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Update in respiratory sleep disorders: Epilogue to a modern review series

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This review series summarizes research in the fields of sleep and breathing, highlighting major progress made in recent years. Based on these advances, we use this epilogue to make predictions for our field and perhaps to help guide further progress.

NEW DIAGNOSTICS

1. **Wearable technologies to diagnose obstructive sleep apnoea (OSA)**: Wearable technologies are increasingly being used to monitor various aspects of health, including sleep.[1] Validation studies on wrist-worn devices suggest that we are rapidly moving towards devices that can reliably monitor and stage sleep.[2] Efforts are underway to diagnose OSA using such technologies.[3] Remote monitoring approaches may also be helpful to provide patient engagement and to allow clinicians to identify and intervene on patients who are struggling with therapy.[4]

2. **Plasma biomarkers to diagnose and risk stratify OSA:** Biomarkers are being used increasingly to diagnose various conditions, for example plasma exosomes and microRNAs are being applied to OSA such that a clinician may ultimately be able to diagnose a patient with OSA based on a blood test.[5,6] Moreover, these

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approaches may provide some insight into why a given patient has OSA and what is the risk of a particular complication.

3. **Genome sequencing for individuals to predict risk of OSA and risk of OSA complications:** Genetics studies are also providing insight into OSA risk and mechanisms.[7] Big data approaches are now being applied to sleep medicine by using huge sample size to answer important questions.[8] By identifying patients at risk of developing OSA, preventative strategies could be used in high-risk patients before complications develop or prior to the occurrence of irreversible changes, for example apoptosis in the hippocampus[9] and age-related changes.[10]

NEW CAUSAL PATHWAYS AND APPROACHES

1. **Individualized therapy:** The appreciation that not all OSA patients get their disease for the same reason has led to the concept that individualized therapy could be used for patients depending on the underlying mechanism of disease[11] For example, a patient with a primarily anatomical problem at the level of the velopharynx may benefit from palatal surgery, whereas a patient with dysfunction in upper airway dilator muscles may have a good response to hypoglossal nerve stimulation.[12] On the other hand, a patient with unstable ventilatory control (high-loop gain), may see improvement in OSA with oxygen or acetazolamide, interventions which can effectively reduce the loop gain.[13] This individualized approach to therapy will require rigorous outcome data and methods to determine underlying mechanisms using clinically accessible data (e.g. plasma markers, sophisticated analyses of sleep recordings, etc.).[14,15]

2. **Drug therapy for OSA:** Advances in our understanding of the neuropharmacology of brainstem control have enabled targeted approaches to therapy.[16] A medication that could be used to augment hypoglossal motor output during sleep, or stabilize the ventilator control or perhaps mitigate OSA complications (e.g. by blocking the end organ impact of oxidative stress or sympathoexcitation) would be a valuable addition to treatment options.

3. **Alterations of microbiome to improve OSA and its complications:** Recent insights into the role of gut bacteria have shown definitively that the microbiome is an important factor in many common diseases including obesity and atherosclerosis. Studies are now suggesting that the intermittent hypoxia which defines OSA can lead to alterations in gut bacteria which in turn can yield metabolic alterations in the circulation with associated end organ effects.[17,18] In future, different dietary and antimicrobial approaches could be used to mitigate the risk of OSA and its complications.

VALUE-BASED PURCHASING AND QUALITY IMPROVEMENT

1. **OSA treatment to prevent complications and to reduce expenditures:** An upcoming trend in healthcare is the move towards *value-based purchasing* such that (in some countries) reimbursement will be tied to improvement in outcomes,

rather than simply rewarding the *quantity* of care provided. This trend will represent an opportunity for the sleep field, for example treatment of OSA, which reduces perioperative complications, at least in some individuals.[19] Similarly, addressing sleep disorders in congestive heart failure, diabetes, COPD and accelerated cognitive decline may serve to improve the wellbeing of these patients from the standpoint of quality of care and health outcomes.[20–22]

FUTURE STUDIES

We anticipate a number of areas of future study and development but summarize a few here:

1. **Big data approaches:** Large databases are now being used by the sleep field to address issues with positive airway pressure (PAP) adherence, to study the natural history of OSA and to predict which patients may be at risk of important complications.[8] Rigorous studies are needed to assess the new technologies, which are being developed to allow patient engagement and feedback, attempting to optimize PAP adherence.[4]

2. **Diet, exercise and sleep are the three pillars of health:** Advocacy for the importance of sleep and sleep health is occurring via large-scale public education efforts in many countries. For example, the general public is now focusing increasingly on issues around cognition and aging, but there is generally minimal appreciation for the impact of healthy sleep on these outcomes.[23–25]

3. **New health care delivery models for OSA:** The recognition that the number of sleep specialists is grossly inadequate for the massive numbers of afflicted OSA patients has led to discussion about alternative health care delivery approaches (e.g. using nurse practitioners or primary care physicians).[26] New technologies may also provide opportunities to diagnose and treat uncomplicated OSA effectively, without the need for direct specialist involvement.

The sleep field is undergoing an exciting period of knowledge expansion and increased appreciation. We hope that this review series has provided food for thought and a pathway to future progress.

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