Letters to the Editor

Adherence to CPAP May Make a Difference for Cardiovascular Outcomes in Patients with OSA

Original Article: Treating Sleep Apnea with Positive Airway Pressure Does Not Reduce Adverse CV Outcomes or Mortality

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To the Editor: The authors of a meta-analysis published last year (the findings of which were summarized in *American Family Physician*) found that the use of positive airway pressure therapy was not associated with cardiovascular benefits in patients with sleep apnea.[1] However, for several reasons, this conclusion should be interpreted with caution.

The meta-analysis included 10 randomized controlled trials (RCTs) with a total of 7,266 patients with sleep apnea who were, for the most part, not excessively sleepy. Of these, 1,583 patients from two studies had central sleep apnea.[2,3] Because the pathophysiology of central sleep apnea is different from that of obstructive sleep apnea (OSA), these two studies should not have been included in the meta-analysis.

Of the OSA-related studies, the largest share of patients (2,717) came from the SAVE study.[4] One limitation of this study was that the mean continuous positive airway pressure (CPAP) use was only 3.3 hours per night, and only 42% of the patients used it for four or more hours per night. Therefore, the lack of cardiovascular benefit from CPAP in this study may simply have been because patients did not use it for a long enough period of time during the night.

Interestingly, two studies in the meta-analysis found that cardiovascular events were significantly reduced in patients who used CPAP for at least four hours per night. One study in which the mean adherence to CPAP therapy was 5.3 hours per night found significantly higher cardiovascular survival in patients who used CPAP. Another study in which the mean adherence to CPAP therapy was 4.5 hours per night found a trend toward a reduction in cardiovascular events in patients who used CPAP. These data suggest that adherence to CPAP therapy in patients with OSA is important and that patients with OSA who use CPAP for at least four hours per night may experience cardiovascular benefits. The possibility of such a benefit has also been recognized in two other recent meta-analyses of RCTs.[5,6]

Until further studies are available, it would be prudent to test patients who have OSA-related symptoms (including those who may not have significant daytime sleepiness) and to offer CPAP therapy to patients who test positive.

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In Reply: We appreciate Dr. Kapoor's interest in the POEMs series. Dr. Kapoor raises four concerns about this particular POEM, which are addressed as follows:

(1) The included trials represented patients typically referred by family physicians for suspected sleep apnea, both with and without excessive daytime sleepiness.[1] In addition, trials specifically enrolling patients at high risk with known cardiovascular events also found no benefit with CPAP in reducing cardiovascular events morbidity or mortality.[2,3] Patients with excessive daytime sleepiness do benefit from an increased quality of life.

(2) The meta-analysis intentionally included studies of patients with central and obstructive sleep apnea and found no benefit with CPAP for reducing adverse cardiovascular events for either group of patients.[1]

(3) A formal analysis of all trials found no significant association between CPAP adherence and reduced risks of cardiovascular events and death or severity of sleep apnea.[1]

(4) Although a post-hoc analysis found an association between CPAP adherence and a reduced risk of

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This series is coordinated by Kenny Lin, MD, MPH, Deputy Editor.

cardiovascular events in some of the individual trials, it is uncertain whether this is a real effect or the result of the compliance effect, whereby compliant patients almost always experience a significant reduction in morbidity and mortality compared with a mixed population of compliant and noncompliant individuals, regardless of the intervention.

In its 2017 recommendation statement on screening for sleep apnea, the U.S. Preventive Services Task Force found inadequate evidence that treatment with CPAP reduces cardiovascular events and death.[4] Although current data are imperfect, unless new studies show benefit, family physicians should not indicate to their patients that treatment with CPAP will prevent cardiovascular events, especially because it is an expensive and uncomfortable intervention.

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Consider Cardiovascular Risk Factors Before Prescribing Triptans for Migraine

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See additional reader comments at: https://www.aafp.org/afp/2018/0215/p243.html

To the Editor: We would like to thank Drs. Mayans and Walling for their review of the treatment of acute migraine headaches, for which triptans are a first-line pharmacologic option. In Table 5, eletriptan (Relpax) is described as the triptan class agent with the least cardiovascular risk. Because patients who are candidates for pharmacotherapy may have cardiovascular risk factors or cardiovascular disease, we will review the literature on this risk assessment.

Because triptans antagonize 5-hydroxytriptamine receptors expressed in the cerebrovascular and coronary vessels, triptans as a class are associated with cardiovascular and cerebrovascular risks related to vessel vasoconstriction. Contraindications to triptans include, but are not limited to, peripheral vascular disease, coronary artery disease, cerebrovascular disease, and uncontrolled hypertension. A 2004 American Headache Society consensus statement noted that the cardiovascular risk for triptans is relatively small, with fewer than one adverse cardiovascular event per 1 million patients exposed.[1]

Eletriptan is a selective 5-hydroxytriptamine receptor 1B/1D antagonist and is approved by the U.S. Food and Drug Administration for the acute treatment of migraine with or without aura in adults. It has been described as more selective for intracranial blood vessels, inducing less contraction in coronary tissues in vitro compared with sumatriptan (Imitrex).[2] Notably, another Letter to the Editor emphasized that this study's conclusion is misleading and that all triptans have similar effects on vasoconstriction.[3] In a single group study of 10 patients without coronary artery disease who received intravenous eletriptan (80 mg over 30 minutes) after a placebo infusion of normal saline over 10 minutes, eletriptan showed no significant effects on constriction of the coronary arteries, as demonstrated by angiography at regular intervals of infusion.[4] However, this theoretical, comparative benefit has not been demonstrated in studies reporting cardiovascular outcomes.

In summary, the proposed lower cardiovascular risk of eletriptan is based on a challenged in vitro study and a small study of intravenous eletriptan (not used in practice) in humans without coronary artery disease. Because triptans as a class have relatively small cardiovascular risk in patients without coronary artery disease, selection is best supported by the clinician's assessment of effectiveness, safety, pharmacokinetics, availability, and insurance coverage.

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Editor's Note: This letter was sent to the authors of "Acute Migraine Headache: Treatment Strategies," who declined to reply.

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