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Medications prescribed to brain injury patients: A retrospective analysis

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Medication side effects

Abstract

BACKGROUND: The purposes of this study were to retrospectively evaluate the frequency of medications used by individuals with either traumatic brain injury (TBI) or cerebrovascular accident (CVA) and to consider the possible relationship between vision symptoms and diagnoses in this sample and the established visual and ocular side effects of the prescribed medications.

METHODS: Charts of patients examined in the Raymond J. Greenwald Rehabilitation Center at the SUNY State College of Optometry from the years 2000 to 2003 were reviewed. Only TBI (n=160) or CVA (n=60) patients were included. Prescribed medications from 12 possible categories were identified. Patients experiencing blurred vision, diplopia, asthenopia, poor depth perception, and/or light sensitivity were identified. Patients with accommodative dysfunction, vergence dysfunction, versional dysfunction, dry eyes, and/or ptosis were also identified.

RESULTS: The 4 most common medication categories taken by TBI patients were anti-anxiety/antidepressants (42.5%), anticonvulsants (26.9%), opiate/combination analgesics (23.8%), and cardiac/antihypertensives (23.1%). For the CVA patients, the medications were cardiac/antihypertensives (66.7%), anti-anxiety/antidepressants (31.7%), vitamins/mineral supplements (26.7%), and anticonvulsants (23.3%). Frequency of vision symptoms and diagnoses in the TBI and CVA patients appeared not to be related to medication use in most cases.

CONCLUSIONS: Anti-anxiety drugs, antidepressants, and anticonvulsants were the overlapping medication categories between the TBI and CVA groups. Medication intake did not affect the frequency of the reported vision symptoms and diagnoses in most cases, suggesting the symptoms and diagnoses were primarily related to either the TBI or CVA itself.

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Little is known about the type and frequency of medications prescribed to the acquired brain injury (ABI) population. Only 1 study has been conducted, which had a relatively small sample size (n=50) and combined all ABI subgroups.[1] The 5 most commonly prescribed medication categories described as a percentage of the total number of prescribed medications (n=300) taken by the 50 patients in that study were antidepressants (10%), cardiac/antihypertensives (9.3%), anticonvulsants (9.3%), vitamin/mineral supplements (8.3%), and general analgesic agents not including narcotic combination analgesics (6%).

Clinically, it can be hypothesized that the established vision and ocular side effects of specific medications would be manifest to a greater degree in the brain-injured popula-

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tion compared with a visually matched, ABI cohort not taking any medications. This was thought to be true, because brain-injured patients often report vague but severe vision symptoms that are similar to some of the known side effects of their prescribed medications.[2-12] For instance, they report intermittent blurred vision, eyestrain with sustained distance or near vision activities, poor depth perception, and light sensitivity. Thus, it is often difficult for the clinician to determine if the reported vision symptom is a side effect of the prescribed medication or a direct sequela of the brain injury itself.

The *primary* purpose of the current investigation was to retrospectively evaluate the frequency of medications prescribed in a large population of patients having either traumatic brain injury (TBI) or cerebrovascular accident (CVA) treated in an ambulatory outpatient, university-based, vision rehabilitation setting. The *secondary* purpose was to determine the possible relation between the vision symptoms/diagnosed vision conditions and the known visual/ocular side effects of the prescribed medications in this sample.

Methods

Charts of active patients in the Raymond J. Greenwald Rehabilitation Center (RJGRC) at the State University of New York (SUNY) State College of Optometry outpatient facility from the years 2000 through 2003 were obtained using a computer-based query. The RJGRC serves mainly patients who are referred from the following institutions: Rusk Institute of Rehabilitative Medicine at New York University (NYU) Medical Center, Bellevue Hospital at NYU Medical Center, Mount Sinai Medical Center's Department of Rehabilitative Medicine, Lenox Hill Hospital, New York Hospital, and the International Center for the Disabled. Some referrals to the unit were also received from other services within the college's University Optometric Center including Primary Care, Low Vision, Contact Lens, Ocular Disease, and Special Testing services as well as outside medical and optometric practitioners. Referred patients were not limited to those with either TBI or CVA; those with other neurologic conditions that affect the visual system, such as vestibular dysfunctions, cranial postsurgical complications, or brain tumors, comprised a sizable patient base.

The query searched for patients examined from October 1, 2000, to October 7, 2003, using either the 99203 (Evaluation and Management, New Patient Expanded Problem-Focused Vision Examination) or 99213 (Evaluation and Management, Established Patient Expanded Problem-Focused Vision Examination) procedure codes and was performed by specific staff members having unique provider numbers. This would include all patients referred to the clinic for a vision rehabilitation examination. The query determined that 486 charts matched the criteria listed above. The initial vision rehabilitation evaluation was chosen, even if it was performed before the query dates.

Table 1 Descriptive characteristics of patient population

	TBI (n=160)	CVA (n=60)
Gender	Men=73 Women=87	Men=33 Women=27
Age range, y	8-91	24-90
Mean	44.9	61.2
Standard deviation	15.8	14.7
Range of years post-injury	0.1-42.0	4.5
Mean	0.1-18.0	2.7

Only the initial vision evaluation encounters were chosen to be reviewed. This evaluative encounter normally includes a visual acuity assessment (distance and near), refractive assessment (distance and near), binocular sensorimotor assessment (distance and near), clinical oculomotor assessment, color vision assessment when indicated, ocular health assessment (including biomicroscopy, applanation tonometry, and dilated fundus examination if the procedure was not performed within the last year), and visual field assessment. In some instances, not all of these areas could be evaluated because of limitations in the patient's cognitive status, language ability, or physical state.

The 486 evaluation encounters were listed according to their medical record numbers. The list was then divided among 3 reviewers (3 of the coauthors). Each began reviewing from the lowest medical record number on their list, until 100 charts were reviewed. Of the 300 charts reviewed, only 220 included either TBI or CVA patients. Of the 220 charts, 160 patients were in the TBI group and 60 in the CVA group. Descriptive information regarding the patient population is summarized in Table 1.

Patients taking medications in the following 12 categories were identified as described in the earlier study by Han[1]: cardiac/antihypertensives, antidiabetics, anti-anxiety/antidepressants, central nervous system (CNS) stimulants, opiate/combination analgesics, anti-asthmatics, anticonvulsants, antipsychotics, antihistamines, hormone supplements, vitamin/mineral supplements, and herbal remedies. The total number of medications (including prescribed as well as vitamins and minerals) taken by each patient was determined. When ascertaining the most commonly prescribed medications, percentages were based on the total number of patients who reported taking at least 1 medication in 1 or more of the 12 categories divided by the total number of either TBI or CVA patients.

The frequency of patients experiencing the established vision symptoms and diagnoses typically associated with the 4 most prescribed medication categories was determined for both the TBI and the CVA subgroups based on the literature as well as the combined clinical experience of the authors.[2-12] To ascertain the impact of the medications on reported vision symptoms and diagnoses, the same frequencies were compared with those found for TBI or CVA patients not taking any medications. Further comparisons

Table 2 Ranking of the 12 medication categories in TBI and CVA patients

TBI group		CVA group	
Medication categories	Percentages	Medication categories	Percentages
Anti-anxiety/antidepressant agents	42.5	Antihypertensive/cardiac agents	66.7
Anticonvulsant agents	26.9	Anti-anxiety/antidepressant agents	31.7
Opiate/combination analgesics	23.8	Vitamins and mineral supplements	26.7
Antihypertensive/cardiac agents	23.1	Anticonvulsant agents	23.3
Vitamins and mineral supplements	9.4	Antidiabetic agents	15.0
Anti-asthmatic agents	8.8	Opiate/combination analgesics	11.7
Hormone supplements	6.3	Hormone supplements	8.3
Antipsychotic agents	5.6	Antipsychotic agents	6.7
CNS stimulants	5.6	Anti-asthmatic agents	3.3
Antihistamine agents	4.4	Antihistamine agents	1.7
Herbal remedies	3.1	CNS stimulants	0.0
Antidiabetic agents	2.5	Herbal remedies	0.0

were also made with similar frequencies calculated for all TBI and all CVA patients.

Results

The total number of medications taken by the TBI and CVA patients was 499 and 246, respectively. In the TBI group, 12.5% (n=20) did not take any medications, whereas 6.7% (n=4) of the CVA patients did not take any medications.

TBI group

Table 2 lists the frequency ranking (in percentage) of the 12 medication categories from highest to lowest in the TBI group. The 4 most commonly prescribed medication categories were anti-anxiety/antidepressants (42.5%), anticonvulsants (26.9%), opiate/combination analgesics (23.8%), and cardiac/antihypertensives (23.1%). For the other 8 medication categories, the percentages ranged from 2.5% to 9.4%.

Tables 3 and 4 compare the patients' vision symptoms and diagnoses with the established side effects for the top 4 medication categories used by patients in the TBI group. In addition, the percentages of TBI patients taking any medications, as well as the percentage of those not taking any medications but also experiencing vision symptoms or diagnoses were listed. For each of the 5 vision symptoms categories, the mean percentages ranged from approximately 40% to 50%, except for the category of "poor depth judgment," which had a mean of approximately 6%. With respect to the 5 categories of vision diagnoses, both versional and vergence oculomotor dysfunctions were the most frequent, with a mean frequency of approximately 50%. In the remaining 3 vision diagnostic categories, mean frequencies ranged from approximately 1% to 15%.

CVA group

Table 2 also lists the frequency ranking (in percentage) of the 12 medication categories from highest to lowest for the

Table 3 Medication categories: vision symptoms—TBI

Medication category	Blurred vision*	Diplopia†	Asthenopia‡	Poor depth judgment§	Light sensitivity‖
Anti-anxiety/antidepressant (n=68)	29.9%	27.1%	29.9%	11.8%	54.4%
Anticonvulsants (n=43)	48.8%	27.9%	41.9%	11.6%	51.2%
Opiate/combination analgesics¶(n=38)	63.2%	36.8%	n/a	n/a	60.5%
Cardiac/antihypertensives (n=37)	43.2%	43.2%	n/a	n/a	54.1%
All TBI (n=160)	51.3%	40.6%	47.5%	6.3%	49.4%
TBI taking any medication (n=140)	52.1%	38.6%	48.6%	6.4%	52.1%
TBI taking no medications (n=20)	50.0%	55.0%	40.0%	5.0%	30.0%

n/a = not applicable with regard to this medication.

* Patients who reported either distance or near blur.[2,4,5,8,10,11]

† Patients who reported either distance or near diplopia.[4,8,10,11]

‡ Patients who reported symptoms of headaches, eyestrain, loss of place when reading, reading slowly, falling asleep when reading, avoiding near vision tasks, and short attention span with near vision tasks. Patients with a history of cognitive therapy were excluded.[4,8,10,11]

§ Patients who reported poor depth judgment during activities of daily living.[4,8,10,11]

‖ Patients who reported sensitivity to light. The patients who reported photophobia secondary to an ocular inflammation were not included.[2,4,8,10,11]

¶ Mainly based on aspirin, nonsteroidal anti-inflammatory medication, ibuprofen.[2,3,4,8]

Table 4 Medication categories: vision diagnoses—TBI

Medication category	Accommodative dysfunction*	Vergence dysfunction†	Version dysfunction‡	Dry eyes§	Ptosis‖
Anti-anxiety/antidepressant (n=68)	3.7%	36.4%	48.5%	10.3%	n/a
Anticonvulsants (n=43)	4.7%	53.5%	46.5%	n/a	0.0%
Opiate/combination analgesics¶(n=38)	n/a	n/a	n/a	28.9%	n/a
Cardiac/antihypertensives (n=37)	2.7%	n/a	54.1%	13.5%	n/a
All TBI (n=160)	13.1%	55.0%	49.4%	15.0%	0.6%
TBI taking any medication (n=140)	10.7%	55.0%	50.7%	14.3%	0.7%
TBI taking no medications (n=20)	30.0%	55.0%	40.0%	20.0%	0.0%

n/a = not applicable with regard to this medication.
* Patients who were diagnosed with an accommodative dysfunction.[4,10,11]
† Patients who were diagnosed with a vergence dysfunction.[4,10,11]
‡ Patients who were diagnosed with poor pursuit, saccades, nystagmus, or impaired fixation.[4,10,11]
§ Patients who were diagnosed with dry eyes.[4,10,11]
‖ Patients who were observed to have a unilateral ptosis.[4,10]
¶ Mainly based on aspirin, nonsteroidal anti-inflammatory medication, ibuprofen.[2,3,4,8]

CVA group. The 4 most commonly prescribed medication categories were cardiac/antihypertensives (66.7%), anti-anxiety/antidepressants (31.7%), vitamins/mineral supplements (26.7%), and anticonvulsants (23.3%). For the other 8 medication categories, the frequency rankings ranged from 0% to 15%.

Tables 5 and 6 compare the patients' vision symptoms and diagnoses to the known side effects for the top 4 medication categories used by patients in the CVA group. The percentage of CVA patients taking any medication as well as those not taking any medication but also experiencing specific vision symptoms or diagnoses were listed. For the 5 vision symptom categories, the mean percentages ranged from approximately 25% to 45%, except for the category of "poor depth judgment," which was approximately 7%. With respect to the 5 categories of vision diagnoses, both versional and vergence dysfunctions were found to be the most frequent, with mean frequencies of approximately 60% and 35%, respectively. In the remaining 3 vision diagnoses categories, mean frequencies ranged from approximately 2% to 12%.

Discussion

Comparison with earlier studies

The primary purpose of this retrospective study was to determine the frequency of medications taken in a large population of patients with either TBI or CVA treated in an ambulatory, university-based vision rehabilitation setting. Twelve medication categories were chosen based on an earlier study conducted by Han.[1] The current analysis shows that 3 of the 4 main categories of drugs taken by both the TBI and CVA groups were the same: anti-anxiety/antidepressants, anticonvulsants, and cardiac/antihypertensives. More than 20% of the patients were found to take any

Table 5 Medication categories: vision symptoms—CVA

Medication category	Blurred vision*	Diplopia†	Asthenopia‡	Poor depth judgement§	Light sensitivity‖
Cardiac/antihypertensives (n=40)	45.0%	25.0%	n/a	n/a	22.5%
Anti-anxiety/antidepressants (n=19)	31.6%	26.3%	52.6%	10.5%	31.6%
Vitamin mineral supplements (n=16)	n/a	6.3%	n/a	n/a	18.8%
Anticonvulsants (n=14)	28.6%	28.6%	71.4%	7.1%	21.4%
All CVA (n=60)	43.3%	31.7%	51.7%	6.7%	26.7%
CVA taking any medication (n=56)	42.9%	30.4%	51.8%	7.1%	26.8%
CVA taking no medications (n=4)	50.0%	50.0%	50.0%	0.0%	25.0%

n/a = not applicable with regard to this medication.
* Patients who reported either distance or near blur.[2,4,5,8,10,11]
† Patients who reported either distance or near diplopia.[4,8,10,11]
‡ Patients who reported symptoms of headaches, eyestrain, loss of place when reading, reading slowly, falling asleep when reading, avoiding near vision tasks, and short attention span with near vision tasks. Patients with a history of cognitive therapy were excluded.[4,8,10,11]
§ Patients who reported poor depth judgment during activities of daily living.[4,10,11]
‖ Patients who reported sensitivity to light. The patients who reported photophobia secondary to an ocular inflammation were not included.[2,4,10,11]

Table 6 Medication categories: vision diagnoses—CVA

Medication category	Accommodative dysfunction*	Vergence dysfunction†	Version dysfunction‡	Dry eyes§	Ptosis‖
Cardiac/antihypertensives (n=40)	0.0%	n/a	55.0%	12.5%	n/a
Anti-anxiety/antidepressants (n=19)	0.0%	52.6%	63.2%	21.1%	0.0%
Vitamin mineral supplements (n=16)	n/a	n/a	43.8%	12.5%	n/a
Anticonvulsants (n=14)	7.1%	35.7%	64.3%	n/a	n/a
All CVA (n=60)	1.7%	36.7%	56.7%	11.7%	6.7%
CVA taking any medication (n=56)	1.8%	37.5%	57.1%	12.5%	7.1%
CVA taking no medications (n=4)	0.0%	25.0%	50.0%	0.0%	n/a

n/a = not applicable with regard to this medication.
* Patients who were diagnosed with an accommodative dysfunction.[4,10,11]
† Patients who were diagnosed with a vergence dysfunction.[4,10,11]
‡ Patients who were diagnosed with poor pursuit, saccades, nystagmus, or impaired fixation.[4,10,11]
§ Patients who were diagnosed with dry eyes.[4,10,11]
‖ Patients who were observed to have a unilateral ptosis.[4,10]

combinations of medications in the top 4 categories for both the TBI and CVA groups. Thus, the ranking of medications from the current study using a larger sample size was consistent with Han's earlier findings.[1]

Possible relationship between medications and vision symptoms or diagnoses in the TBI group

The secondary purpose was to determine the possible relation between vision symptoms/diagnoses and the known visual/ocular side effects of the prescribed medications in this sample. The most common vision symptoms or vision diagnoses elicited by more than 50% of the TBI patients taking 1 or more of the 12 medication categories were (*see* Tables 3 and 4) blurred vision, light sensitivity, vergence dysfunction, and versional dysfunction.

Light sensitivity was reported by 52.1% of TBI patients taking any medication compared with 30% of those not taking any medication. This nearly 2-fold percentage difference suggested that medication intake contributed to the presence of this symptom. With light sensitivity being a known side effect of the top 4 medications studied and being an established visual sequelae of TBI, the number of TBI patients reporting light sensitivity was expected to be high.[2,4,8-10]

Interestingly, the frequency of patients reporting blurred vision (29.9%), diplopia (27.1%), and asthenopia (29.9%) was *less* in those taking anti-anxiety/antidepressant medications compared with all of the TBI patients (blurred vision, 51.3%; diplopia, 40.6%; asthenopia, 47.5%), with TBI patients taking any medications (blurred vision, 52.1%; diplopia, 38.6%; asthenopia, 48.6%), and with TBI patients not taking any medications (blurred vision, 50%; diplopia, 55%; asthenopia, 40%). Additionally, patients taking anti-anxiety/antidepressants showed *less* vergence (36.4%) and accommodative (3.7%) dysfunction compared with all of the TBI patients (vergence dysfunction, 55%; accommodative dysfunction, 13.1%), with TBI patients taking any medications (vergence dysfunction, 55%; accommodative dysfunction, 10.7%), and with TBI patients not taking any medications (vergence dysfunction, 55%; accommodative dysfunction, 30%). The fact that the symptoms were nearly 2 times less in those taking the medications may suggest these drugs do not increase the likelihood of experiencing these symptoms.

A higher frequency of patients taking either anti-anxiety/antidepressants or anticonvulsants reported poor depth perception, 11.8% and 11.6%, respectively, compared with all of the TBI patients (6.3%), with TBI patients taking any medications (6.4%), and with TBI patients not taking any medications (5%). These findings suggest that the symptom of "poor depth perception" was likely to be a side effect of the medication. We speculate that these medications may alter the ability to interpret correctly multiple visual-spatial cues typically needed when making accurate depth judgments.

Similar to patients taking anti-anxiety/antidepressants, patients taking anticonvulsants also manifested less accommodative dysfunction (4.7%) compared with all of the TBI patients (13.1%), with TBI patients taking any medications (10.7%), and with TBI patients not taking any medications (30%). Therefore, accommodative dysfunctions diagnosed in TBI patients taking anticonvulsants were less likely to be a result of a medication side effect.

There was a higher frequency of TBI patients with dry eye (28.9% vs. 20%) and experiencing light sensitivity (60.5% vs. 30%) than those TBI patients not taking any medications. Thus, TBI patients taking prescription analgesics should be monitored carefully for the above vision symptoms and conditions particularly, as they appear to be reported or seen with high frequency in the TBI population.

Possible relationship between medications and vision symptoms or diagnoses in the CVA group

Among the CVA patients, on average, 46% of them taking any of the medications listed in Tables 5 and 6 experienced

blurred vision, asthenopia with near vision activities, vergence dysfunction, or a versional dysfunction. Interestingly, light sensitivity was not experienced as much in the CVA group as in the TBI group. Clinically, evaluation of CVA patients should involve a comprehensive case history, which queries blurred vision and asthenopia, and furthermore should include a careful assessment of vergence and version function.

Off-label uses

Medications in the antihypertensive, antidepressant, and anticonvulsant categories may be prescribed to patients with TBI or CVA for the off-label treatment of the following conditions: attention, arousal, aggression, agitation, restlessness, cognition, and vestibular disorders.[1,13-18] In the current study, the percentage of patients who were not hypertensive or who did not report a cardiac problem, but reported taking an antihypertensive or cardiac medication, was 21.6% (n=8) in the TBI group and 15% (n=6) in the CVA group. The percentage of patients taking anti-anxiety or antidepressant medications, but who did not report a history of depression, was 23.4% (n=25) in the TBI group and 42.0% (n=8) in the CVA group. One might speculate that those patients who were not hypertensive yet who were taking a beta-blocker such as propranolol were being treated for agitation and aggression (a common behavioral sequelae after an ABI).[14,18] Fleminger et al.[18] determined beta-blockers to be the most effective, particularly propranolol, in treating patients at either the initial hospitalization stage or toward later stages in their recovery. Those patients above, who did not report depression, may be receiving an off-label treatment for their behavioral deficits in attention and cognitive arousal, and therefore required the CNS activation effects of the antidepressants.[14]

The results above should help the clinician gain a more comprehensive picture of the nonvisual sequelae of brain injury that can affect the patient's ability to function effectively. Patients not treated for attention, arousal, aggression, agitation, restlessness, cognition, or vestibular disorders may experience a slower rate of progress in their vision rehabilitation program, or they may show poor compliance with treatment and management options recommended at the time of the evaluation.

Clinical applications

The results of this study provide a clearer idea of what vision symptoms and diagnoses to expect and what needs to be investigated further when performing a comprehensive vision examination in these patients. For example, the eye care provider must keep in mind the value of tinted lenses (indoor and outdoor use), polarized sunglasses, or antireflective coatings to address the very common complaint of light sensitivity. The results of this study indicated that TBI patients may be expected to experience more light sensitivity than CVA patients because both the TBI and their medications appear to be contributing factors.

For the optometric member of an interdisciplinary rehabilitation team, TBI patients who exhibit symptoms of anxiety and depression in conjunction with blurred vision, diplopia, asthenopia, vergence, or accommodative dysfunction at the conclusion of the examination may need a referral to a professional who can effectively diagnose and manage these conditions. TBI patients already receiving such treatment and taking anti-anxiety/antidepressants may report symptoms of poor depth perception, as indicated in the current study.

When examining TBI patients taking opiate/combination analgesics, a careful dry eye assessment is necessary. Also, ophthalmic management of the symptoms of blurred vision and light sensitivity would be helpful in improving visual comfort because this is easily treated and might result in a reduction in the severity of their chronic pain.

Study limitations

The relatively small number of patients not taking any medications made it somewhat difficult to provide compelling comparisons between patients taking medications, particularly in the CVA group, with respect to reported vision symptoms or diagnoses. Another question that arose during the analysis was how medication dosage may affect the ABI patient compared with the non-ABI patient.

It must also be noted that the frequency of vision symptoms reported by patients in this study would be expected to be high because the patients were referred directly to the unit because of their vision-related symptoms. Thus, these frequencies may not reflect the extent of vision symptoms experienced by patients in a general outpatient rehabilitation setting.

Future directions

A prospective analysis using a larger sample size should be conducted to control the different study parameters better. Further investigation to determine the frequency of vision symptoms/diagnoses in brain-injured patients not taking any medications would help support or modify the findings and related clinical implications based on this retrospective study.

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