Intradermal Pharmacokinetics of Naloxone Hydrochloride Using Hollow Microneedles of Different Lengths
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3M Drug Delivery Systems

Purpose
In a previous study, intradermal drug delivery of naloxone hydrochloride (approximately 15 min injection time) gave a lower Cmax and a longer Tmax using an array of eighteen 710 micron long microneedles compared to a subcutaneous dose. In this study we explore the intradermal pharmacokinetics of naloxone using longer microneedles and a shorter injection time. A three-way cross-over pharmacokinetic (PK) study was conducted in swine, where the same dose of naloxone hydrochloride was intradermally administered using a hollow microneedle transdermal system (hMTS) injector with microneedles of two different lengths; and also by subcutaneous administration using a syringe.

Methods
One milliliter of naloxone hydrochloride injection, USP (1 mg/mL) was administered to the lower ham of anesthetized swine (n=4) by: a) 3M hMTS injector with an array of eighteen 920 micron long microneedles; b) 3M hMTS injector with an array of twelve 1500 micron long microneedles; or c) subcutaneous injection. Blood samples were collected before the dose and at 2.5, 5, 10, 20, 40, 60, 120, and 240 minutes after start of dosing. Serum was analyzed for naloxone using a LCMS-MS method.

Results
ID injection times using the 920 micron microneedle array, the 1500 micron microneedle array, and the SC injection was 1.4± 0.4 minutes, 2.5 ± 0.9 minutes, and 3 seconds, respectively. The ID doses of naloxone yielded similar PK profiles. The ID Cmax of naloxone in serum for both arrays was approximately 14 ng/mL, whereas the SC Cmax was approximately 5 ng/mL. Tmax for all three groups was less than 10 minutes. The extent of absorption from ID administration with microneedles was greater than by SC injection. A full PK analysis and comparisons will be provided and discussed.

Conclusion
Compared to earlier work with 710 micron long hollow microneedles, the improvements in hollow microneedle array design by lengthening the microneedles to 920 or 1500 microns permitted faster ID delivery and decreased Tmax from 30 minutes to less than 10 minutes.