Migraine History and Outcomes in Military Pilots and Flight Surgeons

Roger R. Hesselbrock; Jared T. Haynes

BACKGROUND: Migraine is a common disorder with significant aeromedical implications. The variability and unpredictable nature of occurrences hampers accurate assessment of future risk. This uncertainty results in a necessarily conservative approach to aeromedical recommendations, which unfortunately may lead to over-restrictive dispositions. Limited long-term follow up information is available on migraine outcomes in pilots, particularly assessing for impact of potential modifiable aggravating factors.

METHODS: This retrospective study reviewed 159 U.S. Air Force pilots with migraine who had been granted aeromedical waivers. As a comparison group, 44 U.S. Air Force flight surgeons with migraine who had been granted aeromedical waivers were reviewed.

RESULTS: Migraine with aura and isolated migraine aura without headache accounted for the majority of migraine subtypes in both male and female subjects. Self-identified triggering factors were identified by 62% of subjects. The most commonly reported triggers were dietary factors, sleep disturbances, stress, caffeine intake, and hormonal factors. Sleep disturbances, stress, hormonal factors, and ethanol triggers were more frequently noted in female subjects. Self-reported positive response to trigger factor modification was noted in 54% of subjects. Subjects reported an average of only 3 migraine attacks in the previous year. Long-term follow up indicated continued aeromedical waiver in 91% of subjects.

DISCUSSION: The majority of subjects had migraine with aura or isolated migraine aura. Significant salutary response to modification of commonly-reported triggering factors was noted. These findings can be incorporated into individualized aeromedically-compatible management strategies to clarify symptom impact on aviation safety, improve symptom control, and increase the possibility of safe return to fly recommendations.

KEYWORDS: migraine, aura, pilots, flight surgeons.

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Migraine is a common neurologic condition that impacts a significant portion of the general population and has important aeromedical implications. It is one of the top three most burdensome neurological disorders in the United States.[12] Migraine occurs in about 12% of the Unites States population, affecting about 18% of women and 6% of men, and worldwide is the second most disabling condition after low back pain.[4] Aeromedically, migraine was the second most frequent neurologic condition assessed by the U.S. Air Force School of Aerospace Medicine (USAFSAM) over a 12-yr period.[17] Migraine has different subtypes, each having discrete, specific diagnostic criteria, with clinical manifestations ranging from painless minor visual disturbances to incapacitating pain and major neurologic deficits.[15] This heterogeneity, coupled with individual variabilities in treatment response, makes aeromedical risk assessment determinations challenging at best. In addition to adverse aeromedical effects from the migraine attack itself, clinically and operationally-significant premonitory and post migraine symptoms may occur, further increasing aeromedical risk.[3,18] Adding further to

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the aeromedical disposition challenge, migraine management options are necessarily more limited in aviators due to concerns of operationally-significant adverse effects that might be irrelevant at ground level, but could be augmented and manifested under stressors of flight. There is a paucity of information specifically addressing migraine in aviators.

This retrospective study looked at trained U.S. Air Force pilots and flight surgeons who had received aeromedical waivers for migraine, and was follow-on from a previous study that reviewed U.S. Air Force pilot applicants with migraine who had received aeromedical waivers.[16] Objectives of our current study were to identify any predictive factors for migraine recurrence, assess any differences by migraine subtypes, identify any gender differences in longitudinal outcomes, and to potentially propose an aeromedically-reasonable period of observation before return-to-fly recommendation for trained aviators.

METHODS

The study protocol was reviewed and approved under Exempt status by the 711th Human Performance Wing Institutional Review Board (protocol FWR20210016E). This study was a retrospective review using information initially obtained from the U.S. Air Force Aeromedical Information Waiver Tracking System (AIMWTS). AIMWTS was queried for information from its inception in approximately 2002, through late 2020. Search criteria included text and International Classification of Diseases codes for migraine and common subtypes such as migraine with aura, and ocular or complicated migraine. Demographic information included age, gender, race, duty status, aeronautical rating, waiver disposition dates, and waiver status. From this list, pilots and flight surgeons with a history of migraine and who had been granted aeromedical waivers were identified. Flight surgeons were chosen for the comparison group due to their similar level of aviation experience and analogous aeromedical standards. The Armed Forces Health Longitudinal Technology Application (AHLTA) and Health Artifact and Image Management System (HAIMS) applications were then queried to obtain additional information on longitudinal clinical course. Information from these sources was entered into a Microsoft Access® database for analysis. Data management used the Microsoft Excel® and Access® applications. Statistical analysis was performed using IBM SPSS® software. Bivariate contingency tables were used, with Chi-squared and Fisher's Exact tests performed to assess differences between groups. Odds ratios and relative risk ratios were then calculated from the bivariate contingency table analysis.

RESULTS

Initial query of the AIMWTS application yielded a total of 1559 U.S. Air Force aviators of all flying classes and aircrew positions who were listed as having been assessed for or had received waivers for the diagnosis of migraine. This list was further refined and yielded the primary study group of 159 pilots, and a second comparison group of 44 flight surgeons. Study group demographics are listed in **Table I**. In the overall group, 74% were listed as Active Duty military status. Regarding racial composition, 141 (88.7%) were listed as White in the pilot group and 39 (88.6%) were listed as White in the flight surgeon group. Aeromedical disposition involvement from USAFSAM, which is recommended by the U.S. Air Force Waiver Guide in most migraine cases, was noted in 145 (71%) of the overall group, 125 (79%) of pilots and 20 (45%) of flight surgeons. Additional specific clinical information was then obtained from the AHLTA and HAIMS applications. **Table II** lists the percentage of subjects that received waivers, broken out by migraine subtype; subjects with multiple or unknown migraine types were not included in this table. Reporting of migraine frequency timing of last reported headache occurrence were highly variable on medical record documentation review, with only 153 subjects (116 pilots, 37 flight surgeons) documenting migraine frequency. For those with reported frequency information, the average number of migraine occurrences in the previous year was 3.2 overall, 2.2 for pilots and 6.5 for flight surgeons. **Fig. 1** lists the frequency and type of medications reported for migraine management. Multiple medication types could be used in a single subject. Aeromedically-incompatible medications would have been discontinued before a waiver would be recommended or granted.

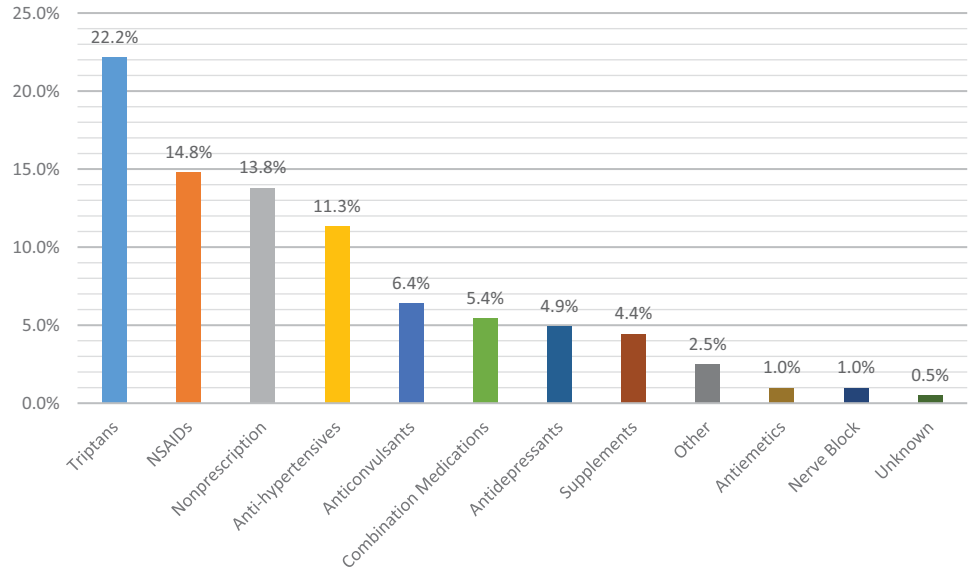
Table I. Study Group Demographics and Observation Time.

	N	M	F	AGE AT DISPOSITION (YR)	OBSERVATION TIME (YR)
Total	203	166	37	38.4 (20-62)	10.0 (1-37)
Pilot	159	140	19	37.0 (20-59)	9.7 (1-34)
Flight Surgeon	44	26	18	43.3 (28-62)	11.1 (1-37)
Male	166	–	–	38.3 (20-62)	10.3 (1-37)
Female	37	–	–	38.6 (24-59)	9.0 (2-28)

Subjects were more likely than not to report that headaches were associated with specific triggers. Self-reported triggering factors for migraine were reported in 125/203 (62%) of the overall group, by 100/159 (63%) of pilots, and 25/44 (57%) of flight surgeons. By gender, 98/166 (59%) of males and 27/37 (73%) of females reported triggering factors. As with medications, more than one migraine trigger factor could be reported in a given subject. **Fig. 2** lists the frequency and type of reported triggering factors. Hormonal triggers were reported by 12/37 (32%) of women (6 pilots, 6 flight surgeons). The presence of hormonal triggers in females was associated with an increase in

Table II. Study Group Migraine Types and Number/Percentage of Waivers Granted.

	WITHOUT AURA/WAIVER GRANTED		WITH AURA OR AURA ALONE/WAIVER GRANTED	
Total	45	38 (84%)	145	135 (93%)
Pilot	32	28 (87%)	121	115 (95%)
Flight Surgeon	13	10 (77%)	24	20 (83%)
Male	35	29 (83%)	122	115 (94%)
Female	10	9 (90%)	23	20 (87%)



Note: anticonvulsants, antidepressants, combination medications and antiemetics are not waiverable for most U.S. Air Force aviators.

Fig. 1. Medications and other treatments used for migraine management.

migraine occurrence with relative risk of 7.64 (95% CI [5.30, 11.01]). Sleep dysfunction was also associated with an increased likelihood of migraine occurrence, with an odds ratio of 3.01 (95% CI [1.21, 7.49], P = 0.01). For those who reported migraines induced or aggravated by sleep dysfunction, compared to male subjects, females had a significant increase with a relative risk of 2.29 (95% CI [1.23, 4.27]).

Self-reported positive response to trigger modification was noted in 109/203 (54%) of the overall group, 89/159 pilots (56%) and 20/44 (45%) of flight surgeons. By gender, 88/166 (53%) of males and 21/37 (57%) of females reported a positive response to trigger modification. Such modifications were specific to the associated identified triggering factor, and could include avoiding foods associated with migraine attacks, reduction in caffeine or ethanol intake, improving sleep hygiene, treating musculoskeletal neck pain, stress management, hormonal modulation and other interventions. Medical record documentation did not include quantified headache calendar information on the degree of trigger modification response. The likelihood of those who reported a response to trigger modification in migraine groups with and without aura was significantly increased, with an odds ratio of 3.77 (95% CI [1.14, 12.44], P = 0.02). There was not a significantly increased response to trigger modification in either the overall migraine with aura (odds ratio 3.43, 95% CI [0.69, 17.06], P = 0.12) or without aura (odds ratio 4.00, 95% CI [0.64, 25.02], P = 0.12) subject groups. When compared by aircrew position, subjects who had either migraine with aura and

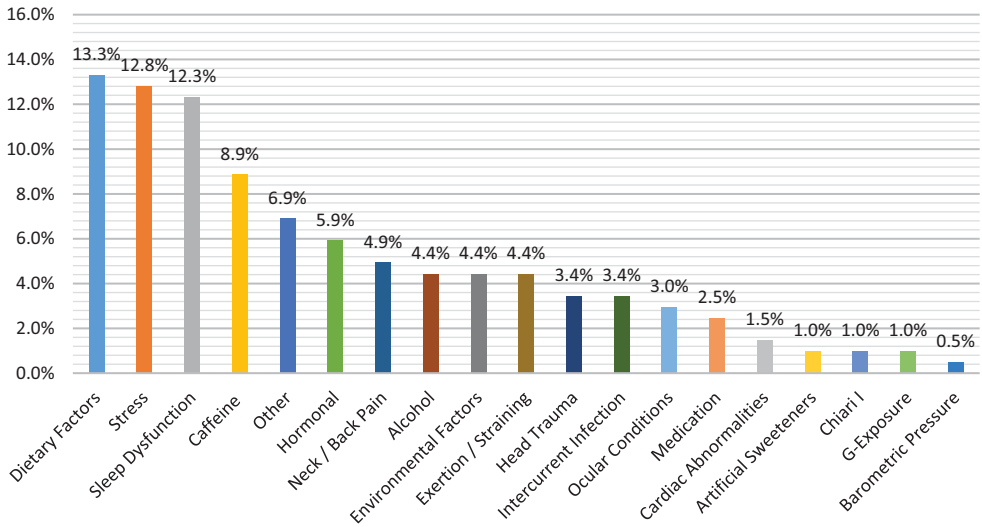


Fig. 2. Self-reported migraine triggering factors.

without aura did not see a significant change in the likelihood of a response to trigger modification with odds ratio of 1.96 (95% CI [0.55, 6.99], $P = 0.18$). However, when comparing by gender, females had a significantly increased likelihood of response to trigger modification, with a relative risk of 2.49 (95% CI [1.23, 5.06]).

Waivers were granted in the majority of subjects. Overall, there was an increased likelihood of receiving an aeromedical waiver in the subject group of migraine with aura (odds ratio 3.83 (95% CI [0.99, 14.81], $P = 0.04$)), compared to the group of migraine without aura (odds ratio 2.10 (95% CI [0.40, 11.07], $P = 0.38$)). Compared by gender, subjects who had migraines either with aura or without aura did not have a significant change in the likelihood of receiving an aeromedical waiver, with an odds ratio of 1.53 (95% CI [0.47, 5.02], $P = 0.21$). However, when compared by aircrew position, flight surgeons had a significantly increased likelihood of receiving an aeromedical waiver (relative risk 2.37 (95% CI [1.23, 4.57])) compared to pilots (relative risk 0.71 (95% CI [0.48. 1.07])).

DISCUSSION

In this study, the majority of subjects reported isolated migraine aura and migraine with aura, rather than migraine without aura. This finding and the finding that most of such cases were recommended for and granted aeromedical waiver were unexpected and somewhat surprising, as transient migraine aura symptoms could be even more hazardous to flight safety than the actual migraine headache. One possible explanation for our findings is that aviators with even minor, isolated transient visual aura symptoms might be more likely to report these symptoms due to both medical and flight safety concerns. Another potential explanation is that nonaura visual symptoms such as blurred vision or difficulty focusing due to pain might have incorrectly been listed as migraine aura. A third possibility is that migraine without aura may be under-reported, especially if infrequent or with less severe manifestations. However, variability in clinical assessments and documentation limited any definitive conclusions on this observation.

Self-reported migraine triggers and a positive response to trigger modification were noted in the majority of our study subjects. Migraine triggers have historically been commonly reported by patients.[13,19] However, subjectivity and heterogeneity of migraine triggers weakens objective conclusions. For example, one study of self-reported headache diary information indicated an average of four triggers per patient.[24] Headache diaries have long been an important tool to better characterize headache type and identify potentially modifiable headache triggers.[9] Newer digital tracking applications can facilitate headache data capture.[7] Multimodal approaches with attention to methodological consistency have been proposed to improve understanding of migraine triggers.[22,23] Lifestyle management techniques incorporating headache diary information have been recommended to address common modifiable headache triggers such as sleep dysfunction, exercise, nutrition, and stress.[27] Patient-provider communication is crucial in disease management, especially with migraine. Involvement of nonphysician healthcare professionals can provide additional avenues for patient interaction and migraine management.[21]

Complementary and integrative/alternative medicine management strategies are used by patients for many conditions, including migraine.[20,30] Nonpharmacological self-management has shown a small beneficial effect in reducing pain intensity and headache-related disability for migraine and tension-type headaches.[25,26] Vitamin, supplement and herbal agents are often aeromedically-compatible and have shown benefit in migraine management, but can have occasional adverse effects such as butterbur-related hepatotoxicity.[6,29] Increased understanding of migraine pathophysiology has facilitated development of novel treatments and individually-tailored management plans.[5] Various medications were reported for migraine management. No information was available in our data set on the use of newer treatments such as calcitonin gene-related polypeptide (CGRP) agents, which have recently shown promising results in selected civil aviation pilots.[10]

There is no accepted consensus on aeromedically-acceptable migraine frequency. Historically, a conservative approach to permanently exclude aviator applicants or trained aviators with any history of migraine was often taken. This gradually evolved to less-restrictive practice. Previous USAF policy for aeromedical waiver in migraine required at least a 1-yr migraine-free and medication-free observation period before waiver consideration.[28] The current U.S. Air Force Waiver Guide does not specify a maximum acceptable migraine frequency, but current policy is generally to only consider waiver recommendation for up to several occurrences annually.[14] The current Federal Aviation Administration (FAA) Aviation Medical Examiner (AME) Guide permits the AME to issue medical certification for up to monthly migraine occurrences. Cases with more frequent occurrences are deferred for Special Issuance medical certification consideration.[8] The USAF and FAA documents provide eligibility criteria guidelines for waiver or certification consideration.

Absolute migraine occurrence frequency is only one variable in aeromedical disposition consideration. The presence or absence of associated neurologic or visual symptoms is another independent factor in aeromedical risk assessment and disposition in migraine. Specific operational environment factors (high performance aircraft, unmanned aircraft, etc.) and aircrew position (pilot, flight surgeon, etc.) are also considered in aeromedical disposition determinations. Our study indicated that subjects with available headache frequency data reported few migraine occurrences in the previous year, which aligns with current U.S. Air Force Waiver Guide information. However, variable migraine frequency and tracking documentation did not permit any conclusive determination of observation time or occurrence frequency for waiver suitability.

A significant strength of our study was access and availability of longitudinal medical record information, which provided objective long-term follow up data. Our study had several important limitations. The retrospective nature of the

study incompletely captured historical information due to variability of clinical assessments and documentation. Only U.S. Air Force members were included for review, which could affect applicability to the overall aviator population. Only cases listed for waiver consideration in the U.S. Air Force aeromedical waiver tracking system were identified for inclusion and review. This almost certainly underestimates the true incidence of pilots with migraine who are actively flying; as was earlier noted, migraine is sometimes not reported to the flight surgeon or aviation medical examiner. For example, cases with less frequent or severe headaches might not be recognized as requiring an aeromedical waiver and thus escape capture in the waiver tracking application. A surprisingly high percentage of study subjects were granted aeromedical waivers. This could reflect consideration of fully trained aircrew status, but more likely reflects a selection bias of waiver authorities not submitting poorly controlled migraine cases or those with frequent or severe auras for aeromedical waiver consideration. Few migraine occurrences were reported by subjects in the most recent previous year. As this is self-reported information, under-reporting of true migraine frequency is possible. There is no accepted standardization regarding the use of headache tracking tools, which further limits data collection at this point. Limited data on female subjects were available in our review, reflective of U.S. Air Force aviator demographics. This makes general applicability challenging and limits any inference on possible differences in migraine among female aviators compared to the nonaviator female population. Gender-related differences in migraine and response to medications have been reported in the general population.[1,11] A systems thinking approach to assess self-management of migraine in women has been suggested to improve management in this cohort.[2] The long sampling period in the study encompassed advances in migraine management and resultant evolution of aeromedical standards. Some subjects encountered earlier in the sampling period would have been eligible for aeromedical waiver based on current aeromedical standards but were disqualified from flying duties based on then-current, more restrictive standards.

CONCLUSIONS

Migraine with aura and isolated migraine aura were reported in the majority of subjects. Self-reported trigger factors and a positive response to trigger modification were noted in the majority of subjects, with hormonal triggers reported in one-third of women. These findings can be incorporated into evaluation guidance to better determine the impact of aura and trigger factors on aviation safety, and thus better guide aeromedical dispositions. Practical recommendations include the following: accurate classification of migraine type based on accepted diagnostic criteria; noting aura symptom type and distribution, particularly for visual aura, to better assess aeromedical risk; screening for potential triggering factors; implementation of trigger factor modification strategies where feasible; and utilization of headache tracking tools for objective information on headache occurrences, potential triggers, and response to interventions. Using these recommendations, an individualized migraine management plan could then be developed.

While the study findings were not novel for the general population with migraine, because aeromedically compatible migraine management options are limited, our results can serve as useful adjuncts to achieve better migraine control and improve the possibility of safe return to fly recommendations. Future studies are recommended to address the impact of newer medications on aeromedical management of migraine and to further explore gender-specific epidemiology and management differences in aviators with migraine.

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