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LETTER

Modafinil: a novel alternative to non-invasive ventilation in hypercapnic respiratory failure?

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Dear editor

Nowadays non-invasive ventilation (NIV) is a common therapeutic option in chronic hypercapnic respiratory failure, especially in chronic obstructive pulmonary disease (COPD).[1] Even though there is not robust data showing mortality or morbidity benefits, it appears to improve quality of life and reduce admissions for exacerbation.[1,2] However, there will always be a group of patients where NIV is not an option, because of poor compliance or side effects.

Parnell et al used modafinil, out of label, in a very small heterogeneous group of hypercapnic respiratory failure patients unwilling to carry out NIV, with good results (benefic effects in blood gases, exacerbation admissions, with no adverse effects).[3]

This pilot study open a new door to control hypercapnic respiratory failure in noncompliance patients with NIV. We understand limitations of this brief study, but consider, however, some key aspects need to take into account to a proper clinical extrapolation.

First, mechanism of acute and chronic hypercapnic are numerous and complex interaction, not only during daytime and night time period, muscular weakness play a central role in this pathways and respiratory central breathing could be influenced to chemical and mechanical properties of lung and upper airways.[1,2]

Second, regarding limits of hypercapnic and how monitoring response to modafinil therapy is a key cornerstone.

Third, other co morbidity as chronic renal failure or neurologic conditions influence by hypercapnic could difficult interaction of modafinil as coincident psychiatric drugs like antidepressive or anxiolytic, that in some cases are associated in chronic respiratory insufficiency.[4–6] Additionally, coexistence of COPD and sleep breathing disorders determinate more complexity in this prescription.[7,8]

In our opinion, the good results shown in these six patients justify the conduct of extended studies on the action of modafinil in hypercapnic respiratory failure. However, if this drug may improve the quality of life, reduce health costs and safe alternative to non-invasive mechanical ventilation are still open questions.

Disclosure

The author have no conflicts of interest in this communication.

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Authors' reply

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Dear editor

Thank you very much for a copy of the letter from Dr Matos and Dr Esquinas for our comments.

We wish to thank them for their feedback and we agree with all their points.

Hypercapnic respiratory failure as discussed under Point No 1 does have many factors that may not yet be fully understood but may contribute to both acute and chronic hypercapnia as Dr Matos and Dr Esquinas suggest. We found the published symposium on sleep-induced hypoxemia in patients with COPD very thought provoking and supportive of their current suggestions,[1] and we have included ideas from it in our planned further study of modafinil.

We plan to commence shortly a further study of 60 patients with chronic hypercapnic respiratory failure who will be openly randomized to standard care or standard care with modafinil 200 mg. We hope that this will give information about modafinil's action and time course that may increase our understanding as mentioned under their Point No 2.

Modafinil is metabolized by the liver and liver disease is an important contraindication along. Renal function including severe chronic renal failure (creatinine clearance <20 mL/min) is not reported to significantly affect the pharmacokinetics of modafinil at 200 mg, although modafinil acid is increased ninefold. However the manufacturers have limited data in severe renal failure.

The comments by Dr Matos and Dr Esquinas with regard to possible benefits to quality of life and health costs compare with standard NIV are important questions that need to be answered. Following our published case series on modafinil we were very interested to read the published study in Thorax.[2] This examined the use of nocturnal NIV in patients with prolonged hypercapnic respiratory failure in COPD. Interestingly this showed that randomization to standard care with nocturnal NIV or standard care alone, showed no difference in re-admission or death rate after 1 year of treatment. With 65% of the NIV arm either dying or being re-admitted compared with 64% receiving the standard care. Since NIV has cost implications and COPD is increasing considerably, treatments used should be cost effective and worthwhile.

Disclosure

The authors report no conflicts of interest in this work.

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