A Study of the Efficacy of a Novel Drug Delivery System (MicroNeedle Device)

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1. *BACKGROUND AND OBJECTIVES*

Many drugs, diagnostic agents, and vaccines used for the diagnosis, treatment and management of disease in human and veterinary medicine must be administered via injection. Adverse effects of this mode of drug delivery include appropriate patient restraint, necessity of administration by trained personnel, pain upon injection, local reaction(s), and problems with drug absorption and distribution. These inherent problems have sparked developments in the area of novel drug delivery systems including the use of microneedles.

Microneedles are designed to be minimally invasive injection devices similar in diameter to a human hair and generally made of stainless steel or silicon. These needles/probes penetrate the skin safely, reliably and painlessly, and can be used for single-use drug delivery eg. insulin or heparin (1, 2). This micro-needle technology can also be used for the delivery of vaccines or for the sampling of biological fluids for diagnostic purposes, eg. blood glucose monitoring (3). In studies in people the delivery of drugs with these devices caused much less pain and enhanced the uptake, bioavailability and, in some cases, the efficacy of the compound administered (4). In many cases intra-dermal delivery systems actually changed the pharmacokinetic profile and enhanced the uptake and bioavailability of the protein being injected which enabled improved efficacy of these compounds as compared to standard delivery after intramuscular or subcutaneous administration.

The purpose of this study is to establish that a novel microneedle delivery system effectively delivers a drug into the systemic circulation, the biologic effects of which can be safely and quickly noted. In this initial project that drug is atropine. The purpose of this pilot study was to verify that this MircoNeedle device successfully delivers a drug with known physiologic effects. Future studies will look at specific drugs which may be effectively delivered with this device and are currently only available for conventional injection eg insulin, heparin, analgesic agents, and vaccines.

2. *METHODOLOGY*

Mature beagles of either sex (neutered or intact) were used in because of their relatively uniform size and easy disposition. Prior to the study each dog was acclimatized and assessed by a veterinarian for general well being on the basis of a physical examination, complete blood count, biochemical profile, urine analysis and electrocardiogram (ECG). Only healthy dogs will be included within the study. The dogs were housed, cleaned, fed and provided water at the Central Animal Facility according to guidelines outlined by the

Canadian Council on Animal Care. They will be permitted food and water on the day of study.

The design for this study was a simple randomized cross-over plan eg, does treatment X (MircoNeedle) have an effect on variable Y (heart rate) in population Z (beagles) compared with a standard treatment protocol (atropine SC via regular needle & syringe) (11 - 14) ?. The study consisted of 2 groups of 10 dogs. On ***Day One*** 5 dogs received atropine administered via the Microneedle device (0.03 mL total volume or ~ 0.044 mg/kg), and 5 dogs received atropine (0.03 mL or ~ 0.044 mg/kg SC) via conventional needle (22 g) and plastic syringe (1 cc).

Results

Date: March 14, 2007
Average Age: 2 years 8 months
Avrage Body Weight: 9.0 kgs.
Atropine: MicroNeedle]
Dose of Atropine Delivered: 0.044 mg/kg SC = 20 microliter

TIME (Micro-needle)	HEART RATE	PERCENT CHANGE
0	72	NA
2 minutes	108	50%
5 minutes	270	275%
10 minutes	263	265%
20 minutes	245	240%
30 minutes	230	219%
Average Change from Baseline		210%

Date: March 14, 2007
Average Age: 2 years 8 months
Average Body Weight: 9.0 kgs.
Atropine: S.C. Injection
Atropine: MicroNeedle [NO] **Dose of Atropine Delivered:** 0.044 mg/kg SC = 0.68 mLs

TIME (s.c. Injection)	HEART RATE	PERCENT CHANGE
0	90	0
2 minutes	106	19.8%
5 minutes	108	20%
10 minutes	150	66.7%
20 minutes	235	161%
30 minutes	210	133%
Average Change from Baseline		76%

Conclusions;

Microneedle showed much faster rate of Atropine absorption when compared to the regular s.c. injection. The rate of change in the heart rates were significantly higher with the microneedle (210% from the baseline vs 133% s.c. injection). The device was proven safe and almost painless as dogs never felt pricks when device was placed and activated as opposed to injection where dogs felt pain as assessed from the withdrawal behavior and sound emitted.