Storage Temperatures of Medications on an Air Medical Helicopter

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Abstract

Introduction: The safety and efficacy of medications stored on air medical helicopters may be adversely affected by extreme temperatures. The purpose of this study was to determine whether temperatures inside an air medical helicopter drug box were within the U.S. Pharmacopeia recommendations for controlled room temperature. This is defined as a temperature between 15° and 30° C (59° and 86° F) with a mean kinetic temperature of less than 25° C (77° F). An additional goal was to determine whether time/temperature indicator labels can reliably monitor mean kinetic temperatures.

Methods: Temperatures were monitored with miniature electronic temperature recorders and color-changing time/temperature indicator labels.

Results: The mean kinetic temperatures for the summer and winter periods were 25.1° C (77.2° F) and 12.7° C (54.8° F), respectively. In the summer, the electronic recorders logged temperatures exceeding 25° C (59° F) 37% of the time and more than 30° C (86° F) 6% of the time. In the winter, temperatures less than 15° C (59° F) were recorded 83% of the time. The mean kinetic temperatures obtained from the electronic recorder and the time/temperature indicator labels differed by less than 0.7° C (1.3° F). The results show that medications on an air medical helicopter are subject to temperatures out of the recommended range and that time/temperature indicator labels can reliably monitor mean kinetic temperatures.

Introduction

Many medications are carried in drug boxes in air medical helicopters (AMHs). These medications may be exposed to extreme thermal conditions that can affect their efficacy and safety and thus may adversely affect patient care in the field. All prehospital medications carry a U.S. Pharmacopeia (USP) label requiring that they be kept within a specific temperature range.[1] The range for most of these medications is "controlled room temperature," which is defined as temperatures between 15° and 30° C (59° and 86° F) with a limit on mean kinetic temperatures (MKTs) to less than 25° C (77° F). The USP defines MKT as "a single calculated temperature at which the degradation of an article would be equivalent to the actual degradation that would result from temperature fluctuations during the storage period."[1] This method averages temperatures exponentially, which is the same way that pharmaceuticals degrade with temperature.

Previous studies have examined whether prehospital medications meet storage requirements and whether degradation occurs. Palmer et al.[2] in 1985 measured summer temperatures by a disk-recording device in a prehospital ground vehicle in Salt Lake City, Utah, for 15 hours. They found that temperatures were far higher than those recommended for safe drug storage.[2] In 1989, Valenzuela et al.[3] reported changes in isoproterenol and epinephrine after being stored in a white metal shed exposed to the summertime sun in Arizona

for 4 weeks. Grant et al.[4] found significant reduction in the biologic availability of thermally stressed epinephrine (1:1000, 1:10,000 solution) when injected into rats.

Johansen et al.[5] in 1993, however, reported no changes in four prehospital medications subjected to 16 hours of variable temperature extremes. A review of the literature does not reveal any reported studies that addressed colder environmental conditions. For cold environmental conditions, temperatures below the freezing point (0° C) may pose a problem for certain drugs, particularly those in aqueous solutions.

The main objective of this study was to determine whether temperatures inside the drug box in an AMH were within the USP recommendations for storage temperatures. Measurements were obtained in both summer and winter to encompass a range of extreme temperatures. A second objective was to determine whether novel time/temperature indicator (TTI) labels can reliably monitor MKT.

Methods

The AMH was kept on a roof heliport in northern New Jersey except in cases of inclement weather, when it was housed in a climate-controlled hangar. The medications were stored in an uninsulated commercial drug box on the helicopter floor. An external cabin heater and air conditioner were available on the roof heliport. Two methods were used to monitor temperatures in the drug box: a miniature electronic temperature recorder (METR) and a set of seven color-changing TTI labels. Data were collected from June 1 to August 10, 1995, and December 27, 1995, to January 17, 1996.

The METR was a matchbox-size HOBO® data logger (Onset Computer Corporation, Pocasset, Mass.) that recorded temperatures at preprogrammed intervals set from 12 to 24 minutes. The accuracy of the METR is listed as ± 0.8° C. Data from the METR were downloaded to a computer, and graphs of temperature versus time were generated. The percentage of time that temperatures were outside of the USP recommended storage range was calculated. The MKTs from METR data were determined using an integrated form of the USP formula.

HEATmarker® TTI labels from LifeLines Technology, Inc. (Morris Plains, N.J.), also were used for this study. The TTI labels are made from a chemical that undergoes a polymerization process resulting in color changes.[6] Exposure to temperature over time causes color changes that correlate with degradation processes occurring in pharmaceuticals. These color changes can be perceived visually; however, a color reflectance den-

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Figure 1

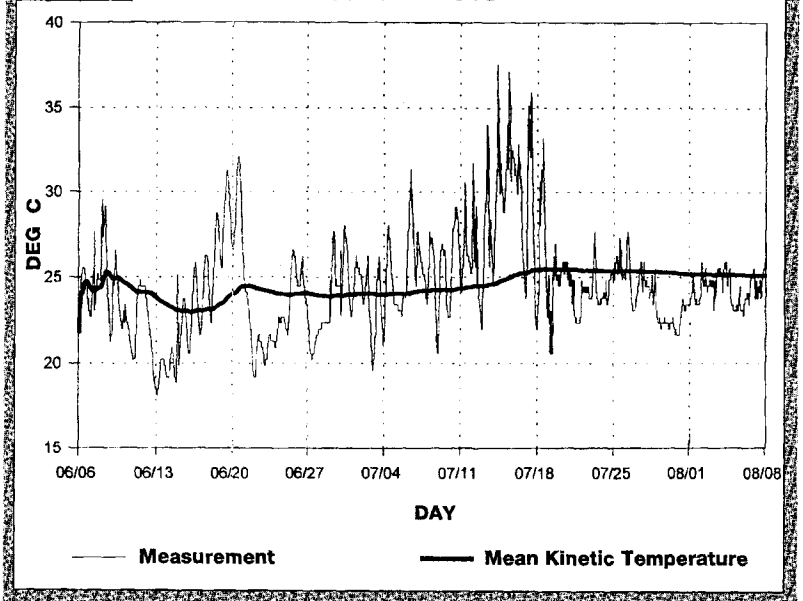
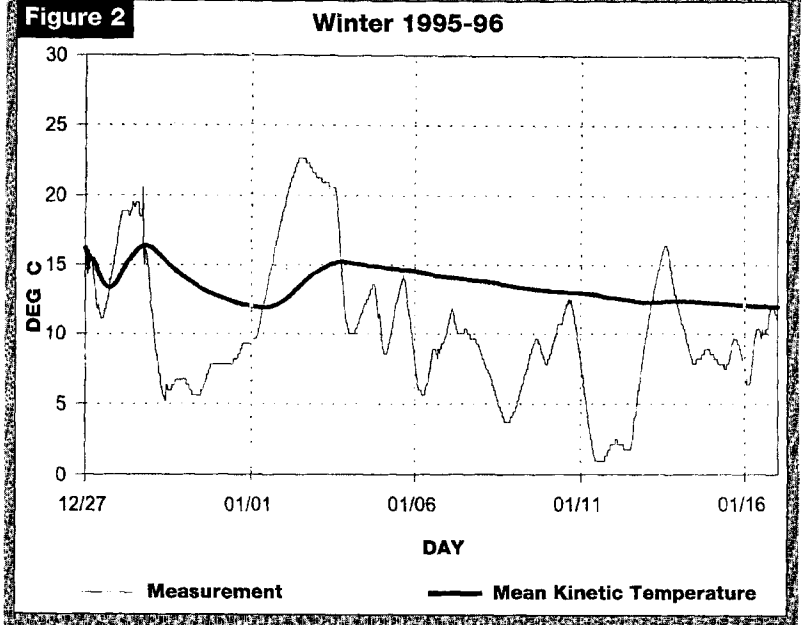


Figure 2



The temperatures recorded by a miniature electronic temperature recorder for a study period in 2001. The temperature measurements are shown along with the calculated mean kinetic temperature.

sitometer (X-Rite model 404GS from X-Rite, Inc., Grandville, Mich.) was used for more objective measurement. The MKTs were obtained from these color changes by calculating the equivalent temperature exposure that would result in the same color change over the measured period.

Results

In the summer, the METR recorded temperatures greater than 25° C (77° F) 37% of the time and greater than 30° C (86° F) 6% of the time, as illustrated in Figure 1. The MKTs calculated weekly for the summer period ranged from 23.8° to 29.4° C (74.8° to 84.9° F). The MKT for the entire summer period was 25.1° C (77.2° F). The MKT calculated from the set of seven TTI labels was 0.5° C lower than that for the METR. The 95% confidence intervals for the TTI labels and the METR were ± 0.4° C and ± 0.8° C, respectively. Thus, no statistically significant difference occurred between the two methods.

In the winter, temperatures less than 15° C (59° F) were recorded 83% of the time and less than 8° C (46.4° F) 32% of the time, as shown in Figure 2. For the winter period, no temperatures below 0° C (32° F) or above 30° C (86° F) were recorded. The weekly MKT ranged from 9.2° to 14.5° C (48.6° to 58.1° F). The MKT for the entire period was 12.7° C (54.9° F). The MKT calculated from the set of seven TTI labels was 0.7° C lower than that for the METR. The 95% confidence intervals for the TTI labels and the METR were ± 0.6° C and ± 0.8° C, respectively. Thus, no statistically significant difference occurred between the two methods. We estimate that we had a power of greater than 90% to detect a difference of more than 2° C between the two methods.

Discussion

Temperatures inside a drug box in an AMH were measured for several weeks in the summer and winter. The results show that, for significant periods, the storage area of the drug box was exposed to temperatures outside those recommended by the USP. These data indicate the AMH program to be out of compliance with current regulations concerning storage of medications.

Protecting against thermal abuse can be accomplished in several ways: continuous climate control of AMH cabins and/or drug boxes, insulation of drug boxes, continuous temperature-recording devices, TTI labels on each pharmaceutical, or frequent rotation of medications. By the nature of prehospital care, even with a continuous climate-controlled environment, medications may be exposed to temperature extremes when in the field. To minimize this exposure, insulated drug boxes may be used. With the frequent rotation of drugs in the prehospital environment, it is difficult to monitor the temperature history of an individual medication using a continuous temperature-recording device in an AMH cabin or drug box.

An alternative approach is to use TTI labels on each drug container. The World Heath Organization has used this type of label on more than 12 million vaccine vials during the past 4 years. Although an exact time/temperature history of medications cannot be obtained, the MKT can be monitored reliably, which is the most relevant indicator of pharmaceutical degradation. This approach, combined with a freeze indicator for the drug box, would provide an excellent way to monitor for thermal abuse.

Using an optical densitometer, the MKTs obtained from the TTI labels and the METR agreed within 0.7° C. This method would not be as precise if color changes were monitored visually. However, a built-in safety factor may be used to show the color-indicating expiration before the standard shelf life expires.

Limitations to this study include the fact that the chemical or bioavailability of the medications were not measured. The fact that drugs are exposed to temperature extremes does not mean they all are no longer effective; however, certain drugs may lose their full potency, or undesirable degradation byproducts may develop.

This study also did not address the length of time that drugs are on the AMH unit before administration. Busier programs will have shorter medication storage time than slower units, whereas certain medications are administered infrequently regardless of call volume.

Conclusion

The results show that medications on AMHs may be subject to temperatures out of ranges recommended by the USP. This exposure may result in premature degradation of medications, which may adversely effect prehospital interventions. Given that providing care on AMHs is expensive, it seems prudent to expend more effort to ensure that prehospital medications are not thermally abused. One solution is to use TTI labels, which can reliably monitor MKTs.

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