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Is Increased Sleep Responsible for Reductions in Myocardial Infarction During the COVID-19 Pandemic?

The COVID-19 pandemic caused by the highly contagious SARS-CoV-2 virus has had devastating consequences across the globe. However, multiple clinics and hospitals have experienced a decrease in rates of acute myocardial infarction and corresponding cardiac catheterization lab activations, raising the question: Has the risk of myocardial infarction decreased during COVID? Sleep deprivation is known to be an independent risk factor for myocardial infarction, and sleep has been importantly impacted during the pandemic, possibly due to the changes in work-home life leading to a lack of structure. We conducted a social media-based survey to assess potential mechanisms underlying the observed improvement in risk of myocardial infarction. We used validated questionnaires to assess sleep patterns, tobacco consumption and other important health outcomes to test the hypothesis that increases in sleep duration may be occurring which have a beneficial impact on health. We found that the COVID-19 pandemic led to shifts in day/night rhythm, with subjects waking up 105 minutes later during the pandemic ($p < 0.0001$). Subjects also reported going to sleep 41 minutes later during the pandemic ($p < 0.0001$). These shifts led to longer duration of sleep during the COVID-19 pandemic. Before the pandemic, subjects reported sleeping 6.8 hours per night, which rose to 7.5 hours during the pandemic, a 44 minute or 11% increase ($p < 0.0001$). We acknowledge the major negative health impact of the global pandemic but would advocate for using this crisis to improve the work and sleep habits of the general population, which may lead to overall health benefits for our society. **(Am J Cardiol 2020;131:127−140)**

The COVID pandemic has had devastating consequences globally including impact on health and economics. However, some hospitals have seen a 38-49% decrease in presentations of acute myocardial infarction (MI).[1−3] Whether this finding represents patients' avoiding medical care due to COVID, which would lead to greater numbers of cardiovascular deaths and higher rates of post-MI complications, versus a true reduction in incidence of MI via unknown mechanisms is unclear.[1−4] Sleep deprivation is common in today's 24/7 society and has been independently associated with risk of incident MI. Furthermore, sleep has been importantly impacted during the pandemic, perhaps due to a lack of regular daily structure, and sleep deprivation is an independent risk factor for MI.[5] We conducted a social media survey to assess potential mechanisms underlying observed reductions in MI. We used validated questionnaires to assess sleep patterns, inhalant use, anxiety and depression. We sought to test the hypothesis that sleep duration has increased in the time of COVID and may beneficially impact overall health.

Methods

Participants were recruited to participate in online surveys through widespread Twitter, Facebook, Craigslist and Reddit advertisements. Participants were incentivized to complete both pre- and during-pandemic online surveys based on random lottery. We received

responses to both surveys from 135 individuals of which 131 included complete data. Of these, 56% identified as female, 43% as male, and 1.5% as non-binary, with an age-range of 14 to 64 years.

Results

We found several effects of the pandemic on sleep. First, mean sleep onset was delayed from 11:30 PM to 12:11 AM (41 minutes, p <0.0001). Second, mean awakening was delayed from 7:00 AM to 8:45 AM (105 minutes, p <0.0001). Third, sleep duration increased by 11% (44 minutes, p <0.0001). This finding was only true for non-inhalant users (non-smokers, nonvapers; p <0.0001). Fourth, we observed no change in subjective sleep based on overall Pittsburgh Sleep Quality Index score. With regards to other potential cardiometabolic risk factors, we observed no decrease in tobacco and vaping consumption, with, if anything, consumption somewhat increased during the pandemic. These findings demonstrate possible increased sleep duration and delayed circadian phase without a major change in sleep quality. The impact of these changes on cardiometabolic health is unclear but would be predicted to be beneficial.

With regards to gender, females had longer sleep latency during the pandemic (28 vs 21 minutes, 95%CI 0.4046 to 13.69), suggesting that they may suffer from greater anxiety due to the pandemic and shelter-in-place orders. Both females and males had increased sleep duration (34 and 50 minutes, respectively). The greater increase for males is due to their average sleep duration being 6 hours 40 minutes prior to the pandemic, while females slept 6 hours 54 minutes prior. During the pandemic, both females and males reported sleeping 7 hours 30 minutes.

Discussion

In conclusion, we believe our findings are important as the increased sleep duration observed during the COVID pandemic may have important health benefits. Short sleep duration is common in today's 24/7 society. Sleep deprivation is also an epidemic and has been associated with incident MI, impaired glucose tolerance, increased obesity risk and pneumonia.[5-8] The reported alleviation of sleep deprivation is likely to have important health benefits for some patients. In particular, males had a noteworthy increase in the duration of sleep (6 hours 40 minutes prior to the pandemic, increased to 7 hours 30 minutes in the setting of stay-in-place orders) which may reduce their cardiovascular disease risk.

Regarding the reported reductions in MI, several mechanisms seem plausible. In theory patients may be reluctant to leave their homes and thus some patients with chest pain may stay home rather than being assessed in the emergency room.[9,10] That is, the rate of MI may not have changed as much as might be suggested by the reduced numbers being seen in the emergency room. Others have suggested that work-related stress may be reduced during the stay-at-home orders. The global pandemic is a stressful time and indeed we found elevated Hospital Anxiety Depression Scale anxiety scores of 7.42 in this cohort. The third potential explanation which seems likely based on our findings is that the increased sleep duration that has been facilitated by the stay-at-home orders has contributed to reduction in sleep-deprivation associated cardiac risk. The fact that men are at increased risk of MI compared to women and reported greater improvements in sleep deprivation, based on our data, is consistent with our purported mechanism.

Our study has limitations. First, we used a prospective sample based on social media and thus have no real way to assess whether there was participation bias in those who responded. Thus, our conclusions are limited to the population studied. *S*Second, we relied on self-report and thus some inaccuracy is possible if not likely. However, we expect such misclassification to be random and thus should bias towards the null hypothesis. Third, we did not assess other cardiometabolic risk factors such as lipids or body weight, but do not believe these improved during the pandemic. In fact, many have referred to the "COVID 10" or "Quarantine 15" to reflect the increase in body weight that many experienced during the stay-at-home orders. Despite these limitations we view our findings are potentially important and worthy of further mechanistic research.

We would advocate for using this global crisis to improve work and sleep habits of the general population, which may lead to overall health benefits for our society.

Disclosures

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Meta-analysis of the Safety and Efficacy of Bempedoic Acid

Low-density lipoprotein cholesterol (LDL-C) is a well-established modifiable cardiovascular risk factor. Therapeutic options such as statins, ezetimibe, or proprotein convertase subtilisin/kexin type-9 inhibitor that reduce LDL-C through upregulation of LDL receptors have shown to reduce the risk of cardiovascular events. A significant number of patients despite receiving high intensity statin therapy, or due to nonadherence or intolerance fail to achieve target goals for LDL-C reduction. Bempedoic acid is a recently approved lipid-lowering drug indicated for treatment of heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease as an adjunct to maximally tolerated statin therapy. Bempedoic acid is activated in the liver and reduces LDL-C through adenosine triphosphate-citrate lyase inhibition working up stream of the statin target 3-hydroxy-3-methylglutaryl-CoA reductase. Several clinical trials have demonstrated pharmacologic efficacy of bempedoic acid in LDL-C reduction.[1–9] However, none of these trials were powered to assess cardiovascular efficacy of bempedoic acid.[10,11] Moreover, while concerns exist that LDL-C-lowering therapies might potentiate the risk of diabetes mellitus (DM), safety of bempedoic acid with respect to DM and other adverse events remained uncertain. Herein, we present a meta-analysis to investigate the effects of bempedoic acid on clinical outcomes.

Eleven randomized controlled trials that enrolled patients with dyslipidemia, established or at risk of cardiovascular disease were selected using PubMed and Embase through 02/2020. Data were abstracted on baseline characteristics of patients (Table 1), and outcomes of interest (percent change in LDL-C, major adverse cardiac events, myocardial infarction, serious adverse events, muscle-related adverse events, nasopharyngitis, urinary tract infection, new/worsening DM, and gout). Risk of bias was assessed following the Cochrane bias risk assessment tool and reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis.[12] The whole process of study search and selection and data abstraction were performed by 2 authors (MUK and MZK), independently. Outcomes were pooled using Mantel Haenszel random effect model. Categorical estimates were reported as risk ratio (RR) and continuous outcomes were calculated as mean difference with 95% confidence intervals (CIs). Heterogeneity was assessed by I^2 tests and publication bias using Egger's test. Statistical significance was set at 0.05. Comprehensive meta-analysis V-3.0 was used for all analyses.

Table 1
Baseline characteristics of participants and trials of bempedoic acid (180 mg) versus placebo

First author (year)	Phase	N	Age (years)	Baseline LDL-C (mg/dl)	Women	CHD	Hypertension	Diabetes	Statin	Ezetimibe	Follow-up (weeks)
Ballantyne (2013)	2	44	57.0	165.0	43.0 (%)	0	0	0	-	-	12
		44	56.0	167.0	30.0 (%)	0	0	0	-	-	
Gutierrez (2014)	3	30	55.3	125.2	43.3 (%)	-	26.7 (%)	100 (%)	-	-	4
		30	56.0	128.4	33.3 (%)	-	26.7 (%)	100 (%)	-	-	
Thompson (2015)	2/3	37	64.0	176.0	46.0 (%)	-	57.0 (%)	-	-	-	8
		19	60.0	185.0	58.0 (%)	-	53.0 (%)	-	-	-	
Thompson (2016)	2/3	100	59.0	166.0	51.0 (%)	0	-	-	-	-	12
		99	60.0	165.0	52.0 (%)	0	-	-	-	100 (%)	
Ballantyne (2016)	3	45	57.0	142.0	69.0 (%)	-	-	-	100 (%)	-	12
		45	56.0	131.0	49.0 (%)	-	-	-	100 (%)	-	
Ballantyne (2018)	3	181	63.8	129.8	60.2 (%)	-	61.3 (%)	19.3 (%)	32.6 (%)	100 (%)	12
		88	63.7	123.0	63.6 (%)	-	58.0 (%)	19.3 (%)	28.4 (%)	100 (%)	
Ballantyne (2019)	3	88	65.0	145.0	54.5 (%)	-	87.5 (%)	51.1 (%)	69.4 (%)	-	12
		41	65.4	141.0	41.5 (%)	-	85.4 (%)	41.5 (%)	65.8 (%)	-	
Ray (2019)	2/3	1488	65.8	103.6	26.1 (%)	97.4	78.9 (%)	28.6 (%)	99.8 (%)	7.8 (%)	52
		742	66.8	102.3	28.7 (%)	98	80.1 (%)	28.6 (%)	100 (%)	7.5 (%)	
Laufs (2019)	2/3	234	65.2	158.5	56.8 (%)	-	67.5 (%)	26.9 (%)	<10 (%)	-	24
		111	65.1	155.6	55.0 (%)	-	67.6 (%)	23.4 (%)	<10 (%)	-	
Lalwani (2019)	2	45	58.0	71.0	51.2 (%)	-	-	-	100 (%)	0	4
		23	58.0	86.0	43.5 (%)	-	-	-	100 (%)	0	
Goldberg (2019)	3	522	64.1	119.4	37.2 (%)	82.8	83.9 (%)	29.7 (%)	90.0 (%)	-	12
		257	64.7	122.4	34.6 (%)	79.8	87.2 (%)	31.5 (%)	89.0 (%)	-	

CHD = coronary heart disease; LDL-C = low-density lipoprotein cholesterol.