K A Jellinger
Institute of Clinical Neurobiology, Kenyongasse 18, A-1070 Vienna, Austria; kurt.jellinger@univie.ac.at

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The specificity of prescription patterns in secondary stroke prevention

We would like to comment on the important report by Landi and colleagues about the factors associated with a reduced likelihood of receiving secondary stroke prevention treatment[1] and present our own data. We have demonstrated that in community-dwelling patients with chronic atrial fibrillation, living alone or in rural areas, history of previous falls, and cognitive and functional impairments are independent factors that result in physicians prescribing aspirin instead of anticoagulants, thus disregarding the common guidelines for stroke prevention.[2 3] We have also shown that in some cases it does not mean malpractice.[3] In elderly patients, a geriatric assessment including a shrewd evaluation of the psychosocial conditions can guide physicians in the selection of the correct treatment, thus avoiding the risks related to anticoagulants in individuals at high risk of falls or with inability to comply with regular blood monitoring.[2–5]

Our data are only partially comparable with those of Landi and colleagues, since in their study a significant number of the reported undertreatment concerns aspirin and triclopidine, drugs that have an unfavourable risk–benefit ratio in comparison with anticoagulants, even when they are prescribed for individuals living alone, with a low education level and poor cognitive or functional performance. In these conditions, low compliance is not enough of a risk and does not justify undertreatment. As a matter of facts, in the clinical conditions described by Landi and colleagues, an ''ageist'' cultural background prevails without real clinical motivation.

The difference between the two sets of data suggests that physicians need to be taught to consider the complexity of the medical scenario and to distinguish incorrect prescribing patterns due to limitations imposed by cultural factors from the rational behavior of physicians who adopt a multidimensional model of care and avoid treatments commonly recognised as beneficial but burdened by a high cost–benefit ratio.

G Bellelli
Rehabilitation Unit ''Ancelle della Carità'' Hospital, 26100, Cremona Italy and Geriatric Research Group, Brescia, Italy

M Trabucchi
''Tor Vergata'' University, Rome Italy and Geriatric Research Group, Brescia, Italy

Correspondence to: G Bellelli, MD, Head, Rehabilitation Unit, ''Ancelle della Carità'' Hospital, 26100, Cremona Italy; giuseppebellelli@libero.it; bellelli-giuseppe@poliambulanza.it

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Authors' reply

The data presented by Bellelli and Trabucchi confirm our findings suggesting that many older adults do not receive secondary stroke prevention treatment.[1] However, we really do not believe that our results indicate only an ''ageist cultural background without real clinical motivations''. Indeed, in our article we recognised that the decision of not to treat could not be considered as ''undertreatment'', but it may be related to the uncertainty about the cost-effectiveness of the treatment in a frail population. These doubts are not always unrealistic, especially among frail post-stroke elderly individuals, who characteristically have a high number and complexity of associated diseases, with a concomitant higher risk of drug interactions and adverse drugs events.[2] Furthermore, the reduced rate of treatment observed in our study is not only explained by potential risks in frail elderly patients, but also by uncertainties about the potential benefits.[3 4] In fact, the most important evidence of antiplatelet or anticoagulant medications after cerebrovascular accidents is substantially based on non-disabling ischaemic stroke. Evidence about the benefits of secondary stroke prevention is much more limited in the frail elderly population with severe physical and/or cognitive impairment. In this respect, it is important to underline the fact that the data presented by Bellelli and Trabucchi are based on a sample of community dwelling patients with atrial fibrillation, that ''per se'' is an indication to treat. In contrast, our study sample, which was based on patients receiving home care programmes indicating that an important and disabling health problem was in place, included a frailer population.[5] In this respect our results can not be generalised to all healthy community dwelling elderly individuals. However, we acknowledge that studies addressing the efficacy of secondary prevention treatment are needed, especially for frail and functionally impaired older individuals who have suffered a stroke.

F Landi, G Onder, R Bernabei
Centro Medicina dell'Invecchiamento, Istituto di Medicina Interna e Geriatria, Universita' Cattolica Sacro Cuore, Rome, Italy

Correspondence to: Dr F Landi; francesco_landi@rm.unicatt.it

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Relationship between stridor and sleep apnoea syndrome: is it as simple as that?

We read with interest the article by Hirayama *et al*[1] in which the authors, using an original imaging method, low field magnetic resonance fluoroscopic study, proposed that upper airway obstruction precedes laryngeal occlusion causing the stridor in patients with multiple system atrophy (MSA). This issue of nocturnal stridor in MSA is of great importance since it is a common cause of sudden death and a recognised prognostic factor in this disease.[2] It affects about 19% of patients as shown in our series and by others.[3] We feel that the relationship proposed between obstructive apnoeic respiratory events and stridor is not as simple as suggested by the authors and must be considered in light of classical standardised polysomnographic (PSG) data.

In our own series, 18 consecutive patients with MSA were assessed for night-time disturbances by all-night standard PSG with continuous synchronised audiovisual recording. Nocturnal stridor occurred in 10 patients and, except in one patient, was always accompanied by breathing disorders, mostly apnoeic, with or without significant oxygen desaturation. In four patients, obstructive sleep apnoeas (OSA) occurred without stridor, and one of these patients presented predominantly with central apnoea that also occurred while awake. Among the patients with stridor, four presented predominantly OSA and one mainly central apnoea. Mixed and prolonged apnoea, up to 53 s, was seen along with stridor in five patients and was isolated in two others. Episodes of mixed apnoea were typical in their occurrence as

they were always preceded by heavy, prolonged inspiratory effort and stridor, indicating upper airway obstruction. Such episodes were not detected in OSA patients without stridor. Apnoeic events of any type were in most cases followed by the recurrence of snoring and not by an inspiratory stridor sound.

Thus, there seems to be a wide variety of combined sleep-related breathing disorders ranging from a majority of obstructive apnoeas to stereotyped mixed apnoeas of very long duration and sometimes preceded by stridor in MSA.

Nocturnal breathing disturbances in MSA are due to the complex involvement of multiple brainstem nuclei, leading to a defect in the respiratory control system independently of the occurrence of stridor.[2] Among these breathing disorders, OSA are the most common and may occur in non-obese MSA patients even in the absence of stridor, thus indicating that the mechanism underlying the two events is different. The higher incidence of OSA observed in MSA patients may also be due to the severity of bradykinesia and the fact that patients with severe MSA lie predominantly, if not always, in the supine position while asleep. The reduction of nocturnal obstructive events during lateral position in patients with OSA has already been reported.[4] In our patients, who were audio monitored, stridor was not followed by typical obstructive apnoea nor was the apnoea ended by a stridor. Thus, we believe that stridor and OSA in MSA are different and independent events. We also found that mixed apnoea occurred stereotypically and was very prolonged and often preceded by a harsh sound typical of stridor, as documented by audio monitoring.

Non-invasive continuous positive air pressure (CPAP) should be proposed for relief of sleep breathing disorders. It has been used successfully to treat stridor and OSA in MSA patients.[5] In our series, nine patients accepted CPAP treatment (six with stridor and sleep apnoea and three with isolated OSA). One patient died before initiation of the treatment and two patients without sleep complaints dropped out after one week because of lack of tolerance despite having a severe apnoea/hypopnoea index. Since the onset of CPAP treatment, both patients and their spouses reported better sleep, improved daytime alertness and wellbeing. For some patients, getting used to CPAP took up to a month, after which it was generally well tolerated. After a mean follow up period of 10 months, the patients' compliance with the continued use of CPAP was satisfactory and their relatives did not report any recurrence of stridor.

Thus we feel that the relationship between stridor and sleep apnoea is far from clear, especially considering the polysomnographic association of stridor and mixed apnoea that we found. Complex supranuclear neurological dysfunction may account for this association, but further studies are however needed to clarify this issue and better establish the indications for CPAP.

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I Ghorayeb, B Bioulac
Service d'Explorations Fonctionnelles du Système Nerveux, Bordeaux cedex, France

F Tison
Service de Neurologie, CHU de Bordeaux, Bordeaux, France

Correspondence to: Dr I Ghorayeb, MD, PhD, Service d'Explorations Fonctionnelles du Système Nerveux, Hôpital Pellegrin, Place Amélie Raba-Léon, 33076 Bordeaux cedex, France; imad.ghorayeb@umr5543.u-bordeaux2.fr

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Authors' reply

We would like to thank Dr Ghorayeb *et al* for their interest in our paper and their comments. We agree with the view that the relation between stridor and apnoea in MSA is very important.[1] Unfortunately, in our experimental procedure, we could not establish a correlation between the image of the vocal cords and upper airway and stridor symptoms because it is difficult to record airflow and vocal sound simultaneously in a magnetic resonance imaging (MRI) recording.[2]

In obstructive sleep apnoea syndrome (OSAS), even when the upper airway was obstructed completely, the vocal cords were not obstructed. Therefore, stridor does not develop although snoring may occur in OSAS. In contrast, MSA patients had an obstructed upper airway, which was frequently accompanied by stenosis of the vocal cords. However, we did not find stenosis of the vocal cords without stenosis of the upper airway. If the stridor is produced by stenosis of the vocal cords and snoring is produced by stenosis of the upper airway, snoring should be accompanied by stridor in all MSA patients. In fact, we observed that the initial narrowing of the larynx and pharynx produced snoring. Ghorayeb *et al* point out that OSA (SAS with upper airway obstruction) can commonly occur even in non-obese patients with MSA without the presence of stridor. We agree with this observation, but in this study, we did not find stenosis of the vocal cords without upper airway stenosis, so none of our patients developed stridor without snoring. We observed the patients in the MRI room to identify the sleep state and the presence of snoring and stridor, and we found that the highest pitch vocal sound appeared after heavy and prolonged inspiratory effort. This phenomenon is very similar to Ghorayeb *et al*'s observation of apnoea and stridor. We also suppose that the phenomenon of apnoea in MSA patients occurs with confinement of stenosis of the upper airway. Therefore, we think that some patients in MSA with SAS can be treated with CPAP similar to OSAS patients. However, the effect of CPAP could be diminished, since the respiratory centre is eventually involved with the progression of disease in MSA, and central apnoea and abnormal respiration may appear. Further study is required to clarify the indication of CPAP in patients with MSA.

The mechanism of SAS in MSA is unclear. Our study showed complete obstruction of the upper airway and vocal cords occurred in MSA even with the presence of tongue atrophy and without narrowing of the larynx. Thus, we suggest that there is another mechanism involved distinct from that of OSAS. Some reports have stated that a dystonia-like phenomenon was present in the vocal cords in the stridor through electromyographic study, suggesting a similar mechanism to be present in the progression of upper airway obstruction.[3 4]

M Hirayama, G Sobue
Department of Neurology, Nagoya University Graduate School of Medicine, Nagoya, Japan

H Fukatsu
Department of Radiology, Nagoya University Graduate School of Medicine, Nagoya, Japan

Y Koike
Department of Health Sciences, Nagoya University Graduate School of Medicine, Nagoya, Japan

Correspondence to: Professor G Sobue; sobueg@med.nagoya-u.ac.jp

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BOOK REVIEWS

Biological psychiatry, Vol 1 and 2

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The European editors of these two volumes have brought together contributions from all over the world and from a range of relevant specialties. Although the majority of the authors work in psychiatry, the other disciplines represented include neurology, psychology, physiology, and pharmacology. Guided by clear concepts regarding the anatomy of the book overall as well as the individual chapters, the editors have succeeded in providing an integrated and comprehensive review of biological psychiatry.

The introductory chapters address conceptual and measurement issues in biological psychiatry. The next section comprises a series of chapters on basic principles, reviewing key topics such as animal models, monoaminergic transmitter systems, neuroendocrinology, immunology, psychophysiology, neuropsychology, brain imaging,