Long-term progestin therapy for female chronic respiratory insufficiency?

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Summary End-stage chronic obstructive pulmonary disease often leads to hypercapnic respiratory failure. Oxygen supplementation therapy may further aggravate hypercapnia and not all patients are compliant with non-invasive ventilation. This case documents successful control of chronic respiratory failure with medroxyprogesterone in a postmenopausal woman during 1-year follow-up.

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textbf{KEYWORDS}
Chronic obstructive pulmonary disease; Cyclical treatment; Hypercapnia; Medroxyprogesterone; Menopause; Respiratory stimulation

Introduction
The prevalence of chronic obstructive pulmonary disease (COPD) is increasing in both men and in women. Non-invasive ventilation is proposed for the hypercapnic respiratory failure in end-stage COPD but not all patients are compliant. In non-compliant patients, respiratory stimulation with progestins\textsuperscript{1,2} could be an option in those whose progesterone receptors are not down-regulated by high levels of androgen, i.e. in women.\textsuperscript{3} We previously showed that medroxyprogesterone acetate (MPA) markedly improves arterial blood gases in short term in chronic respiratory insufficiency.\textsuperscript{4} In postmenopausal women, the beneficial respiratory effects were maintained at least for 3 weeks after cessation of MPA therapy.\textsuperscript{4,5} Whether these beneficial effects are maintained long term is not known.

Case report
We followed the effects of a cyclic MPA therapy in a 76-year old woman with severe COPD and chronic respiratory insufficiency. Despite maximal bronchodilator therapy, her forced expiratory volume was 1.49 l (68% of predicted) and forced expiratory volume in one second 0.87 l (50% of predicted). Because of her tendency for carbon dioxide retention, she was not eligible for long-term oxygen therapy. She was not willing to use non-invasive
ventilation, and continued to suffer from regular morning headaches. A cyclic regimen of 2 weeks on and off MPA 60 mg daily was started. MPA was divided in two doses of 30 mg each, which were administered in the evening 2 h apart to achieve maximum concentrations during night. There were no changes in her regular medication except introducing MPA. No oral steroids, antibiotics, neurological medicines or analgetics were administered. Her blood gases improved and her morning headaches vanished with treatment.

Due to tenderness of her breasts, MPA dose was halved during the second cycle, but her blood gases deteriorated. The gradual increase of MPA back to the dose of 60 mg per day was successful without side effects. By now, our patient has used MPA on a cyclic regimen for 12 months, and her blood gases have continued to improve (Table 1). MPA seems to maintain its efficacy in long term and is well tolerated. Despite respiratory stimulation, her nocturnal and exertional dyspnoea improved rather than aggravated. The initial tenderness of breasts was the only adverse effect observed. The patient attributed her improved quality of life to the therapy and preferred to continue.

### Discussion

MPA stimulates breathing in males\(^1,2\) and in females.\(^4\) However, studies investigating the long-term efficacy and feasibility of progestins to control respiratory insufficiency are lacking. Our case study suggests that blood gases, morning headaches and quality of life may markedly improve during progestin therapy in patients with respiratory failure due to end-stage COPD. The present case report also provides evidence that the beneficial effects are maintained in long-term therapy.

Based on our previous observations of prolonged respiratory effects in postmenopausal women, our patient used MPA on a cyclical basis.\(^4,5\) The prolonged effect seems to be specific for women, since in healthy men the ventilatory effects subside within 14 days after a 2-week treatment with MPA of 60 mg daily.\(^2\) Progesterone concentrations are low in both men and postmenopausal women but down-regulation of progesterone receptors by androgens,\(^3\) may shorten the progestin effect in men. In premenopausal women, the secretory pattern of progesterone is strongly affected by the phase of the menstrual cycle. Therefore, it may be more physiological to administer progestins on a cyclical than on a continuous basis.

Patients with end-stage COPD often need hospitalisation due to hypercapnic respiratory failure. Therefore, any new treatment options to avoid hypercapnia would be of high interest. Selected cases of respiratory insufficiency could respond to progestins with respiratory stimulation. Comprehensive studies into the feasibility and the efficacy of long-term MPA therapies in postmenopausal women are therefore warranted.

### References


### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before MPA</th>
<th>During MPA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preceding</td>
<td>Baseline</td>
</tr>
<tr>
<td>PaCO(_2) (kPa)</td>
<td>5.7–7.6</td>
<td>6.8</td>
</tr>
<tr>
<td>PaO(_2) (kPa)</td>
<td>5.1–5.9</td>
<td>6.1</td>
</tr>
<tr>
<td>pH</td>
<td>7.33–7.44</td>
<td>7.37</td>
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<tr>
<td>HCO(_3) (mmol/l)</td>
<td>26.7–41.9</td>
<td>26.0</td>
</tr>
<tr>
<td>BE (mmol/l)</td>
<td>3.2–8.1</td>
<td>2.2</td>
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</tbody>
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