

Appendix C: Protocol

Current Practices for Benign Headache Disorders and Perspectives on Peripheral Nerve Blocks Among Emergency Physicians in Canada: Protocol for a National Survey

Authors:

*Dilan Patel^{1,2}, BSc, dilpatel@ohri.ca
Monica Taljaard^{1,2}, PhD, mtaljaard@ohri.ca
Krishan Yadav^{2,3}, MD, MSc, kyadav@toh.ca
Daniel James^{2,3}, MD, dajames@toh.ca
Jeffrey Perry^{1,2,3}, MD, MSc, jperry@ohri.ca

Author Affiliations:

1. School of Epidemiology and Public Health, University of Ottawa, K1G 5Z3 Ottawa, Ontario, Canada.
2. Ottawa Hospital Research Institute, ON K1Y 4E9 Ottawa, Ontario, Canada
3. Department of Emergency Medicine, University of Ottawa, Ontario, Canada

***Corresponding Author**

Dilan Patel
dilpatel@ohri.ca
Clinical Epidemiology Program, Department of Emergency Medicine
Ottawa Hospital Research Institute
The Ottawa Hospital, Civic Campus
1053 Carling Ave., Ottawa, ON, K1Y 4E9

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If amendments are to be made to this protocol, we will provide the date of each respective amendment as well as the rationale in this section.

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ABSTRACT:*Background:*

Treatment options for primary headache disorders, including acute and chronic migraine, tension headache and cluster headache in the emergency department (ED) are broad. The current standard of care, which includes nonsteroidal anti-inflammatory drugs (NSAIDs) and dopamine antagonists, may be considered suboptimal due to slow onset and often requires intravenous administration which may cause harmful side effects to patients. Other viable treatment options such as peripheral nerve blocks (PNBs), including occipital nerve blocks, sphenopalatine ganglion blocks and trigger point injections are less often utilized due to limited certainty on efficacy and safety from existing trials, compared to the current standard of care.

Objectives:

Our objective is to survey Canadian emergency physicians (EPs) to determine their current practice for benign headache disorders in the ED and determine EP perspectives on the use of PNBs for benign headache disorders in the ED.

Methods:

We will conduct a cross-sectional postal survey of a random sample of 500 EPs listed in the Canadian Medical Directory. We will utilize a modified Dillman technique including an initial survey with a small unconditional gift card (\$5 Tim Horton's coffee card) and up to four additional reminder mailed surveys sent every three weeks to non-responders. For the last survey reminder, we will use a special contact with a courier envelope. A survey instrument will be developed in collaboration with emergency physicians and experts in pain management and appropriately translated to French for francophone physicians. We will pilot the survey and carry out cognitive interviews to determine content and face validity and non-verbal cues of our questionnaire and modify the instrument accordingly.

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Discussion:

It is not currently known how primary headaches are treated in the ED given the wide variety of treatment options. This survey will provide insight on current practice patterns and determine if other known alternatives are currently being used. Results from this survey will provide useful information to guide the design of a future randomized controlled trial to test the effectiveness of alternate treatment options such as SPG blocks for the treatment of primary headache disorders in the ED.

BACKGROUND:

Headaches are a common neurological problem and can be disabling and negatively impact quality of life. The most common headache disorders in primary care are primary headaches, including migraine, tension-type headache and trigeminal autonomic cephalalgias (such as cluster headache) with a global prevalence of 10%, 40% and 0.1% respectively.¹ These headaches are benign in nature and differ from secondary headaches. According to the Global Burden of Disease, migraine alone was the sixth highest cause worldwide of years lost to a disability, and headaches collectively ranked third.^{2,3}

According to a US-based study, non-traumatic headaches account for 2.2% of emergency department (ED) visits per year; among this proportion, 98% are benign with the remainder being rare secondary headaches presenting in forms such as subarachnoid hemorrhage (SAH) or other life-threatening forms.⁴ Diagnosing headaches in the ED is challenging and requires thoughtful consideration among emergency physicians (EPs). Primary headaches are difficult to diagnose mainly due to lack of awareness and impracticality of the international headache society (IHS) criteria; according to a ED based study, primary headaches were diagnosed for 16% of headache presentations, whereas 84% of headaches were not diagnosed.⁵ Guidelines and policies have been implemented by the American College of Emergency Physicians to guide the management of acute headaches⁶, as well as rules such as the Ottawa Subarachnoid Rule, to identify life-threatening forms of headache.⁷⁻⁹

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Treatment options for primary headaches in the ED are diverse. First-line treatment options for primary headaches include nonsteroidal anti-inflammatory drugs (NSAIDs) such as intravenous (IV) ketorolac, oral or IV acetaminophen, antidopaminergic agents such as IV metoclopramide, prochlorperazine or haloperidol, oxygen therapy for cluster headaches and corticosteroids such as dexamethasone for reduction of headache recurrence.¹⁰ Other medications which may be used consistently are IV fluids if dehydration is present, antiemetics such as dimenhydrinate which is useful against akathisia associated with prochlorperazine use, ondansetron, abortive therapy such as triptans, other butyrophenones such as droperidol, ergotamine, magnesium, IV sodium valproate and parenteral opioids.^{10,11}

If first-line medications fail to relieve pain, recommended second-line medications include IV ketamine, IV propofol and peripheral nerve blocks (PNBs) such as the occipital nerve block (ONB), sphenopalatine ganglion (SPG) block or intranasal lidocaine, and trigger point injections.¹⁰ These first-line treatment options are recommended, however may act with significant delay, cause rare but potentially serious side effects or fail to control symptoms of headache. For example, haloperidol is known to cause extrapyramidal symptoms such as acute dystonia, akathisia, neuroleptic malignant syndrome, parkinsonism, tardive dyskinesia and anticholinergic effects, among others.^{12,13}

A controversial medication option is the use of parenteral opioids for the treatment of benign primary headaches in the ED. According to a US-based survey, opioids were administered or prescribed in over 50% of migraine visits in the ED.¹⁴ Many societies and committees recommend against using opioids for migraine and other primary headaches.¹⁴⁻¹⁶ Opioids are disadvantageous as a treatment option since their use has been associated with increased frequency of recurrent ED visits, can impair the effectiveness of other migraine treatments, promotes chronic migraine and medication overuse headache and is associated with more psychiatric disorders when dependence is built on

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opioid use.¹⁷ The prevalence of administration or prescription of opioids as a first line treatment for benign headache disorders in the ED among EPs in Canada is currently unknown.

PNBs which target peripheral nerves in the head and neck have gained recent interest for the optimal management of primary headaches in the ED. PNBs are understudied and potentially less often utilized as a treatment option in the ED. These minor bedside procedures involve a subcutaneous local injection of a small volume of a local anesthetic agent to target areas such as the greater or lesser occipital nerve, or sphenopalatine ganglion to promote neural blockade and break the pain cycle. Randomized controlled trials (RCTs) have been conducted to study the efficacy and safety of occipital nerve blocks on various forms of headache.^{18–22} Several RCTs currently exist which study SPG blocks or intranasal administration of anesthetics^{23–29}; the results are mixed, some trials found SPG blocks to provide statistically significant pain relief^{23,25,27,28} and some found no difference compared to placebo.^{26,29} To our knowledge, no trial currently exists which studies the SPG block or intranasal lidocaine in Canada among the adult population for benign headaches in the ED. The SPG block is the least invasive of the PNBs especially with its intranasal route of administration, compared to the subcutaneous injection across the scalp of occipital nerve blocks or trigger point injections. For this reason, we also seek to investigate EP perspectives and attitudes towards using PNBs for benign headaches in the ED. Results from this survey will lay the foundation to study SPG blocks in the form of an RCT in Canada to potentially achieve a more successful and faster management of benign primary headaches in the ED compared to current standard of care.

OBJECTIVES:

The primary objective of this survey is to understand current practice patterns for benign primary headaches among EPs. This objective will provide insight into unanswered and important questions such as if EPs cotreat primary headaches with ketolorac and dopamine antagonists, if dexamethasone is used to prevent headache recurrence and the frequency of opioid use across Canada.

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Secondary objectives are to determine EP perspectives on PNBs in terms of frequency of use, effectiveness, preference, and comfort level. Additionally, we will further investigate the SPG block in terms of preferred route of administration and inquire about the optimal time point to reassess pain after giving a PNB. Lastly, we will inquire about the minimal clinically important reduction in pain on a standard pain scale to safely discharge a patient presenting with a benign headache, home. This will inform the choice of an effect size to use in the sample size calculation for the future trial.

METHODS:

Study design and Setting:

We plan to conduct a national postal survey of a random sample of 500 Canadian EP's listed in the Canadian Medical Directory³⁰ according to a modified Dillman's tailored design method for survey design and administration.³¹ We will use simple random sampling to select our sample.

Survey instrument construction:

The survey instrument will be developed in collaboration with physicians consisting of clinical experts in emergency medicine and pain medicine. The survey will be piloted with a random sample of 20 EP's and revised based on feedback. The survey should take 10-15 minutes to complete and will consist of binary questions (yes/no answers) and likelihood questions (i.e., always, most of the time, some of the time, almost never, never) on Likert scales. Survey questions will capture demographic data such as EP level of experience and address the following: 1) Current practices for benign headache assessment and treatment in the ED; 2) Challenges and limitations of current practice if any; 3) Perspectives on PNBs, specifically the SPG block; 4) The optimal time to reassess pain after administering a PNB; 5) The minimal clinically important relief of pain for safe discharge home.

We will pilot the first draft of the survey instrument and perform cognitive interviews as a psychologically derived method to understand how individuals respond to our questionnaire prior to

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administering the survey. Based on this interview, we will modify questions accordingly based on feedback and reactions to questions.

The survey instrument will be translated to French by a research coordinator fluent in the language, for francophone physicians, and approved by language services

Data Collection Strategy:

The survey will be administered according to the following procedure: (i) initial survey with an incentive (\$5 Tim Horton's gift card) with the first survey and (ii) a reminder of survey completion through a new survey instrument, every three weeks for a total of four times, with the final notification using a special contact (e.g., Xpress post). Previous surveys have demonstrated >50% response rates using these methods.³²⁻³⁴ For letters that are returned to sender due to unknown or outdated address, we will search the College of Physicians and Surgeons or equivalent in their respective jurisdiction to determine if there has been a change in primary practice location and attempt to re-send to their current practice location.

Survey responses and data will be input into Microsoft Excel v. 16 and statistical analyses will be conducted using SAS v. 9.4 (SAS Institute Inc. Cary, NC, USA). Incentives will be provided for survey respondents up front and attached with the mail in survey. All data management and study coordination will be at the Ottawa Hospital Research Institute.

Sub-studies

We will conduct a sub-study with half of the survey respondents (n = 250) receiving hand-signed recruitment and reminder letters and the other half of the survey respondents receiving electronically signed recruitment and reminder letters. The rationale for this is to determine if there is a difference in response rates between hand signatures compared to electronic signatures. This would provide useful recommendations for future postal surveys.

Analysis and Sample Size Calculation:

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We will use descriptive statistics to describe the results from the survey including and frequencies and percentages for categorical variables. Comparisons will be conducted using chi-squared tests for categorical variables (i.e. differences based on EP level of experience).

A random sample of 500 emergency physicians listed in the Canadian Medical Directory will be surveyed. The large sample size will reduce sampling error and improve generalizability. The random sample will be selected using a computer-generated randomization sequence. A random sample of 500 EP's with a response rate of 50% is adequate to estimate the primary outcome (i.e., the proportion of survey respondents who use each class of drugs "always" or "most of the time") using a two-sided 95% confidence interval with a margin of error no greater than 6.2% assuming the most conservative prevalence estimate of 0.5.

ETHICAL CONSIDERATIONS:

Prior to collecting any data, this protocol will be reviewed by the Ottawa Health Science Network Research Ethics Board. In the cover letter of our designed survey, we will state that participation is voluntary and survey responses will be kept confidential. Responding to a survey will be considered implied consent. We will keep sensitive information such as personal identifiers confidential and will be store separately from the data collected in the survey instrument.

CLINICAL IMPLICATIONS

Since headache presentations are prevalent and complex with multiple treatment options, it is important to understand frequently used medications in an EP's treatment plan across Canada. Based on this survey, we would have a better sense of a Canada-wide EP perspective on commonly used treatment methods for benign headache disorders, and insights on alternative treatments such as PNBs. We hope to fill the gap in headache treatment by providing evidence on current treatments and insight towards the SPG block which may be faster and more effective at relieving pain and reduce the use of opioid and other medications with known side effects.

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