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Research Paper

Suicide risk reduction in youths with attention-deficit/hyperactivity disorder prescribed methylphenidate: A Taiwan nationwide population-based cohort study

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ABSTRACT

Background: Attention-deficit/hyperactivity disorder (ADHD) youths have increased suicide risk. Nevertheless, the beneficial effects of methylphenidate (MPH) on suicide attempt have received relatively little attention.

Aims: To investigate the MPH usage and the risk of suicide attempt among ADHD youths.

Methods: We identified 84,898 youths less than 18 years old with ADHD diagnosis between 1997 and 2013 from National Health Insurance, and examined whether MPH use affected suicide attempt risk using Cox proportional-hazards models.

Outcome and results: Among ADHD youths, reduction of suicide risk was found in patients prescribed 90–180 days of MPH after adjusting for confounding factors (hazard ratio (HR): 0.41, 95% confidence interval (CI): 0.19–0.90) and a greater reduction in those prescribed more than 180 days of MPH (HR: 0.28, 95% CI: 0.17–0.48).

Conclusions and implications: We observed a 59% suicide attempt risk reduction among ADHD youths prescribed between 90 and 180 days and a 72% risk reduction in those prescribed more than 180 days of MPH. The protective benefit observed by the group prescribed MPH for longer duration underscores the importance of psychoeducation and compliance enhancement as part of ADHD management. Indication bias is identified as a limitation of this study, and future self-case control study to investigate the association between suicide attempt and ADHD medication is

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; MPH, methylphenidate; NHIRD, National Health Insurance Research Database; HR, hazard ratio; CI, confidence interval

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suggested.

What this paper adds: This nationwide population-based cohort study showed that among ADHD youths, reduction of suicide risk was observed in patients prescribed MPH for duration 90 days and longer, underscoring the importance of appropriate ADHD pharmacotherapy and enhancing drug compliance.

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is the most common childhood neurodevelopmental disorder that can affect people across their lifespan and is characterized by persistent hyperactivity, impulsivity, impaired attention and distractibility (Wilens, Biederman, & Spencer, 2002). It is well established that ADHD is significantly associated with impairments in day-to-day life, daily functioning at school or at work, as well as on social and emotional development (Buitelaar & Medori, 2010), family stress and healthcare consumption (Banaschewski et al., 2014), increased risk of accident and injury (Chang, Lichtenstein, D'Onofrio, Sjolander, & Larsson, 2014) and increased suicidality (Impey & Heun, 2012). Pharmacotherapy including MPH and atomoxetine can effectively reduce ADHD symptoms at all ages (Asherson, Chen, Craddock, & Taylor, 2007). Additional benefits of stimulant therapy for core symptoms of ADHD are decreased risk for substance use disorder (Faraone & Wilens, 2007), injury (Dalsgaard, Leckman, Mortensen, Nielsen, & Simonsen, 2015), fracture (Chou, Lin, Sung, & Kao, 2014a) and improved functional outcomes (Subcommittee on Attention-Deficit/Hyperactivity Disorder, 2011).

It is estimated that suicide claims approximately 1 million lives worldwide every year, and as many as 60% of incidences occur in Asia (Vijayakumar, 2005). In most of the developed world, suicide is among the top 10 leading causes of death for individuals of all ages, and is the third leading cause of death among adolescents, after motor vehicle accidents and homicide (Bridge, Goldstein, & Brent, 2006). Numerous studies have found that ADHD is associated with suicide-related events (Chronis-Tuscano et al., 2010; Impey & Heun, 2012; James, Lai, & Dahl, 2004) and self-harm (Allely, 2014; Meszaros, Horvath, & Balazs, 2017). In a review of six prospective studies measuring annual suicide rates, ADHD subjects were reported to have 1.3–13.6 times greater annual suicide rates in comparison to the general population (Impey & Heun, 2012). A Finnish study of a treatment-naive 1986 birth cohort found that, when compared with adolescents without ADHD, those with ADHD had more suicidal ideation (57% vs. 28%, $p < 0.01$) and self-harm (69% vs. 32%, $p < 0.01$), with a clear conclusion that ADHD is a risk factor for both suicidal ideation and self-harm (Hurtig, Taanila, Moilanen, Nordström, & Ebeling, 2012). In Taiwan, Chou et al. conducted a national population-based study from the National Health Insurance Research Database (NHIRD) and found that ADHD patients were at a 4.65-fold greater risk of developing self-poisoning than the control patients were (0.9% vs 0.1%; $P < .001$, Odds ratio: 4.65, 95% Confidence interval (CI): 2.4–8.9) (Chou, Lin, Sung, & Kao, 2014b).

Evidence has confirmed that the rates of suicide ideation, self-injury and suicide attempts are significantly increased in untreated ADHD populations (James et al., 2004). However, the roles of ADHD treatment across disparate measures of suicidality are mixed (Bangs, Tauscher-Wisniewski et al., 2008; Bangs, Wietecha, Wang, Buchanan, & Kelsey, 2014; Chen et al., 2014; Paternite, Loney, Salisbury, & Whaley, 1999). A longitudinal population-based study using a Swedish national registered database exploring the incidence rate of suicide-related events amongst individuals with ADHD did not identify an increase in risk for suicide-related events with ADHD treatment (hazard ratio (HR) = 0.89, 95% CI 0.79–1.00) (Chen et al., 2014). A meta-analysis of 14 clinical trials of adverse-event data associated with atomoxetine treatment reported a statistically significant elevated risk for suicidal thoughts amongst atomoxetine-treated children and adolescents when compared with patients receiving a placebo (Mantel-Haenszel incidence difference of 0.5, 95% CI 0.1–0.8) (Bangs, Tauscher-Wisniewski et al., 2008). Recently, in a separate meta-analysis, Bangs, Wietecha et al. (2014) reported there was no evidence of increased risk for suicidal behavior in atomoxetine-treated pediatric or adult patients (Bangs, Wietecha et al., 2014). Relatively few studies using data for suicide-related events associated with MPH have been reported (Paternite et al., 1999). Summaries of Product Characteristics (SPCs) for MPH list suicidality as a contraindication for usage, contain a warning relating to the emergence of suicidal behaviours, and list suicidal ideation as a rare and serious adverse event (Savill & Bushe, 2012).

The mixed findings regarding the effects of MPH across measures of suicidality provides the impetus for our study herein. Thus, as our starting point, we hypothesize that MPH treatment reduces the risk of suicide attempts and that the beneficial effect is influenced by duration of exposure to treatment amongst younger populations newly diagnosed with ADHD whose data is captured within the nation-wide population database in Taiwan.

2. Methods

2.1. Data source

Taiwan's National Health Insurance (NHI) was implemented in March 1995 and established a single-payer insurance system covering the delivery of health care for 92% of the national population at that time. This government-supported insurer centralized the disbursement of all healthcare funds including outpatient, ambulatory, dental service and hospital inpatient care, and, as of 2009, NHI coverage had grown to 99.5% of medical claims (National Health Insurance Administration, 2013).