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Migraine and suicide

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In the year 2000, the WHO reported that approximately one million people died of suicide - this represents one death due to suicide every 40 s worldwide [101]. At least 100,000 of these deaths occured among individuals 15-24 years of age. Suicide rates in the USA doubled between 1960 and 2001 and now the US Centers for Disease Control and Prevention have shown that suicide mortality is the third leading cause of death for Americans aged 10-24 years [1]. Among adolescents and young adults committing suicide, approximately 90% have some sort of mental illness, with depression and substance abuse constituting the majority of diagnoses [102]. In studied cohorts of depressed adolescents, 35-50% attempted suicide; furthermore, 5-10% of these adolescents diagnosed

with a major depressive disorder died of suicide within 15 years [2].

Researchers have also shown that patients with migraine frequently exhibit comorbidity with

depressive and anxiety disorders [3,4]. However, whether there is a link between migraine and suicide is not fully understood or investigated. If there is a link, is it directly related to migraine itself or its comorbid psychiatric disorders or both? Furthermore, is the link related to certain migraine subtypes? Recently, our team of researchers surveyed 7900 students aged 12–14 years at five middle schools in Taiwan looking for data to help define the linkages [5,6]. Of this cohort, 121 students were diagnosed to have chronic daily headache (CDH), in other words, more than 15 headache days/month and more than 2 h/day for more than 3 months. After a face-to-face interview with these subjects,

our psychiatrist found that adolescents with CDH had higher frequencies of psychiatric disorders (47%), including major depression (21%) and panic disorder (19%) [6]. In addition, our psychiatrist rated the current suicidal risk of these adolescents based on the Mini-International Neuropsychiatric Interview-Kid (MINI-Kid) Suicidality Module (score ranging from 0 to 36) [7]. The results showed a mean suicidal score of 4.8, with scores ranging from 0 to 36. With a score of 10 or more, 24 of our subjects (20% of our study group) were rated to have a 'high' current suicidal risk. Subjects in this high suicidal risk group were more likely to be female (odds ratio [OR] = 10.3) or have major depression (OR = 3.0) or any anxiety disorder (OR = 4.1). Intriguingly, when we started

> looking into the data describing the headache subtypes, we found that our subjects with migraine were more likely to have high suicidal risk than those

without (OR = 4.3). The frequencies of high suicide risk were 50% for subjects with migraine with aura, 21%, migraine without aura and 7.5% without migraine. After statistically controlling our data for gender, as well as major depression and anxiety disorders, the association between migraine headache and suicide risk remained for migraine with aura (OR = 7.8) but no longer for migraine without aura. This finding strongly implies that migraine with aura is an independent factor in assessing suicide risk. In addition, being a female as a risk factor is in line with the general concept that shows that men have a higher rate of completed suicide, but women a higher rate of attempted suicide [101].

Breslau and colleagues first described a possible link between migraine with aura and suicide in 1991 [4,8]. They studied a random sample of 1007 young adult members of a large Health Maintenance Organization (HMO; Detroit, MI, USA). Their results, when looking at episodic headache, showed patients with migraine with aura were more likely to have lifetime suicide attempts (OR = 4.3) or suicidal ideation (OR = 2.4) than those without. However, there are some differences between our studies and theirs:

- Our study used an adolescent cohort aged 12-14 years with CDH versus HMO subjects aged 21-30 years with episodic headache
- Our study assessed current suicidal risk evaluated by a psychiatrist using the MINI-Kid Suicidality Module versus the HMO group's lifetime suicide attempt and suicidal ideation evaluated by questionnaire
- Our subjects with migraine with aura were diagnosed by neurologists versus HMO patients responding to a questionnaire 'The exact underlying pathophysiology

That notwithstanding, the most important finding is the same; both and suicidality is unknown, but a shared studies showed that migraine with predisposition mechanism is the popular aura but not migraine without aura is an independent risk factor for

higher suicidal risk. Although these two epidemiological studies demonstrated this link, extrapolation to other older age groups is still not evidenced. Moreover, no similar findings have been shown in clinic-based samples.

The exact underlying pathophysiology of the association between migraine and suicidality is unknown, but a shared predisposition mechanism is the popular theory to explain it, that is, migraine as well as major depression, some anxiety disorders and suicidality are related to dysfunctions in the serotonergic neural activities [3,9,10]. The occurrence of suicide consists of two parts, namely the idea of suicide and the impulse to perform the act. A study of teenage suicide victims showed that hypofunctioning of the serotonergic nervous system is not only related to major depression but also to impulsivity [10]. Nevertheless, the reason why the association occurs only with migraine with aura but not migraine without aura needs further studies. Besides serotonin, there are some other possible explanations. For example, chronic pain may increase the idea to end one's own life. Personality may also play some role. It is still unknown whether migraine with aura is related to an impulsive personality that might, for example, increase suicide behavior. Of note, the discrepancy of suicide comorbidity may at least provide evidence that migraine with and without aura have evolved as two different disease entities.

Predicting suicide is an exceedingly difficult task in young people. However, it has been shown that among youths, one suicide attempt raises the risk of suicide completion by 15-fold [11]. There are an estimated 8-25 attempted suicides for each teen suicide death and four of five teens who attempt suicide have given clear warnings [103]. Our study suggests that, in headache clinics, suicidality deserves more attention among adolescents with CDH, especially those with migraine with aura. In fact, other researchers have noted that CDH is one of the leading diagnoses in pediatric headache clinics, accounting for at least a third of all patients [12,13]. Migraine with aura has seldom been raised as an issue in patients with CDH since most headache

> experts believe that patients with chronic migraine, one subtype of CDH, usually suffer from migraine without aura [14]. This concept is also demonstrated in the diagnostic criteria of chronic migraine, in which only the frequencies of migraine

without aura are counted [15,16]. Our study implies that the role of migraine with aura should be emphasized in adolescents with CDH owing to its prediction to an increased risk of suicide.

Our team believes that there are still some unsolved issues. Further work is needed to investigate the association between migraine with aura and suicide risk in different age groups of populations and clinic-based samples. In addition, the complex relationship among migraine with aura, depression and suicidality should be further explored, including the use of brain imaging and other biometric methods to delineate the underlying mechanisms that establish this link.

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