M1030-05-033

Assessment of Local and Systemic Bioavailability of Lidocaine from Two Lidocaine Topical Delivery Systems using Pharmacokinetic and Skin (Tape) Stripping Analyses

S. Shukla[1], S. Thomas[1], DC Hammell[1], A. Bunge[2], H. Hassan[1], A. Stinchcomb[1]
[1]School of Pharmacy, University of Maryland, Baltimore, MD,
[2]Chemical & Biological Engineering, Colorado School of Mines, Golden, CO
sshuk001@umaryland.edu

aaps PharmSci 360 ADVANCING PHARMACEUTICAL SCIENCES, CAREERS, AND COMMUNITY

PURPOSE

The site of action for many topical dermatological drug products is in the skin and/or in the surrounding local tissues. Therefore, the local bioavailability of the active pharmaceutical ingredient (API) from topical delivery systems (TDS) may influence their therapeutic efficacy and may be relevant for evaluating bioequivalence of such products.

OBJECTIVES

The goal of this study is to obtain a mechanistic understanding of the local and systemic bioavailability of an API from a topically administered drug product. The bioavailability of lidocaine from two commercially available lidocaine TDS (A and B) were assessed both in serum and stratum corneum (SC) samples obtained from healthy volunteers.

METHODS

PK Study Design

Two different lidocaine TDS, 5% products (A and B, 140 cm^2 each) were included in the crossover study. Serum concentrations were determined after application of two TDS of the same product to the upper arms in healthy volunteers. TDS were applied for 10 h and blood samples were collected for 15 h following the application of TDS. Serum samples were analyzed using a validated liquid chromatography mass spectroscopy (LC-MS/MS) method and pharmacokinetic (PK) analysis was conducted using Phoenix WinNonlin® to calculate the area under the concentration (AUC) vs. time curve and maximum concentration (C_{max}) of lidocaine from each product (A and B).

Tape Stripping Study Design

In a following session with each volunteer, six TDS pieces (each 8.25 cm^2) of each product were randomized to six sites on the volar forearms (12 total sites for the two TDS). All TDS pieces were removed 10 h post application, and a 5 cm^2 section of each site was tape stripped to determine the amount of lidocaine in the SC either immediately (designated "uptake") or after 5 h and 14 h of "clearance" (i.e., 15 h and 24 h, post application). Tape stripping of each site was conducted for a minimum of 12 tape strips and up to a maximum of either 30 tape strips or when the site reached six times the baseline transepidermal water loss (TEWL) value determined using a Delfin VapoMeter. Successive tape strips were grouped together based on combined SC weight of at least 750 µg or 6 tapes, whichever came first. Lidocaine was extracted from the skin tape strip groups using methanol, which was analyzed using a validated high pressure liquid chromatography (HPLC) method. All data is reported as mean ± standard deviation.

METHODS

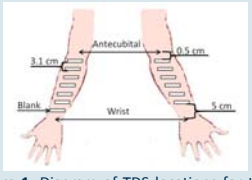

Figure 1. Diagram of TDS locations for tape stripping sites on the volar forearm.

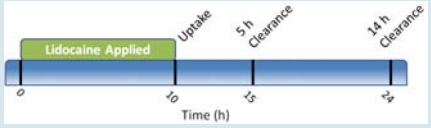

Figure 2. Tape stripping clinical study design. Tape stripping occurs at 10, 15 and 24 h post TDS application.

RESULTS

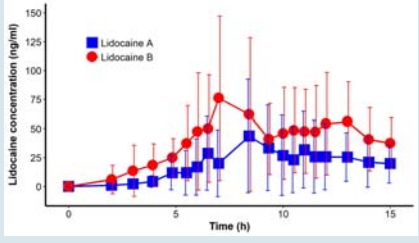

Figure 3. Lidocaine serum concentration versus time from five volunteers (mean ± SD) following 10 h administration of two TDS (Lidocaine A; blue square, Lidocaine B; red circle).

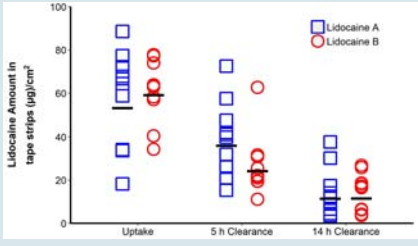

Figure 4. Amount of lidocaine (mean represented by line) in tape strips per TDS (Lidocaine A; blue square, Lidocaine B; red circle). Amount of lidocaine was quantified in duplicate at three different time points, immediately following TDS removal, 5 h and 14 h following TDS removal.

Table 1. Non-compartmental analysis and tape stripping results from five volunteers

Product	A	B
Non-compartmental analysis		
AUC (ng*h/mL)	271.1 ± 275.0	556.5 ± 346.6
C_{max} (ng/mL)	55.9 ± 45.7	93.0 ± 66.0
Stratum Corneum Lidocaine Amount (2 replicates; mean and 90% CI)		
Uptake (µg/cm²)	53.0 (33.5 - 84.0	59.1 (48.7 - 71.8
5 h Clearance (µg/cm²)	36.0 (24.6 - 52.6)	24.1 (18.2 - 32.1)
14 h Clearance (µg/cm²)	11.4 (5.6 - 23.5)	11.5 (5.5 - 24.1)
Percent Cleared from SC following patch removal		
5 h Clearance (%)	32.1	56.4
14 h Clearance (%)	74.7	76.4

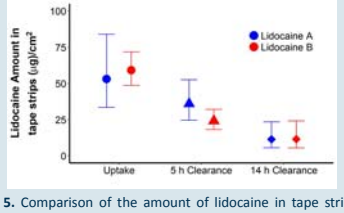

Figure 5. Comparison of the amount of lidocaine in tape strips of 5 volunteers (mean ± 90% CI of the log-transformed geometric mean in each volunteer; n = 10) in at three times following TDS removal: immediately, 5 h and 14 h.

CONCLUSIONS

Five healthy volunteers have completed the study to date. The limited dataset indicates that systemic bioavailability of lidocaine is comparable in the serum (Table 1 and Figure 3) with respect to the maximum concentration of lidocaine, and local bioavailability in the SC appears comparable from the two TDS with respect to amount of lidocaine at uptake and 14 h clearance (Table 1, Figure 4 and 5). The complete dataset in twelve volunteers with a combination of PK and in vivo skin tape stripping may provide insight into the relationship between systemic and local bioavailability of the two lidocaine TDS and thus enhance our understanding of local bioavailability at or near the site of action.

FUNDING

Funding for this project was made possible, in part, by the Food and Drug Administration through grant 1U01FD004947. The views expressed in this poster do not reflect the official policies of the U.S. Food and Drug Administration or the U.S. Department of Health and Human Services; nor does any mention of trade names, commercial practices, or organization imply endorsement by the United States Government.

UNIVERSITY of MARYLAND SCHOOL OF PHARMACY