SHORT COMMUNICATION

PILOT STUDY ON POTENTIAL DEGRADATION OF DRUG EFFICACY RESULTING FROM ANTARCTIC STORAGE, TRANSPORT AND FIELD CONDITIONS

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INTRODUCTION

Field Medical Box items for British Antarctic Survey (BAS) Field operations in Antarctica are provided by the Pharmacy Department of the Plymouth Hospitals NHS Trust. The logistic chain to provide summer season Field Medical Box items is shown in Table I, with an indication of approximate temperatures and timescales such supplies are required to withstand.

Field medical boxes carry a range of pharmaceutical drugs for medical emergencies. The manufacturers recommend that the majority of these drugs should be stored at room temperature – instead they are subjected to extended periods of storage at sub-zero temperatures. Although information is available on the stability of some of these drugs under high temperature storage conditions (1-3), there is currently no information available on their stability under sub-zero conditions.

Some manufacturers specifically warn against freezing (eg for tetracaine, lidocaine gel and hydrocortisone cream) due to either crystallisation or lack of stability data (chemical or physical).

We have performed a pilot study on a group of eleven drugs commonly carried in field medical boxes in order to determine

Table I. Logistic chain to provide summer season Field Medical Box items to Antarctica.

| Location                          | Average temp. (°C) | Extreme temp. (°C) | Timescale     |
|-----------------------------------|-------------------|--------------------|---------------|
| Storage in Pharmacy Dept          | 17                | 23                 | 4 months      |
| Pharmacy to UK port via road      | 13                | 26                 | 1 week        |
| Ships hold storage:               |                   |                    |               |
| Passage in temperate latitudes    | 22                | 28                 | 1 week        |
| Passage in tropical latitudes     | 26                | 34                 | 2 weeks       |
| Southern Ocean latitudes          | 5                 | -5                 | 2 weeks       |
| Snowcat and Skidoo transportation | -5                | -15                | 1 day         |
| Storage at research station       | 2                 | -10                | 4 weeks       |
| Storage in field location         | -5                | -20                | 10 weeks      |
| Winter storage and field use      | -10               | -40                | 6 months      |
whether drug degradation occurs under these conditions, and if so, to what extent drug efficacy is reduced.

METHODS

Ten vials/packets of each drug were obtained; half were stored at the temperature recommended by the supplier, and the other half subjected to average/realistic summer field conditions (-15°C) for a period of 4 weeks. Alternatively, one tube of gel/cream was aliquoted into 5 polypropylene tubes for each arm of the study. Samples were then analysed by stability-indicating High Performance Liquid Chromatography (HPLC) methods to determine whether any drug loss had occurred in the frozen samples relative to their controls.

In addition, after 4 weeks at -15°C followed by thawing, a second set of five vials, packets or aliquots were subjected to repeated freeze-thawing (x 4) over a 3 week period, followed by HPLC analysis.

RESULTS AND DISCUSSION

Eleven Field Medical Box drugs were tested for stability over both 4 weeks at -15°C and 7 weeks at -15°C with 5 freeze-thaw steps. The results presented in Table II demonstrated that all drugs were found to be stable after both freezing and freeze/thawing with the exception of hydrocortisone cream.

Some manufacturers specifically warn against freezing particular drugs/drug formulations (eg tetracaine injection, lidocaine gel and hydrocortisone cream). Tetracaine concentrations were found to remain stable after storage at -15°C in this study, but it is recommended that freezing be avoided due to the

| Drug                                                                 | % rem. after 4 weeks -15°C | % rem. after 4 weeks -15°C + 5 freeze-thaws |
|----------------------------------------------------------------------|-----------------------------|--------------------------------------------|
| Epinephrine injection                                               | 97.0 ± 1.8                  | 101.1 ± 0.6                                |
| Cefuroxime powder for injection (Zinacef)                          | 98.9 ± 1.2                  | 98.9 ± 1.1                                 |
| Chlorpheniramine injection (Chlorphenamine)                        | 97.2 ± 1.0                  | 99.1 ± 1.9                                 |
| Erythromycin tablets                                                | 98.8 ± 2.0                  | 97.0 ± 0.9                                 |
| Hydrocortisone cream                                                | 89.2 ± 7.5                  | 73.5 ± 3.9                                 |
| Hydrocortisone sodium succinate powder for injection (Solu-Cortef) | 99.4 ± 1.0                  | 100.2 ± 0.7                                |
| Lidocaine HCl gel                                                   | 96.8 ± 3.2                  | 100.3 ± 1.8                                |
| Lidocaine HCl injection                                             | 98.8 ± 1.5                  | 99.9 ± 0.9                                 |
| Nalbuphine HCl injection (Nubain)                                   | 99.6 ± 2.2                  | 99.3 ± 1.5                                 |
| Paracetamol tablets                                                 | 100.4 ± 1.2                 | 100.6 ± 2.0                                |
| Tetracaine HCl eye drops (1.0% Minims)                              | 95.4 ± 1.0                  | 99.2 ± 1.0                                 |
| Tetracaine HCl eye drops (1.0% Minims)                              | 101.1 ± 1.0                 | -                                          |
| 0.7µm filtered                                                      |                             |                                            |
potential risk of tetracaine crystallisation. The presence of such crystals could cause corneal abrasions.

In this study (n=5), 0.7µm filtration before analysis did not result in a decrease in measured tetracaine concentration, suggesting either that any crystals formed were less than 0.7µm in size, or that no crystals were formed in this instance. The potential for crystallisation on freezing was also found to apply to other eye (Minims) medications such as fluorescein sodium, cyclopentolate hydrochloride and pilocarpine nitrate.

Lidocaine was found to be stable in gel formulation, however hydrocortisone levels in the cream formulation were found to decrease to below acceptable levels after freezing, particularly after numerous freeze-thaw cycles. Hydrocortisone cream is water based, which may result in the dessication of excipients on freezing. It is possible that hydrocortisone ointment (which is paraffin-based) would be stable under the same conditions.

Therefore it is recommended that hydrocortisone cream and the eye medications mentioned above should not be stored in Field Medical Boxes subjected to freeze/thaw temperature ranges. Further studies are planned on other Field Medical Box items, and their possible replacements.

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