous sets, samples were collected at 0, 1, 24, 48, 72, and 96 hours after infusion. Such times are identified as T_0, T_1, T_2, T_3, T_4, and T_5, respectively, representing a pH measurement in each situation investigated.

With regards to the temperature, samples were exposed to two different situations: when the IAS was kept at 22 ºC and when the distal portion entered the incubator adjusted at 37 ºC.

Regarding the investigation of light influence, samples were exposed to three different conditions: the whole IAS in the dark, the system exposed to the lightning of room light bulbs, and the solutions contained in the distal portion of the intravenous sets exposed to fluorescent light produced by the phototherapy equipment.

Dobutamine hydrochloride solutions were stored in two types of IAS, colorless (CIAS) and amber (AIAS). Colorless devices protected against the light (PIAS) were used for controlling the experiment.

The results were manually recorded and stored in electronic spreadsheets using descriptive text and figures. Analysis of arithmetic mean ± standard deviation was used to investigate pH variations in the different situations studied.

Results

We analyzed 180 pH values. Of these, 20 (11.1%) were measured from samples of dobutamine hydrochloride in its marketed form, 20 (11.1%) were DW5 and NS diluents under the same condition, 20 (11.1%) were solutions composed of these elements, and 120 (66.7%) were samples according to the study situation at the predefined time periods.

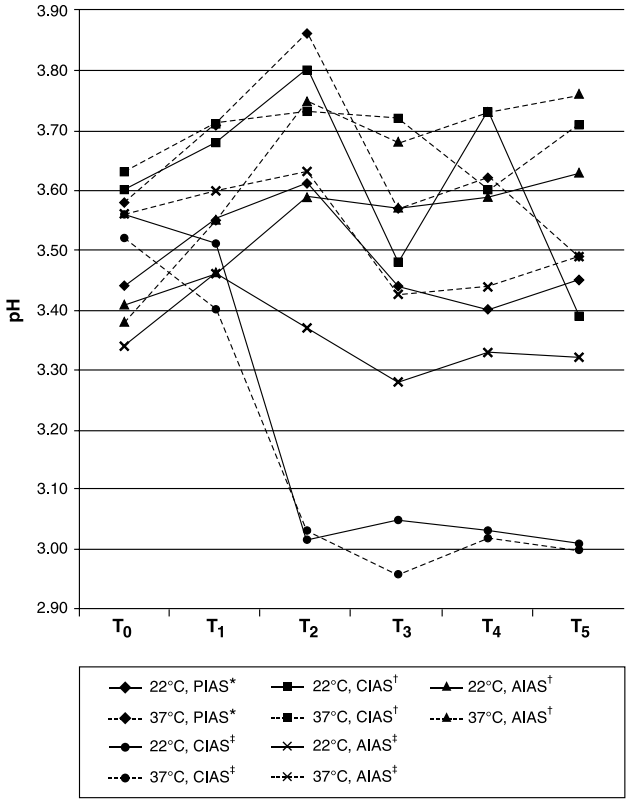
The pH values of dobutamine hydrochloride aimed at dilution in DW5 ranged between 3.10 and 3.31, their mean being 3.23±0.06; the pH values of dobutamine hydrochloride diluted in NS ranged between 3.07 and 3.36 with mean value of 3.27±0.08; the pH values of DW5 were between 4.43 and 5.10, their mean being 4.70±0.20; and the pH values of NS ranged from 5.33 to 6.34 with mean values of 5.86±0.35. The marketed form of dobutamine hydrochloride had a mean value of 3.25±0.07 and, after dilution, the value was 3.49±0.08 (DW5 3.46±0.08; NS 3.52±0.07).

With regard to the temperature, we found mean pH values of 3.45±0.19 for the solutions at 22 ºC and 3.55±0.20 at 37 ºC.

In terms of illumination, we found mean pH values of 3.62±0.09 in the dark, 3.63±0.07 under room fluorescent lightning, and 3.31±0.16 when exposed to phototherapy equipment, with this last situation showing the lowest pH values (2.96) and mean (3.15) and the highest variations in the solutions (0.31).

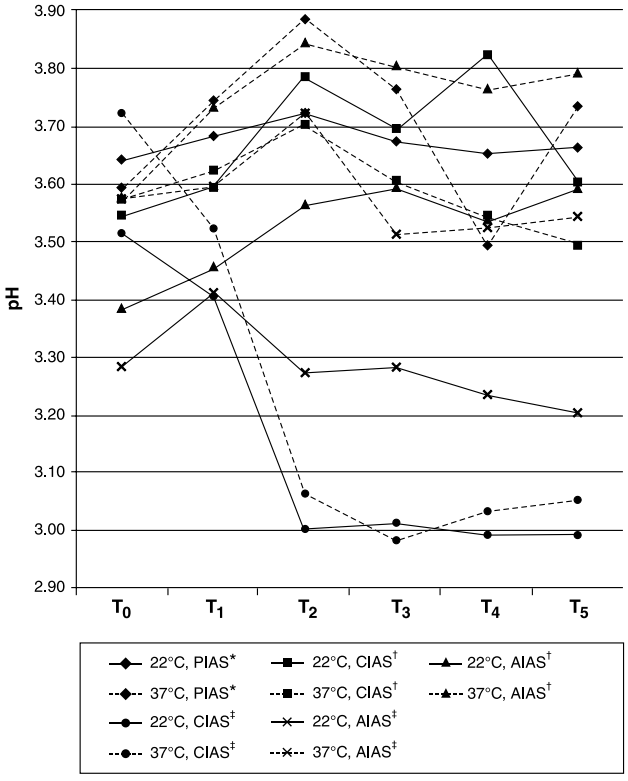
The solutions kept in CIAS had lower pH values (3.17±0.03) than those placed in AIAS (3.55±0.03).

When exposed to the light energy emitted from a close, direct and constant source of fluorescent light bulbs installed in the phototherapy equipment, regardless of diluent and temperature, the solutions kept in the CIAS had significant reduced pH values up to T_2, changing from colorless to pinkish. On the other hand, the solutions placed in AIAS had more constant pH values and did not go through such physical alteration (Figures 1 and 2).



T_0 = 0 hour of infusion; T_1 = 1 hour of infusion; T_2 = 24 hours of infusion; T_3 = 48 hours of infusion; T_4 = 72 hours of infusion; T_5 = 96 hours of infusion; PIAS = protected intravenous administration system; CIAS = colorless intravenous administration system; AIAS = amber intravenous administration system.
* Darkness.
† Room fluorescent lighting.
‡ Light emitted by the phototherapy equipment.

Figure 1 - Values of hydrogen-ion potential of dobutamine hydrochloride in DW5 according to exposure to light, temperature, intravenous administration system and time (São Paulo, Brazil, 2007)



T_0 = 0 hour of infusion; T_1 = 1 hour of infusion; T_2 = 24 hours of infusion; T_3 = 48 hours of infusion; T_4 = 72 hours of infusion; T_5 = 96 hours of infusion; PIAS = protected intravenous administration system; CIAS = colorless intravenous administration system; AIAS = amber intravenous administration system.
* Darkness.
† Room fluorescent lighting.
‡ Light emitted by the phototherapy equipment.

Figure 2 - Values of hydrogen-ion potential of dobutamine hydrochloride in NS according to exposure to light, temperature, intravenous administration system and time (São Paulo, Brazil, 2007)

Discussion

Drug and diluents, in their marketed form, were found to have pH values in agreement with reference values.[3]

Regardless of the diluent used, pH values of solutions remained similar to those of the marketed form of the drug and lower than those considered safe for infusion in peripheral veins in terms of prevention of local complications caused by the intravenous therapy, highlighting the need of administration using central catheters.[12,13]

The small difference between the mean pH values and the standard deviation of solutions at 22 or 37 ºC suggests that temperature is not responsible for alterations in the chemical behavior; however, it was not possible to compare such data with the literature due to the lack of studies assessing the stability of these solutions at temperatures close to 37 ºC.

It is important to mention that most NICUs in Brazil do not have controlled thermal conditions and, therefore, continuous infusion solutions are exposed to the variations of the day-night pattern and to the high temperatures of the tropical climate. In addition, there is electronic equipment at NICUs which favors environmental warming.

The small difference in the mean pH values and in its variations after comparison of solutions stored in the dark with solutions exposed to room fluorescent lightning suggests that this type of illumination did not cause any alterations in the chemical behavior.

With regard to the change in the color of the solutions exposed to close, direct, and constant lightning produced by phototherapy equipment, we could not find support in the literature to the use of these fluids or to the statements that the amount of the therapeutic principle present in such fluids is kept up to 90% of its initial concentration. It is also not possible to assume that the drug is stable. Experiments assessing such solutions by means of high performance liquid chromatography (HPLC) are needed.

It is also worth mentioning the need of studies using other types of phototherapy, such as Super LED, which emits high intensity light by means of a set of LED of superior physical-chemical composition.[14]

According to recommendations of the Centers for Disease Control and Prevention (CDC), IAS replacement just after 72 hours, provided that they remain closed, is classified as category IA.[15] Hence, studies guaranteeing the stability of dobutamine hydrochloride for a period longer than 24 hours could also contribute to the reduction of risks of bloodstream infection associated with handling of catheters, in addition to providing support to the review of residue disposal procedures, collaborating to environmental preservation and reduction of hospital costs.

Conclusions

Heat and lighting produced by room fluorescent light bulbs seem not to cause changes in the chemical behavior of dobutamine hydrochloride solutions; however, it is possible to conclude that there is a stronger influence of the light produced by the phototherapy equipment on the chemical profile of the solution studied and that the use of AIAS may contribute to preserve the initial characteristics of the drug.

It is important to highlight the relevance of further studies on this topic for the detection of alterations in the pharmacological concentrations of the solutions analyzed with the purpose of verifying if the nursing clinical practice related to the care provided to newborns at NICUs is adapted to the peculiarities of the drug treatment so that routine interventions are based on scientific evidence promoting the improvement of nursing and, as a consequence, that medical care is increasingly beneficial, safe and focused on the integral and individual needs of patients and their families.

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