

TITLE: LASER-DOPPLER MEASUREMENTS OF SKIN BLOOD FLOW DURING SYMPATHETIC BLOCKADE IN PATIENTS WITH REFLEX SYMPATHETIC DYSTROPHY

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Introduction

Reflex sympathetic dystrophy (RSD) is characterized by persistent limb pain and sympathetic hyperactivity. Lumbar sympathetic blockade (LSB) with local anesthetics is used for the treatment of lower extremity RSD.⁽¹⁾ Skin capillary blood flow (SBF) and skin temperature (ST) increase with regional sympathetic blockade.⁽²⁾ Laser doppler flowmetry (LDF) permits noninvasive real time measurement of SBF.⁽³⁾ Children and adolescents often receive LSB under heavy sedation or general anesthesia, which may confound immediate interpretation of efficacy. Changes in SBF and ST before, during, and one hour post LSB were studied using simultaneous LDF and skin thermometry in patients with RSD.

Materials and Methods

Ten patients with lower extremity RSD underwent a total of 27 LSBs at L2 under inhalational/intravenous analgesia following informed consent and approval by the Committee on Clinical Investigation. There were 3 adults (40, 32, and 27 yrs old) and 7 children and adolescents (10 to 19 yrs old). Lidocaine 1% 3-5 cc was injected as a test dose, followed by bupivacaine 0.375%, 0.25-0.35 cc/kg in increments. SBF and ST were compared pre- and 1 hour post- block by paired t-test.

Results

25/27 attempted LSB were successful on the first or second attempt; 2 were unsuccessful despite apparently correct needle placement as judged by fluoroscopy and contrast injection. Pre-block SBF in the toes on the affected limb was significantly lower than in the contralateral limb ($p < 0.01$).

Mean SBF increased 18-fold in the affected toes ($p < 0.0001$) and 2-fold in the affected thighs ($p < 0.001$) post-block. Mean SBF decreased by 37% in the contralateral toes post-block ($p < 0.01$). For all successful blocks, an increase in toe SBF of more than 10-fold was detected within 4 minutes after local anesthetic injection. ST changes lagged behind SBF changes by 3-7 minutes, and were less dramatic in anesthetized patients. In three instances, local anesthetic injection produced no detectable changes in SBF or ST, and the operator elected to repeat the procedures 20 minutes later with successful results.

Discussion

LDF during the performance of LSB can be a useful monitor in children and adolescents (who often require heavy sedation or general anesthesia) for immediate detection of increased toe SBF as an early index of effective sympathetic blockade.

References

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2. J Auton Nerv Syst 15:309-318, 1986.
3. N Engl J Med 311:1534-1537, 1984

Table 1 MEASUREMENTS OF SKIN BLOOD FLOW AND TEMPERATURE

SBF	Affected Toe		Contralateral Toe		Affected Thigh		Contralateral Thigh	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Temp	25.1 ± 2.4	32.6 ± 3.4*	25.8 ± 3.2	26.2 ± 2.3	26.2 ± 2.1	29.1 ± 1.7*	29.1 ± 1.7	30.8 ± 1.7

Pre = Before Block; Post = one hour after block. SBF = Skin blood flow ml/100 gm/min. Temp = Temperature Centigrade. Comparison pre- and post-block ** = $p < 0.01$; * = $p < 0.001$. † = Comparison between affected and contralateral extremities pre-block

TITLE: SUSTAINED RELEASE OF DIBUCAINE FROM A BIODEGRADABLE POLYMER MATRIX: A POTENTIAL METHOD FOR PROLONGED NEURAL BLOCKADE

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Introduction

Currently, to provide regional blockade for periods longer than 1 day, clinicians must use either local anesthetic infusions via an indwelling catheter, repeated blocks, or neurolytic agents. Application of a timed-release local anesthetic preparation adjacent to nerves could potentially be a useful alternative.

Biodegradable polyanhydride polymers have been shown to be an effective method for sustained release of medications in humans and animals for weeks to months. These matrices are well-tolerated when implanted in the brain¹. For several drugs tested, *in vivo* release parallels *in vitro* release at pH 7.4, 37 °C. The aim of this study was to examine *in vitro* release of the local anesthetic dibucaine (D) from a polymer matrix. D was chosen for its potency, hydrophobicity, and spectroscopic properties.

Methods

(1,3 bis(p-carboxyphenoxy) propane-sebacic acid anhydride copolymers (20:80) were synthesized as described previously², and D (free base) was incorporated by compression molding in 5%, 10% and 20% weight ratios in 200 mg matrices. Release experiments were performed in 2 ml phosphate-buffered saline, pH 7.4, 37 °C. Released D and polymer subunits were measured by absorption spectroscopy.

Results

D was released for over two weeks (Figure 1). At higher drug/polymer ratios, release occurred more rapidly. From days 2 to 8, mean release rates were 12.0, 33.2 and 71.5 µg/ml/hr, respectively for 5%, 10% and 20% preparations.

Discussion

Model calculations (based on minimal blocking concentrations from 10 to 100 µM) suggest that the amounts of drug incorporated and released may be sufficient to provide degrees of neural blockade for at least a two week period. *In vivo* experiments are in progress to test this hypothesis.

Acknowledgements

Dr. Gary Strichartz provided helpful discussions.

References

1. Select. Canc. Therap. 5(2): 55-65, 1989
2. J. Biomed. Mat. Res. 19: 941-955, 1985

Figure 1 Cumulative Percent Release of Dibucaine from Polyanhydride Matrices

