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ABSTRACT & COMMENTARY

Fluvoxamine Reduces the Risk for Hospitalization from COVID-19

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SYNOPSIS: Researchers found fluvoxamine (100 mg twice a day for 10 days) lowered the risk for hospitalization among high-risk outpatients diagnosed with COVID-19.

SOURCE: Reis G, Dos Santos Moreira-Silva EA, Medeiros Silva DC, et al. Effect of early treatment with fluvoxamine on the risk of emergency care and hospitalisation among patients with COVID-19: The TOGETHER randomized, platform clinical trial. *Lancet Glob Health* 2021; Oct. 27;S2214-109X(21)00448-4. [Online ahead of print].

Despite the widespread availability of COVID-19 vaccines, effective treatments that prevent or delay illness progression are urgently needed. Ideally, novel therapies should be oral, inexpensive, widely available, and carry a low risk of adverse events. There is some evidence suggesting fluvoxamine, an oral selective serotonin reuptake inhibitor used to treat depression, may reduce the risk for hospitalization due to COVID-19.[1] Reis et al studied the efficacy of fluvoxamine vs. placebo in preventing hospitalization among outpatients with an early diagnosis of COVID-19.

This was a randomized, platform, placebo-controlled clinical trial conducted in 11 cities in Brazil. Patients included in the study were at least age 18 years and presented to an outpatient care setting with an acute illness consistent with COVID-19. Symptoms started within seven days of the screening date; patients tested positive at screening, or tested positive within seven days of symptom onset. Patients also needed at least one more criterion that put them at high risk for hospitalization, which included diabetes mellitus, hypertension, cardiovascular disease, symptomatic lung disease, tobacco use, obesity, organ transplant recipient, chronic kidney disease (stage IV or on dialysis), immunosuppression or use of corticosteroid therapy equivalent to at least 10 mg of prednisone per day, history of malignancy in the preceding five years or actively undergoing cancer treatment, or

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had not taken the COVID-19 vaccine. Patients were randomized 1:1 to receive either fluvoxamine 100 mg orally twice a day for 10 days or placebo. An ECG was conducted at baseline for all participants. The primary endpoint was medical admission to a hospital for COVID-19 within 28 days of randomization.

There were 1,497 patients enrolled, of which 741 were randomized to fluvoxamine and 756 to placebo. The median age was 50 years (range, 18-102 years) and 862 were women. The two groups were well balanced in terms of age, body mass index, and comorbidities. Hospitalization occurred in 79 of 741 of fluvoxamine recipients vs. 119 of 756 for those who received placebo; relative risk (RR), 0.68; 95% Bayesian credible interval (95% BCI): 0.52-0.88. Seventeen deaths occurred in the fluvoxamine group and 25 deaths occurred in the placebo group in the primary intention-to-treat analysis (OR, 0.68; 95% CI, 0.36-1.27; $P = 0.24$). The number needed to treat was 20. Fluvoxamine was well tolerated and there were no significant differences in adverse events between those who received fluvoxamine vs. placebo.

■ COMMENTARY

The available treatments for COVID-19 (i.e., monoclonal antibodies and remdesivir) are given intravenously. An effective oral agent would be a game changer. The oral direct-acting antiviral molnupiravir has generated considerable interest after it was shown to reduce the risk for hospitalization by 50% in those with early COVID-19.[2] Reports indicate a novel protease inhibitor, Paxlovid, may be 89% efficacious, bringing it to a level similar to that seen with monoclonal antibody therapy.

However, other oral options remain an important goal. Since it received FDA approval in 1997, fluvoxamine has shown a good safety record and generally is well tolerated. There is growing evidence, as shown by the study from Reis et al and others, suggesting fluvoxamine is an effective, safe, and relatively inexpensive treatment option for outpatients with mild COVID-19. The mechanism of action against SARS-CoV-2 is not well understood and needs further investigation. It may be because of anti-inflammatory properties, such as reducing platelet aggregation, decreasing mast cell degranulation, interfering with endolysosomal viral trafficking, regulating inositol-requiring enzyme 1α-driven inflammation, and increasing melatonin levels.[3] Thus, there are likely to be other drugs used in clinical practice that can be similarly repurposed against COVID-19 that are waiting to be discovered.

The study by Reis et al was well-designed and is the largest randomized trial to date to investigate the effect of fluvoxamine against COVID-19. However, there were a few limitations and unanswered questions. First, it is uncertain whether fluvoxamine will be as efficacious against other strains of COVID-19, such as the delta variant. Second, whether fluvoxamine can help those already hospitalized (i.e., prevent ICU admission) is uncertain. Third, the study was conducted in one geographic area with a relatively homogeneous population, so the results might not be applicable to other regions and should be considered preliminary. Fourth, it is unknown whether fluvoxamine is beneficial for vaccinated patients. Finally, the follow-up duration was relatively short and did not measure the effect of fluvoxamine on persistent symptoms (i.e., long COVID) or late deterioration.

The findings in this study are interesting and further support a role for fluvoxamine in the treatment of early COVID-19 in outpatients. Considering the prevalence of vaccine hesitancy, an inexpensive oral drug that prevents hospitalizations, especially in the unvaccinated, could produce important economic and public health benefits. ■

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ABSTRACT & COMMENTARY

Looking Back, COVID-19 Vaccination Woes Were Predictable

By Seema Gupta, MD, MSPH

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SYNOPSIS: Efficacy, protection duration, side effects, and FDA approval factored into decisions about choosing a COVID-19 vaccine.

SOURCE: Kreps S, Prasad S, Brownstein JS, et al. Factors associated with US adults' likelihood of accepting COVID-19 vaccination. *JAMA Netw Open* 2020;3:e2025594.

The success of any strategy to ensure maximum vaccine uptake depends on the rate of acceptance and hesitancy. The United States remains the leader in both COVID-19 cases and related deaths on a per capita basis.[1] As vaccines have become available, most experts agree widespread public acceptance of a COVID-19 vaccine is imperative for stemming the pandemic.

The wide availability of COVID-19 vaccines presents our best pathway to herd immunity and recreating some sense of normalcy in the United States. Currently, only 60% of the population has been fully vaccinated.[2] This has led to some improvements in case and death rates, but vaccination efforts remain uneven across the country. Certain communities continue to carry an inequitable burden of disease and remain more susceptible to morbidity and mortality. To achieve herd immunity, overcoming vaccination resistance and hesitancy is critical.

Before COVID-19 vaccines were widely available, Kreps et al surveyed 1,971 U.S. adults to gauge what factors might play into decision-making (median age = 43 years; 51% of respondents were women, 73% were white, 14% were Black, and 10% were Latinx). The authors used a choice-based conjoint analysis to estimate the probability of choosing and receiving a vaccine. For each of the five choice tasks, respondents analyzed two hypothetical vaccines and picked an option (vaccine A, B, or neither). Attributes analyzed included minor and major adverse effects, protection duration, efficacy, FDA approval, endorsements, and national origin.

Researchers learned the more efficacious the vaccine, the more likely respondents were to seek the shot. An increase in the duration of vaccine protection from one year to five years and a decrease in the incidence of major adverse effects from one in 10,000 to one in 1 million also were associated with a higher probability of choosing a vaccine.

A vaccine that had received only an FDA emergency use authorization, not full approval, was associated with a lower probability of choosing a vaccine. If a vaccine originated outside the United States, respondents were less likely to seek the solution, especially if the shot was made in China. Vaccines with CDC and World Health Organization (WHO) endorsements carried more weight with respondents than any vaccines endorsed by then-President Trump.

■ COMMENTARY

The unprecedented politicization of the public health response to the COVID-19 pandemic has led to less-than-sufficient deployment of public health measures, resulting in more lives lost, more suffering, and an economic fallout. But was it all predictable? Could we have avoided it? Well, yes and no. Studies like those from Kreps et al clearly outlined a range of factors that may be associated with a better understanding of vaccine resistance and hesitancy. But recommendations and advice regarding a vaccine may be more complicated in the context of COVID-19 compared with other diseases, such as the seasonal influenza. Factors associated with higher probability of choosing a vaccine, such as better efficacy, low incidence of major adverse effects, and endorsements by the CDC and WHO, currently exist.[3] But the FDA has been slow to approve vaccines, and the ongoing politicization of science, from mask-wearing to vaccine mandates and school openings, has led to an erosion of the public's confidence in vaccines.[4,5]

Vaccines were a chance to redeem failures in the U.S. coronavirus response. But it did not happen, and more lives are lost daily as a result. For policymakers and health experts alike, the lesson may be that even perceptions of political influence, much less interference during a pandemic response, significantly undermine the viability of countermeasures deployed, including a vaccine as a strategy to end that pandemic. Perhaps, in the next pandemic (which is sure to happen), we will try to remember that. ■

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ABSTRACT & COMMENTARY

Reduce the Risk of Autoimmune Disease with Vitamin D, n-3 Fatty Acid Supplements

By Joseph E. Scherger, MD, MPH

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SYNOPSIS: A randomized, controlled trial that included older adults showed vitamin D_3 2,000 units daily or n-3 fatty acids 1,000 mg daily over five years reduced the incidence of autoimmune diseases 25% to 30%.

SOURCE: Hahn J, Cook N, Alexander E, et al. Vitamin D and marine n-3 fatty acid supplementation and prevention of autoimmune disease in the VITAL randomized controlled trial. American College of Rheumatology Meeting Abstracts. Nov. 7, 2021. https://bit.ly/30QgHqA

In a randomized, controlled trial, Hahn et el recruited almost 26,000 adults with a mean age of 67.1 years (71% non-Hispanic whites, 20% Black, and 9% other racial/ethnic groups; 51% women). Participants took vitamin D_3 2,000 units daily and/or n-3 fatty acids (i.e., omega-3 fatty acids) 1,000 mg daily, or placebo.

During a median follow-up of 5.3 years, there were 117 confirmed cases of autoimmune diseases in the vitamin D_3 group vs. 150 in the placebo group. In the n-3 fatty acids group, there were 123 confirmed cases. The autoimmune diseases included psoriasis, rheumatoid arthritis, autoimmune thyroid disease, polymyalgia rheumatic, and others. The authors reported the number needed to treat with both supplements for five years to prevent one autoimmune disease was 167.

■ COMMENTARY

Although these results are modest, they reached statistical significance. Notably, one of the authors of this study previously wrote that vitamin D supplementation beyond 800 units daily was not of benefit in preventing disease.[1] The causes of autoimmune diseases remain a mystery, but the leading postulation today implicates a leaky gut and an unhealthy microbiome.[2] Vitamin D is a prohormone that is not readily available in food unless we consume organs from animals.[3] While vitamin D may be obtained through the skin by sunshine converting cholesterol to the vitamin, this conversion declines with age.[4] Hence, vitamin D deficiency is common in seniors.[5] This study provides welcome evidence suggesting vitamin D supplementation is of benefit in preventing disease. Omega-3 fatty acids (called n-3 fatty acids in this trial) have a history similar to vitamin D. We know they are important for health, but there is little evidence indicating their supplementation provides benefit.[6]

Although the strength of these findings does not confirm that all or most adults should take vitamin D or omega-3 fatty acids as supplements, this study shows these supplements may be of benefit in preventing autoimmune diseases. I take these supplements and recommend them to my patients older than age 50 years. ■

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ABSTRACT & COMMENTARY

Importance of Age in the Application of Coronary Artery Calcium Detection

By Michael H. Crawford, MD

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SYNOPSIS: Using coronary CT strategy as a diagnostic first line in patients with symptoms suggestive of coronary artery obstruction revealed relying on the coronary calcium score alone is inadequate for younger patients with a higher frequency of non-calcified obstructions.

SOURCE: Mortensen MB, Gaur S, Frimmer A, et al. Association of age with the diagnostic value of coronary artery calcium score for ruling out coronary stenosis in symptomatic patients. *JAMA Cardiol* 2021; Oct 27. doi: 10.1001/jamacardio.2021.4406. [Online ahead of print].

Although a coronary artery calcium (CAC) score of 0 is associated with a low likelihood of obstructive coronary artery disease (CAD), that does not mean risk is nonexistent. Since early coronary plaques may not be calcified, the relationship between CAC and obstructive disease may be age-related. Investigators from the Western Denmark Heart Registry used data about consecutive real-world patients who exhibited symptoms suggestive of CAD and underwent coronary calcium scoring followed by CT angiography (CTA) to test this association.

In Western Denmark, CTA is a first-line diagnostic test for non-emergency patients with suspected obstructive CAD. For this analysis, Mortensen et al included all patients older than age 18 years who underwent CTA between 2008 and 2017. Only patients with inconclusive test results, missing results, or a history of known CAD were excluded. The authors obtained clinical data from the Danish National Patient Registry. They categorized the severity of CAD as none (0% luminal stenosis and Agatston score of 0), nonobstructive (1% to 49% stenosis), or obstructive (> 49%). The primary endpoint was myocardial infarction and all-cause death. All analyses were corrected either for age and sex or age, sex, smoking, diabetes, and symptom characteristics.

Among the study cohort of 23,759 patients (45% men, mean age = 58 years), 54% recorded a CAC score of 0. The prevalence of obstructive CAD in patients with a CAC score of 0 in the overall population was 6%. In those younger than age 40 years, it was 3%; age 40-49 years, it was 5%; age 50-59 years, it was 6%; age 60-69 years, it was 6%; and older than age 70 years, it was 8%. Overall, 14% of patients with obstructive CAD recorded a CAC score of 0; percentages declined with age: 58% in those younger than age 40 years, 34% in those age 40-49 years, 18% in those age 50-59 years, 9% in those age 60-69 years, and 5% in those age 70 years or older. Although the distribution by age was similar, overall, women with obstructive CAD more often recorded a CAC of 0. The overall diagnostic value of a CAC score of 0 for excluding obstructive CAD was a 63% lower likelihood than expected based on other clinical characteristics. However, this varied across different age groups, ranging from 32% in those younger than age 40 years to 82% in those age 70 years and older. This effect was more pronounced in women younger than age 40 years (18% vs. 41% in men younger than age 40 years). During the mean follow-up of four years, the primary outcome occurred in 31% of patients with a CAC score of 0, with an adjusted multivariable hazard ratio (HR) of 1.51 (95% CI, 0.98-2.33). The HR varied with age, from 1.80 in those younger than age 60 years to 1.24 in those older than age 60 years. The authors concluded the diagnostic value of a CAC score of 0 varied with age. There was less value in younger patients with symptoms suggestive of obstructive CAD. Those younger than age 60 years with a CAC score of 0 made up a large proportion of those experiencing the primary endpoint.

■ COMMENTARY

Because of the logistical issues surrounding stress testing, many chest pain units have moved to using CTA to diagnose obstructive CAD. However, when coronary calcium is present, CTA becomes less accurate for detecting stenoses. Thus, CTA often is preferentially directed at younger patients who are less likely to exhibit significant calcium. In fact, many younger patients will show no detectable coronary calcium. The risk of obstructive CAD in such patients is low, but it is not zero.

Mortensen et al hypothesized the diagnostic value of the CAC score would be age-related, based on the pathophysiology of atherosclerosis wherein calcium deposition is a later manifestation of coronary plaques. In this study, a CAC score of 0 was more common in younger patients, especially women (55%). The prevalence of obstructive CAD in those with a CAC score of 0 was low, ranging from 3% in those younger than age 40 years to 8% in those older than age 70 years. However, in those with obstructive CAD, 14% overall recorded a CAC score of 0; the proportion was higher in younger patients (58% in those younger than

age 40 years vs. 5% in those older than age 70 years). Consequently, the diagnostic value of a CAC score of 0 was less in younger patients and women. Although the overall risk of the combined primary outcome of myocardial infarction or all-cause mortality was low in patients with a CAC score of 0 (< 1%), one out of three events occurred in patients with a CAC score of 0. Thus, CTA is necessary in younger patients with symptoms suggestive of CAD, since relying on the CAC score alone is problematic.

There were weaknesses here. A referral bias to CT scan cannot be excluded, but this was the recommended approach. This was a relatively low-risk population (less than 1% experienced the primary outcome). More importantly, the authors observed changes in management based on the CT scans, but those changes were not considered in the analyses. Also, researchers did not consider the severity of calcium deposition. Nevertheless, this was a large, real-world study, with baseline characteristics representative of everyday practice patients. ■

ABSTRACT & COMMENTARY

Intensive Monitoring for Asymptomatic Atrial Fibrillation Did Not Prevent Strokes

By Joshua D. Moss, MD

Associate Professor of Clinical Medicine, Cardiac Electrophysiology, Division of Cardiology, University of California, San Francisco

SYNOPSIS: Screening with an implantable loop recorder resulted in dramatically higher rates of atrial fibrillation detection and ensuing anticoagulation, but without a significant decrease in risk of stroke or systemic embolism by six years of follow-up.

SOURCE: Svendsen JH, Diederichsen SZ, Højberg S, et al. Implantable loop recorder detection of atrial fibrillation to prevent stroke (The LOOP Study): A randomised controlled trial. *Lancet* 2021;398:1507-1516.

Anticoagulation lowers the risk of stroke in patients with clinically diagnosed atrial fibrillation (AF). Further, more-intensive ambulatory monitoring helps clinicians detect more asymptomatic or "subclinical" AF better than conducting periodic ECGs or short-term Holter monitoring. Svendsen et al investigated whether anticoagulation guided by intensive AF screening with an implantable loop recorder (ILR) could prevent strokes.

At four centers in Denmark, 6,004 patients (mean age = 74.7 years; 47.3% women) with at least one risk factor for stroke (other than age) but no previously diagnosed AF or indication for anticoagulation were randomized in a 1:3 ratio to ILR monitoring or usual care. Required risk factors for stroke included hypertension (90.7%), diabetes (28.5%), prior stroke (17.6%), or heart failure (4.4%). The CHA_2DS_2-VASc score for most patients was 3 or higher. In the ILR group, automated remote transmissions were reviewed daily, and oral anticoagulation was recommended if AF lasting at least six minutes was detected. In the usual care control group, patients were followed per routine with their general practitioner and participated in an annual interview with a study nurse. The primary outcome was the combined endpoint of stroke or systemic arterial embolism, with multiple secondary outcomes, including cardiovascular and all-cause mortality. No patients in the control arm crossed over to the ILR group, and 81 patients in the ILR group did not receive an ILR. The median duration of ILR monitoring was 39.3 months, with 11.7% of ILR patients prematurely discontinuing monitoring (before three years without outcome, AF, or death). Total median follow-up was 64.5 months.

AF was diagnosed at significantly higher rates in the ILR group compared with the control group (31.8% vs. 12.2%), and oral anticoagulation was initiated at similarly higher rates (29.7% vs. 13.1%), most within the first month of AF diagnosis. More ILR patients who started anticoagulation for AF eventually discontinued anticoagulation (5.8% vs. 3.6%). The primary outcome of stroke or systemic embolism occurred less frequently in the ILR group (0.88 events per 100 person-years) than the control group (1.09 events per 100 person-years), but these differences were not statistically significant. Neither cardiovascular death rates nor all-cause mortality rates were significantly different between groups. In subgroup analyses, ILR patients with systolic blood pressure in the highest tertile (a reading of at least 157 mmHg or higher) demonstrated significantly lower rates of stroke or systemic embolism than control patients (3.46% vs. 6.74%; HR, 0.51; 95% CI, 0.31-0.83). Similar differences were not seen for patients with lower blood pressure. Rates of major bleeding, hemorrhagic stroke, and traumatic intracranial hemorrhage were not significantly different between groups. The authors concluded long-term ECG monitoring with an ILR resulted in significantly higher rates of AF detection and ensuing anticoagulation, but no significant decrease in the risk of stroke or systemic embolism by 5.4 years of follow-up.

■ COMMENTARY

The relationship between AF and risk of stroke or systemic embolism is well established but complex. Longer episodes of AF (> 23.5 hours) have been shown to be associated with higher risk than shorter episodes, although even shorter episodes may portend significant risk in patients with higher CHA_2DS_2-VASc scores. Not all cardioembolic strokes occur at or near the time of an AF episode, and not all strokes in patients with AF are caused by cardiac thromboembolism. Anticoagulation to prevent thromboembolism might increase the risk of hemorrhagic stroke. All these factors make it difficult to predict the benefits of intensive arrhythmia monitoring in asymptomatic patients, or when anticoagulation is warranted, questions that may become increasingly important as more patients turn to commercially available wearable monitoring devices like smartwatches. However, the LOOP study offers both a great deal of useful information and new hypotheses to test.

Loop recorders are a safe way to continuously monitor for AF long-term. In 1,420 patients with the device implanted, the ILR was explanted for complications in only nine (eight of whom received a new device). Higher rates of anticoagulation in this patient population were not associated with significantly more bleeding complications over almost six years. That is not to say therapeutic anticoagulation could not have led to some episodes of intracranial bleeding, but that feared event did not occur more often in the ILR group.

More aggressive monitoring, and the ensuing increase in anticoagulation rates, did not result in significantly lower rates of stroke or systemic embolism over six years. However, the event curves did appear to start separating at two to three years follow-up, and they continued to separate thereafter. Only 16.4% of participants were followed for the primary outcome at year 6, necessitating caution in interpretation. But it is not unreasonable to think a larger study or longer follow-up could have led to a different conclusion. Additionally, several factors may have biased outcomes against the ILR group. First, it is possible there was a lower average burden of AF (and lower overall stroke risk) in anticoagulated patients in the ILR group, if longer and/or more frequent episodes were required for AF detection in the control group. It also is possible AF was detected more often with "usual care" than might otherwise be expected, given participation in a clinical trial and higher awareness of AF.

AF is a cause of stroke and a marker of stroke risk. Of the 67 patients in the ILR group who recorded a primary outcome, only 17 experienced an event after AF was first detected, 15 of whom were on anticoagulation. There was no temporal relationship between AF episodes and stroke. More severe hypertension may warrant higher vigilance for AF and more aggressive initiation of anticoagulation, a hypothesis generated from the compelling subgroup data. Anticoagulation for AF will warrant a risk-benefit discussion and shared decision-making with patients. In my own practice, I still recommend anticoagulation for AF episodes longer than six minutes with higher CHA_2DS_2-VASc scores when a direct-acting oral anticoagulant is an option. In the absence of symptoms, I would not advocate for routine ILR monitoring. However, I suggest a higher level of vigilance for patients with more severe hypertension. ■

PHARMACOLOGY UPDATE

Pilocarpine Hydrochloride Ophthalmic Solution 1.25% (Vuity)

By William Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Assistant Clinical Professor of Medicine, University of California, San Francisco.
Dr. Chan is Associate Clinical Professor, School of Pharmacy, University of California, San Francisco.

The FDA has approved eye drops to treat presbyopia, commonly known as age-related blurry near vision. Presbyopia is a progressive condition that affects adults older than age 40 years. The solution includes pilocarpine, a cholinergic muscarinic receptor agonist used to treat glaucoma (miotic). Pilocarpine ophthalmic solution 1.25% is distributed as Vuity.

INDICATION

Pilocarpine ophthalmic solution (OS) can be prescribed to treat presbyopia.[1]

DOSAGE

The recommended dosage is one drop in each eye once daily.[1] Pilocarpine OS is a 1.25% solution available as a 2.5 mL fill in 5 mL bottles.

POTENTIAL ADVANTAGES

Pilocarpine OS onsets rapidly (approximately 15 minutes) and lasts about six hours. It does not affect distance vision.[1] Allergan uses a proprietary pHast technology that allows the drops to rapidly adjust to the physiologic pH of the tear film.[2]

POTENTIAL DISADVANTAGES

Pilocarpine causes reduced illumination and may cause accommodation spasm.[1] The drug appears to be "fully" effective in about 25% to 30% of test subjects.[1] Exercise caution when night driving and during other hazardous occupations in poor illumination. Rare cases of retinal detachment have been reported with other miotics.[1] The most common (more than 5%) adverse reactions were headache and conjunctiva hyperemia. Less common reactions (1% to 5%) were blurred vision, eye pain, visual impairment, eye irritation, and increased lacrimation.[1]

COMMENTS

Pilocarpine adjusts the pupil by contracting the iris sphincter muscle.[1] This improves near and intermediate visual acuity while maintaining some pupillary response to light. Its efficacy was evaluated in two 30-day, randomized, double-masked, vehicle-controlled studies in subjects with presbyopia. Subjects ranged from age 40 to 55 years, with 375 randomized to pilocarpine OS and 375 randomized to the vehicle. The primary efficacy endpoint was the proportion of subjects gaining three lines or more in mesopic high contrast, binocular distance-corrected near visual acuity without losing more than one line (five letters) of corrected distance visual acuity at day 30, three hours after administration.

A statistically significant proportion of participants achieved the efficacy endpoint vs. those on the vehicle (31% in study 1 and 26% in study 2 vs. 8% and 11%, respectively, for the vehicle).

CLINICAL IMPLICATIONS

Presbyopia is a highly prevalent refractive condition that results in loss of accommodation and visual ability to focus on objects at different distances associated with aging. It is estimated to affect 128 million Americans, or nearly half the U.S. adult population.[2] Current treatment options for presbyopia correction include reading glasses; bifocal, trifocal, or progressive glasses; contact lens, and surgical correction.[3] The pharmacologic approach involves miotics, which increase the depth of field by exerting a pinhole effect, such as carbachol and pilocarpine.[3] Pilocarpine OS may be useful for certain settings where reading glasses may not be convenient. The cost of pilocarpine OS is $73.49 per 2.5 mL. ■

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CME QUESTIONS

1. Supplementation with vitamin D3 and/or omega-3 fatty acids may be of benefit in the prevention of:
a. Alzheimer's disease.
b. colorectal cancer.
c. autoimmune disease.
d. Parkinson's disease.

2. Based on the study by Kreps et al, a factor associated with higher probability of choosing a hypothetical COVID-19 vaccine included:
a. short wait time to receive a vaccine.
b. low incidence of major adverse effects.
c. an endorsement from former President Trump.
d. FDA emergency use authorization.

3. Which is correct regarding the known putative mechanism of action of fluvoxamine against SARS-CoV-2?
a. It acts as a protease inhibitor.
b. It acts as a chain terminator.
c. It causes multiple mutations in viral nucleic acid.
d. It is unknown.

4. Deploying an implantable loop recorder in patients at risk for atrial fibrillation compared to a control group showed:
a. more atrial fibrillation detection.
b. lower mortality.
c. fewer strokes.
d. more major bleeding.

5. A study of coronary CT studies as a first-line approach in patients with non-emergency symptoms suggestive of coronary artery disease showed that a coronary artery calcium score of 0:
a. completely excluded obstructive disease.
b. was less common in younger patients.
c. was of less diagnostic value in younger patients.
d. was less common in women.