Cerebrospinal fluid volume–depletion headaches in patients with traumatic brachial plexus injury

Clinical article

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Object. Patients with brachial plexus injury (BPI) present with a combination of motor weakness/paralysis, sensory deficits, and pain. Brachial plexus injury is generally not believed to be associated with headaches. However, CSF leaks may be associated with CSF volume–depletion (low-pressure) headaches and can occur in BPI secondary to nerve root avulsion. Only a few cases of headaches associated with BPI have been reported. It is unknown if headaches in patients with BPI occur so rarely, or if they are just unrecognized by physicians and/or patients in which the focus of attention is the affected limb. The aim of this study was to determine the prevalence of CSF volume–depletion headaches in patients with BPI.

Methods. All adult patients presenting at the Mayo brachial plexus clinic with traumatic BPI were asked to complete a questionnaire addressing the presence and quality of headaches following their injury. The patients’ clinical, injury, and imaging characteristics were subsequently reviewed.

Results. Between December 2008 and July 2010, 145 patients completed the questionnaire. Twenty-two patients reported new onset headaches occurring after their BPI. Eight of these patients experienced positional headaches, suggestive of CSF volume depletion. One of the patients with orthostatic headaches was excluded because the headaches immediately followed a lumbar puncture for a myelogram. Six of the other 7 patients with positional headaches had a clear preganglionic BPI. The available imaging studies in these 6 patients revealed evidence of CSF leaks: pseudomeningoceles (n = 5), CSF tracking into soft tissues (n = 3), CSF tracking into the intraspinal compartment (n = 3), CSF tracking into the pleural space (n = 2), and low-positioned cerebellar tonsils (n = 2).

Conclusions. In this retrospective study, 15.2% of patients (22 of 145 patients) with traumatic BPI suffered from a new-onset headache. Seven of these patients (4.8%) experienced postural headaches clearly suggestive of CSF volume depletion likely secondary to a CSF leak associated with the BPI, whereas the other 15 patients (10.3%) suffered headaches that may have represented a variant of CSF depletion headaches without a postural characteristic or a headache from another cause. These data suggest that CSF volume–depletion headaches occur in a significant proportion of patients with BPI and have been underrecognized and underreported.

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Key Words • intracranial hypotension • cerebrospinal fluid leak • low cerebrospinal fluid pressure headache • posttraumatic headache • orthostatic headache • peripheral nerve

In recent years, the syndrome of intracranial hypotension has become well defined and accepted. Patients with intracranial hypotension typically present with postural headaches due to reduced CSF volume. A wide variety of spontaneous, traumatic, and iatrogenic causes affecting the brain and spinal cord leading to CSF hypovolemia have been identified. Surprisingly, only 2 patients with BPI resulting in CSF hypovolemia and intracranial hypotension have been reported,12,14 despite the relatively common pattern of injury and its potential overt source of CSF leakage. Because the clinical picture of BPI is dominated by motor deficits, sensory deficits, and pain, headaches may not be reported. It is unknown if the prevalence of headache in patients with BPI is low, or if the headaches are unrecognized by physicians and/or patients because the focus of care is the affected limb. The aim of this study was to determine the prevalence of low-pressure headaches in adult patients with BPI.
Methods

Patients and Outcome Measures

Between December 2008 and July 2010, all adult patients with traumatic BPI presenting at our multidisciplinary brachial plexus clinic were asked to complete a questionnaire on the presence and quality of headaches following their injury (Appendix). This short questionnaire was designed by a neurologist (B.M.) specializing in headaches who has extensive experience with low-pressure headaches. The patients answered the questionnaire in the clinic, either at their initial evaluation or at a follow-up visit if they had not previously filled out the questionnaire. Patient and injury characteristics, as well as the available imaging, were subsequently reviewed.

For analysis, the patients were divided into 3 groups: Group 1, those patients who did not develop headaches; Group 2, those patients who developed nonpositional headaches; and Group 3, those patients who developed positional (orthostatic) headaches after their BPI. One patient included in Group 3 because of the development of positional headaches after BPI was excluded from the analysis because the headaches were clearly related to a lumbar puncture performed at the time of a myelogram, rather than the BPI itself.

To evaluate whether an important recall bias was present, especially for patients answering the questionnaire at a follow-up visit that may have been distant from the time of injury, a subanalysis was performed for patients answering the questionnaire within 6 months or less of their injury included (Appendix). This short questionnaire was designed by a neurologist (B.M.) specializing in headaches who has extensive experience with low-pressure headaches. The patients answered the questionnaire in the clinic, either at their initial evaluation or at a follow-up visit if they had not previously filled out the questionnaire. Patient and injury characteristics, as well as the available imaging, were subsequently reviewed.

Statistical Analysis

The data were summarized descriptively using standard methods: categorical variables were summarized as number out of the total and percentage, while continuous variables were summarized as means. To assess if certain factors were associated with the development of positional headaches, continuous variables were evaluated using nonparametric Kruskal-Wallis rank-sum tests. Chi-square tests were used to compare categorical variables; when expected cell counts were less than 5, Fisher exact tests were performed. All statistical tests were 2-sided, and the threshold of statistical significance was set at $\alpha = 0.05$.

Results

During the study period, 145 adult patients who had sustained a traumatic BPI completed the questionnaire. The mean duration between completing the questionnaire and the BPI was 17.8 ± 19.0 months (range 1 month to 10 years). Of these 145 patients, 123 patients did not develop headaches (Group 1), 14 reported new onset nonpositional headaches (Group 2), and 8 patients developed positional or orthostatic headaches (Group 3), which were consistent with CSF volume depletion (low-pressure headaches). One of the patients with positional headache developed headaches after a lumbar puncture for a myelography examination; because the mechanism for the development of these headaches is different, this patient was excluded from analysis of this group of patients. Beside being positional, the other characteristics of the headaches in Group 3 were variable (Table 1). Headaches resolved spontaneously between 2 weeks and 2 months after injury.

In Group 3, 6 of 7 patients had evidence of a preganglionic BPI (Table 2); 5 patients had panplexal injuries with evidence of preganglionic injury at all levels (3 patients) or at the upper (1 patient) or lower (2 patients) nerve roots, and 1 patient had a preganglionic injury of the C-5 and C-6 nerve roots. The other patient, without a CT myelogram investigation, suffered from positional headaches after her BPI. Her injury, secondary to a fall associated with a shoulder dislocation and proximal humerus fracture, had a postganglionic localization based on clinical assessment (mechanism, improvement of motor function, and Tinel signs in the infraclavicular region) and electrodiagnostic testing. Imaging studies available in 6 of these 7 patients (CT myelogram in 5 patients and cervical MRI in 1) revealed evidence of CSF leak and/or low intracranial pressure in all 6 (Figs. 1 and 2): between 1 and 5 pseudomeningeal vessels (n = 5), CSF tracking in the soft tissues (n = 3), CSF tracking into the intraspinal compartment (n = 3), CSF tracking into the pleural space (n = 2), and low-positioned cerebellar tonsils (n = 2).

The mean age, mechanism of trauma, and presence of other injuries were not significantly different between the 3 different groups of patients (Table 2). There were more females in the group of patients that developed positional headaches (3 of 7 [42.9%]) than in the nonpositional headache group (4 of 14 [28.6%]) or the no headache group (21 of 123 [17.1%]) and less concomitant head injury in the positional headache group (2 of 7 [28.6%]) than in the other 2 groups (6 of 14 [42.9%] and 49 of 123 [39.8%], respectively). The patients who developed positional headaches were more likely to have evidence of preganglionic injury (6 of 7 [85.7%]) in comparison with patients with nonpositional headaches (11 of 14 [78.6%]) and with patients without new-onset headaches (85 of 123 [69.1%]); however, these differences were not statistically significant.

The subanalysis of patients who answered the questionnaire within 6 months or less of their injury included 57 patients. The mean duration between the injury and answering the questionnaire was 3.8 ± 1.7 months. Of these 57 patients, 7 (12.3%) developed new-onset headaches, of which 4 (7.0%) were nonpositional and 3 (5.3%) were positional.

Discussion

This study demonstrates that BPI is associated with the development of new-onset headaches in a significant proportion of patients (15.2% [22 of 145]). These post-BPI headaches may be either positional (5.5% [8 of 145]) or nonpositional (9.7% [14 of 145]).

The positional headaches that developed after a BPI likely represent low-pressure headaches, better described as CSF volume–depletion headaches. Postural headaches are the typical manifestation of intracranial hypotension. The variability in their location, characteristics, and associated symptoms (nausea, emesis, visual changes, and others) is not unusual and has been well described. The pathophysiology of preganglionic BPI can provide a direct expla-
nation for the association between CSF volume–depletion headaches and traumatic BPIs. In BPI, forceful distraction of the arm away from the body can stretch nerves, leading to nerve root avulsions. In some cases, rents in the dura and/or arachnoid occur at one or more levels, with subsequent formation of nerve root pseudomeningoceles. Given the exponential relationship between CSF volume and CSF pressure, the loss of small amounts of CSF that usually occurs in pseudomeningoceles associated with BPIs may be sufficient to cause major changes in intracranial pressure. Symptoms of CSF volume depletion, such as positional headaches, may therefore occur. Imaging evidence of CSF leaks was noted in all patients who underwent imaging and had new-onset positional headaches. The imaging findings included pseudomeningoceles, but also CSF tracking into the soft tissues, intraspinal and/or pleural spaces, as well as low-positioned cerebellar tonsils (Figs. 1 and 2). Two cases reported in the literature\textsuperscript{10,12} were also shown to have a CSF-pleural fistula from BPI, one of which\textsuperscript{12} was associated with intracranial hypotension. In a series of 60 cervical myelographies performed for BPI, 6 studies that were performed within 10 days of the injury showed CSF leakage rather than discrete pseudomeningoceles.\textsuperscript{15} It is possible that in the patients who developed positional headaches, the increased volume of CSF lost within the soft tissues and intraspinal and pleural spaces may have caused larger changes in CSF pressures.

In the scientific literature, the classic origins of CSF volume depletion include CSF leaks, true hypovolemic state (reduced total body water), and CSF shunt overdrainage.\textsuperscript{8} Cerebrospinal fluid leaks are described as either spontaneous or not; secondary causes include traum-

TABLE 1: Characteristics of headaches in patients with positional headaches

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Case No.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>history of headaches</td>
<td>no</td>
</tr>
<tr>
<td>associated symptoms</td>
<td></td>
</tr>
<tr>
<td>loss of consciousness</td>
<td>yes</td>
</tr>
<tr>
<td>nausea</td>
<td>no</td>
</tr>
<tr>
<td>emesis</td>
<td>no</td>
</tr>
<tr>
<td>hearing changes</td>
<td>no</td>
</tr>
<tr>
<td>dizziness</td>
<td>yes</td>
</tr>
<tr>
<td>diplopia</td>
<td>no</td>
</tr>
<tr>
<td>characteristics of headaches</td>
<td></td>
</tr>
<tr>
<td>all over</td>
<td>yes</td>
</tr>
<tr>
<td>1 side</td>
<td>no</td>
</tr>
<tr>
<td>area</td>
<td>no</td>
</tr>
<tr>
<td>pressure</td>
<td>no</td>
</tr>
<tr>
<td>throbbing</td>
<td>yes</td>
</tr>
<tr>
<td>always</td>
<td>no</td>
</tr>
<tr>
<td>intermittent</td>
<td>no</td>
</tr>
<tr>
<td>positional</td>
<td>yes</td>
</tr>
<tr>
<td>duration</td>
<td>1 mo</td>
</tr>
</tbody>
</table>

* F = frontal; FO = frontooccipital; P = parietal.

TABLE 2: Clinical characteristics of patients with traumatic BPI in each group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>type of headache</td>
<td>none</td>
<td>nonpositional</td>
<td>positional</td>
<td></td>
</tr>
<tr>
<td>no. of patients</td>
<td>123</td>
<td>14</td>
<td>8†</td>
<td></td>
</tr>
<tr>
<td>mean age in yrs (range)</td>
<td>33.5 (16–72)</td>
<td>31.1 (17–57)</td>
<td>31.7 (20–48)</td>
<td>0.95</td>
</tr>
<tr>
<td>M/F ratio</td>
<td>102:21</td>
<td>10:4</td>
<td>4:3</td>
<td>0.11</td>
</tr>
<tr>
<td>mechanism of trauma: MVA or MCA (%)</td>
<td>70 (56.9)</td>
<td>9 (64.3)</td>
<td>3 (42.9)</td>
<td>0.60</td>
</tr>
<tr>
<td>other injuries (%)</td>
<td>110 (89.4)</td>
<td>13 (92.9)</td>
<td>7 (100)</td>
<td>0.91</td>
</tr>
<tr>
<td>head injury (%)</td>
<td>49 (39.8)</td>
<td>6 (42.9)</td>
<td>2 (28.6)</td>
<td>0.84</td>
</tr>
<tr>
<td>preganglionic injury (%)</td>
<td>85 (69.1)</td>
<td>11 (78.6)</td>
<td>6 (85.7)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

* MCA = motorcycle accident; MVA = motor vehicle accident.
† One patient was excluded from the analysis because the positional headaches were clearly secondary to a lumbar puncture.
In our patients with positional headaches, the headaches did not appear to be related to the spinal tap associated with CT myelography, except for 1 patient (who was removed from the analysis). It is possible that patients with pseudomeningoceles present with symptoms similar to those observed in patients with spontaneous intracranial hypotension, including posture-related headaches. However, traumatic BPI is typically not included in the causes leading to pseudomeningoceles associated with intracranial hypotension. This is not surprising considering that, to date, only 2 patients with BPI resulting in CSF hypovolemia and intracranial hypotension were reported in the literature. The present study suggests that CSF volume-depletion headaches are not uncommon in this population and that this traumatic origin should be added to the causes of secondary CSF leaks causing CSF hypovolemia.

One of the patients with positional headaches had a presumed postganglionic injury; the pathophysiology of CSF volume depletion as described above does not appear to explain her positional headaches. Although un-
likely, it is possible that this patient had an unidentified preganglionic injury component with an associated CSF leak. Another possibility is that the patient suffered a traumatic CSF leak without a preganglionic injury, either at the level of the dura of the spinal nerves or at another level from a subclinical associated spinal trauma. In so-called spontaneous CSF leaks, in which a trivial trauma can be an inciting event,2 the exact cause often remains unknown, which could be the case in this patient. This patient may also have been prone to develop a CSF leak by harboring an underlying weakness of her meningeal sac in certain regions, a contributing factor frequently suspected in patients with spontaneous CSF leaks.7 Finally, mechanisms other than CSF volume depletion could have been involved, given that orthostatic headaches may occur in the absence of CSF leaks.8

Approximately 10% of patients (14 of 145) developed nonpositional headaches after their BPI. These headaches may represent a variant of CSF volume–depletion headaches. The typical manifestation of intracranial hypotension is orthostatic (postural) headaches, but a broader clinical spectrum is recognized.9 Constant lingering or chronic daily headaches that may or may not be worse in the upright position, exertional headaches, “second half of the day” headaches, paradoxical orthostatic headaches, intermittent headaches, and cervical or interscapular pain have all been described.7,8 Some of these new-onset nonpositional headaches may also be related to causes other than CSF volume depletion. These headaches may represent posttraumatic headaches secondary to head injury (mild, moderate, or severe),11 or be secondary to whiplash injury.2,11 Some authors also propose that posttraumatic headaches may be an exacerbation of an underlying primary headache disorder related to stress and anxiety resulting from the injury.13 It is also possible that these patients developed cervicogenic headaches different from whiplash-associated headaches. The upper cervical zygapophysial joints (C1–2, C2–3, and C3–4) as well as pathologies at lower cervical levels can produce headaches;1 pathologies at both locations are possible in these patients with traumatic BPI. Finally, it has been proposed that anterior scalene spasms, which could have occurred in our patients with traumatic BPI, may cause headaches.6 It has been hypothesized that anterior scalene contractions can compress the cervical plexus as it exits deep to this muscle or can lead to tension on the origin of the muscle (at the transverse cervical processes) leading to compression of the occipital nerves.16

The absence of new-onset headaches in the majority of patients, even given the large proportion with evidence of at least a small amount of CSF leak (pseudomeningoceles in 56 of 123 [45.5%]), can be explained. Similar to patients undergoing lumbar puncture, in which only 1%–36% develop headaches,3 only a proportion of patients with pseudomeningoceles and potential CSF leak from BPI developed headaches (21 of 66 [31.8%]). As for headaches after lumbar puncture, in which the volume of CSF removed may or may not be a risk factor,3,5 continuous CSF leakage may be required for headaches to develop in the patients with traumatic BPI. The factors contributing to a persistent communication between the subarachnoid space and the extradural spaces are not well defined, but may include the arachnoid integrity, the volume of the leak, and the capacity of the surrounding tissues to absorb CSF.4 In our patients developing positional headaches, the location of the preganglionic injury was variable; due to a small number of patients (n = 7), we cannot determine if a particular location or type of preganglionic injury is associated with a higher likelihood of developing positional headaches. Finally, some patients could have experienced CSF leakage and CSF volume depletion without developing headaches, as is described for patients with spontaneous CSF leaks.2,7–9 However, our patients were not specifically investigated to identify CSF volume depletion (for example, with CSF pressure measurements and MRI of the brain with Gd injection).

Fortunately, most patients with CSF volume depletion improve spontaneously regardless of treatment.7,8 This was the case for all our patients, who improved spontaneously without any treatment. For patients with continuous symptoms, confirming the diagnosis of CSF volume depletion would be important. This can be accomplished with a determination of CSF opening pressure and examination, radioisotope cisternography, head and spine MRI, and myelography/CT myelography.8 Conservative treatment could include traditional bed rest, hydration/overhydration, caffeine, and/or theophylline, although their effectiveness has not been well demonstrated.8 In patients who failed an initial trial of conservative management, an epidural blood patch could be considered. Although it would not seal the CSF leak in these patients, the epidural blood patch could provide relief through volume replacement resulting from dural tamponade.9 Finally, surgery to address the CSF leak should be performed, as was required in the 2 cases of intracranial hypotension after a BPI that were reported in the literature.7,14

The major limitation of this study is the retrospective nature of the questionnaire. Patients answered the questionnaires within 10 days and 10 years (mean 17.8 months) after their injury, which could be associated with a significant recall bias. However, the subanalysis of patients who answered the questionnaire within 6 months or less of their injury appeared to indicate a similar occurrence of post-BPI headaches when compared with the entire cohort: 12.3% developed a headache and 5.3% developed positional headaches compared with 15.2% and 5.5% for the entire cohort. A recall bias may still be present, but a questionnaire given within 6 months or less of the injury is reflective of a prospective study that would be conducted in most brachial plexus practices. It would be very difficult, if not impossible, to question all patients with BPI about headache in the acute setting because they are not typically referred immediately. Our study can therefore be considered a prospective study, even if the questionnaire has a retrospective nature.

In view of this recall bias, the occurrence of post-BPI headaches in this population, especially minor or very transient ones, was likely underestimated. We became aware of 2 examples of recall biases. One patient (4 years after the event) answered that he did not suffer from headaches after his injury, but the neurology notes several years earlier clearly mention severe headaches postinjury that lasted a week and completely resolved; this patient
was included in Group 1 (did not develop headaches according to the questionnaire). Another patient initially answered (3 months after the event) he did not suffer from new-onset headaches, but on a subsequent clinic visit (5 months after the event), mentioned having suffered from headaches. The questionnaire was revised with him, and this patient was included in Group 3 (developed positional headaches). It is unclear why he initially answered he did not have headaches. Another limitation of the study is the retrospective nature and limited availability of the imaging review: none of the patients with positional headaches had Gd-enhanced brain MRI at the time of their headaches, the available cervical spine MR images or CT myelograms may not have been performed at the time of their headaches or may have been conducted in a delayed fashion, and no serial imaging studies were available to correlate the imaging findings with the presence and/or resolution of the headaches.

Conclusions

In this retrospective study, 15% of patients (22 of 145) with traumatic BPI suffered from a new-onset headache after their injury, and a third of these patients (8 of 22) had clear characteristics of CSF volume–depletion (intracranial hypotension) headaches. We believe that postural headaches have been underrecognized and underreported, probably due to the presence of other more threatening concomitant injuries. This study demonstrates that headaches after BPI, likely secondary to CSF leaks associated with the injury, occur in a significant proportion of patients.

Appendix

Questionnaire

1. Have you ever seen a physician for headaches before your accident? Yes/No
   If yes, what was your doctor’s diagnosis (please circle): Migraine, tension headache, other headache, I don’t remember.
2. With the accident, did you lose consciousness? Yes/No
   If yes, for how long were you actually unconscious?
   For what period of time, if any, are you amnestic (the approximate duration of time that you do not remember)?
3. After the accident, did you develop:
   a. Headache
   b. Nausea
   c. Vomiting
   d. Change in hearing
   e. Dizziness
   f. Double vision
   If you developed headache, what type of headache was it (circle all that apply)
   a. All over the head
   b. On one side
   c. In one area of head (name the area_________)
   d. Pressure-like
   e. Throbbing
   f. Present all the time
   g. Intermittent (came and went)
   h. The headache was present when sitting or standing and would go away by lying down
   i. Associated with nausea or vomiting
   j. Associated with visual changes
4. Have the headaches resolved now? Yes/No
   For how long did you have these headaches before they resolved?

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Spinner, Hébert-Blouin, Mokri. Acquisition of data: Hébert-Blouin. Analysis and interpretation of data: Hébert-Blouin. Drafting the article: Hébert-Blouin. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Spinner. Statistical analysis: Hébert-Blouin. Study supervision: Spinner.

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