A Double-Blind, Placebo-Controlled Study of Transnasal Sphenopalatine Ganglion Blockade with Tx360® in the Treatment of Chronic Migraine: Evaluation of Patient Functional Outcomes

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Background

The Sphenopalatine Ganglion (SPG) is a small concentrated structure of neuronal tissue that resides within the pterygopalatine fossa (PPF) in close proximity to the sphenopalatine foramen. The SPG is innervated by the maxillary division of the trigeminal nerve and has a sensory, parasympathetic, and sympathetic component. It has been implicated in several orofacial pain conditions including migraine. Access to this structure can be gained via a small area of mucosa just posterior and superior to the tail of the middle turbinate on the lateral nasal wall. Blocking the SPG using local anesthetics may relieve pain associated with chronic migraine.

The purpose of this study is to evaluate the safety and efficacy of 0.5% bupivacaine sphenopalatine ganglion blockades for the treatment of chronic migraine delivered via the Tx360® device. This device contains a small, flexible, soft plastic tube that is advanced below the middle turbinate just past the pterygopalatine fossa. The plastic tube can then be rotated laterally on a preset track and extended into the intranasal space. A total of 0.3 cc of anesthetic (0.5% bupivacaine) is injected through the tube and directed to the mucosa covering the SPG. The procedure is performed similarly in each nostril.

Objectives

This pilot study aimed to evaluate the Tx360® device through the review of patient reported outcomes in a chronic migraine population.

Primary Objective

- To compare the impact of pain questions before treatment and 24 hours post treatment using the Tx360® device with 0.5% bupivacaine vs. saline.

Secondary Objectives

- Compare the change in Headache Impact Test (HIT-6) scores from baseline to end of treatment for bupivacaine vs. saline.
- Patient satisfaction with treatment for bupivacaine vs. saline.

Demographic Characteristics

Fifty-five subjects were screened for this study, meeting the proposed sample size of 42 subjects. The study population consisted of 41 subjects randomized per protocol. Subjects included 10 males and 31 females between the ages of 18-67 and a mean age of 41.30 with a diagnosis of ICHD-II definition of chronic migraine. The average length of chronic migraine diagnosis was 8.58 years. Subjects, on average, experienced 15.24 migraines and 23.63 headaches in a month during baseline. Of the randomized population, 34 were Caucasian, 4 were African American, and 3 Other. Forty subjects completed treatment, although 3 subjects had protocol violations and were therefore removed from the study. A total of 38 subjects were analyzed; 26 subjects treated with bupivacaine and 12 with saline.

Methods

This was a 2 center, randomized, double-blind, placebo controlled study consisting of 55 screened subjects, 18 to 67 years of age, meeting the definition of chronic migraine. Subjects were asked to complete a daily baseline headache diary for 28 days. Following the baseline period, subjects meeting the diagnostic criteria for chronic migraine per diary analysis were randomized 2:1 receiving either 0.3 cc of 0.5% bupivacaine or saline delivered to the mucosal surface of the SPG though each nares with the Tx360® device. The procedure was repeated twice weekly for 6 weeks. Subjects continued to complete a daily headache diary throughout the treatment period and 1 month post treatment. Also during the treatment period, subjects completed a battery of questionnaires 15 and 30 minutes post treatment, as well as 24 hours post treatment.

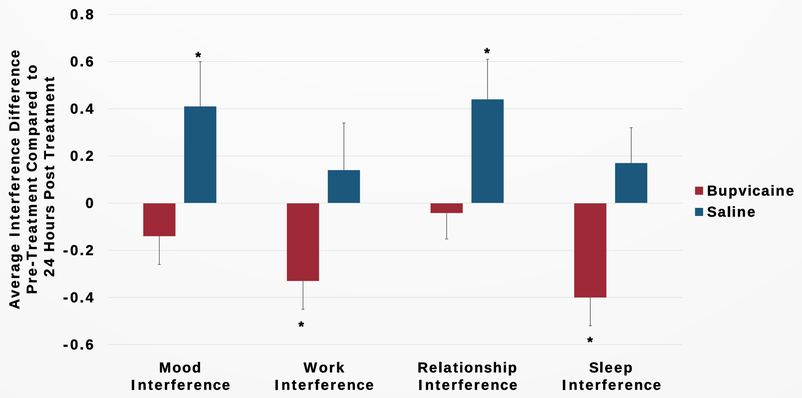
Results

Subjects Treating with Bupivacaine Experienced Significant Reductions in Pain Levels 24 Hours Post Treatment

		Bupivacaine		Saline	
		M_{diff}	p – value	M_{diff}	p – value
Worst Pain	Before Treatment / 24 Hours Post Treatment	- 0.38	.004*	0.01	.97
Least Pain	Before Treatment / 24 Hours Post Treatment	- 0.25	.002*	- 0.07	.56
Average Pain	Before Treatment / 24 Hours Post Treatment	- 0.32	< .001**	- 0.06	.65
Percent Relief	Before Treatment / 24 Hours Post Treatment	6.11	.005*	- 0.17	.95

Subjects in the bupivacaine group reported significantly lower levels of pain 24 hours after treatment (measured by greatest level of pain, least level of pain, average pain and percent relief). There was no significant change reported by subjects receiving saline as a sham treatment.

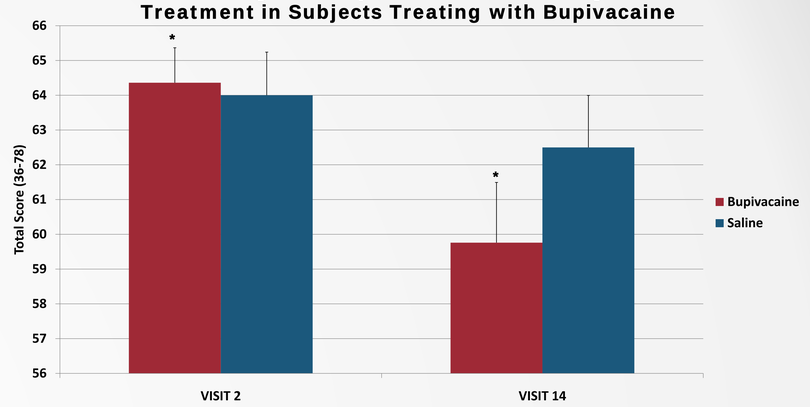
Mood, Work, Relationship, and Sleep Interference Ratings Significantly Decreased for Subjects Treating With Bupivacaine



The bupivacaine group also reported a significantly improved ability to accomplish normal work related tasks (p = .004) and improved sleep (p < .001). The saline group showed increased impairment in their mood (p =.03) and relationships with others (p =.01). When looking at between group differences, all quality of life measurements, including general activity, mood, walking ability, work, relationships, sleep, and enjoyment of life, were significantly different between the bupivacaine and saline groups (p < .001).

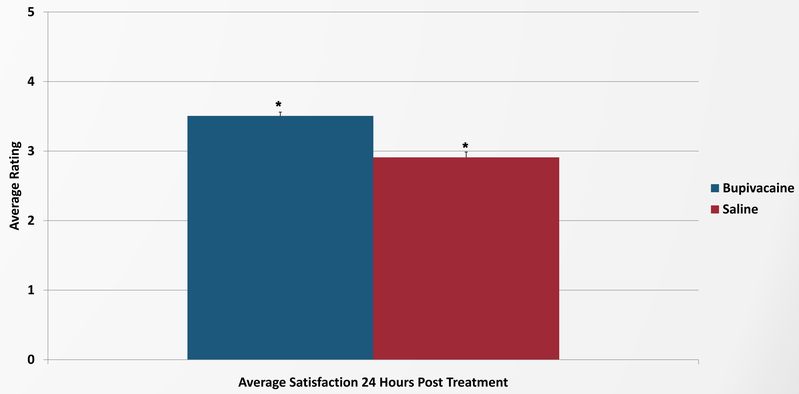
Results

HIT-6 Scores Significantly Decreased Following 6 Weeks of Treatment in Subjects Treating with Bupivacaine



HIT-6 scores significantly decreased in the bupivacaine group (-4.75, p = .005) from baseline to the end of the treatment period (6 weeks) while again there was no significant change for the saline group (-1.55 p = .09). Average treatment satisfaction scores at the end of the treatment period (6 weeks) were significantly higher for Group A compared with Group B. (3.50 vs. 2.91, p < .001).

Satisfaction Scores Were Significantly Higher for the Bupivacaine Group Compared to the Saline Group



Conclusion

Repetitive SPG blocks utilizing 0.5% bupivacaine delivered by through a Tx360® device significantly reduced pain associated with chronic migraine. Furthermore, subjects reported better sleep and increased function at work over the 6 week time of the study. Additionally, subjects receiving the active treatment had significant improvement in HIT-6 scores at the end of the treatment period vs. baseline. These results suggest that repetitive SPG blockade with 0.5% bupivacaine administered with the Tx360® device may be an efficacious treatment and improve clinical outcomes for patients with chronic migraine.

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