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CASE REPORT

Episodes of shortness of breath induced by prednisone

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ABSTRACT

Although anecdotal reports pointing to the occurrence of episodes of shortness of breath due to prednisone use have been published, systematic evidence is lacking. In this manuscript we report on an n=1 trial in a patient using prednisone for polymyalgia rheumatica. With this approach we can confirm that prednisone may cause episodes of dyspnoea and we provide potential explanations for this side effect.

KEYWORDS

Shortness of breath, hyperventilation, prednisone

INTRODUCTION

Prednisone has been used effectively in many diseases and is prescribed frequently by many doctors. Prednisone is known to cause many side effects. Its use may lead to the development of diabetes mellitus, osteoporosis and myopathy in skeletal muscles and in muscles involved in respiration.[1] Although many patient stories on the internet describe that use of prednisone may lead to transient episodes of shortness of breath accompanied by hyperventilation, this has not been described in medical literature. Through a so-called N-of-1 study we describe an association between prednisone and shortness of breath.

CASE REPORT

A 71-year-old woman complained of pain in the upper and lower extremities. She had difficulty in combing her hair and the pain was associated with extreme tiredness and morning stiffness. A diagnosis of polymyalgia rheumatica (PMR) was made. Her complaints decreased shortly after high dosages of prednisone.

A few weeks after starting prednisone the patient complained of shortness of breath at rest and on mild exertion. The patient had the feeling that she could not inhale enough oxygen. Her past history was uneventful and she had smoked cigarettes until 32 years ago (about 20 pack-years).

During a routine outpatient visit (with use of 20 mg prednisone a day) the patient had a breathing frequency at rest of 26 per minute. Blood gas analysis showed a respiratory alkalosis (pH 7.63; pCO_2 17 mmHg; HCO_3- 17.4 mmol/l and pO_2 132 mmHg (*table 1*; normal values). A possible cardiac cause was excluded after a thorough cardiological examination (ECG, echocardiogram, cardiac MRI and coronary angiography were normal). A pulmonary cause was also considered unlikely (X-thorax, lung function test, exercise testing and right catheterisation were all normal). All the tests were performed while she was taking prednisone.

Her breathlessness decreased when the dose of prednisone was lowered. When she had an exacerbation of the PMR it was always necessity to increase the dose of prednisone, as the other therapeutic options, such as non-steroidal anti-inflammatory drugs and methotrexate, were unable

Table 1. *Normal values blood gas*

pH	7.35 – 7.45
pCO_2	35 – 45 mmHg
$pHCO_{3^-}$	22 – 26 mmol/l
BE	-2.0 – 3.0 mmol/l
pO_2	75 – 100 mmHg
O_2 saturation	0.92 – 0.98

BE = base excess

to control the PMR symptoms. As an increase in the dose of prednisone clearly led to an increase in her shortness of breath, we hypothesised that prednisone was the cause of the dyspnoea.

N-OF-1 STUDY

To demonstrate the association between prednisone and shortness of breath, one of the authors undertook a total of five home visits to the patient. During this period the patient's condition was stable. Because of the PMR symptoms, she was taking 2 mg prednisone every morning. The patient was still experiencing PMR symptoms with this dosage, but was unwilling to take the higher dose because of the shortness of breath associated with higher dosages of prednisone. However, she did take 4 mg of prednisone when the pain was severe. The patient noticed a clear increase in her shortness of breath when she took the higher dose. The time between taking the (extra) prednisone and the shortness of breath was about six hours and disappeared after 12 to 14 hours.

We therefore decided to test whether there was a linear association between the prednisone dosage and her respiratory symptoms. This was achieved by measuring several parameters while she was taking different amounts of prednisone: three measurements with the normal dose of 2 mg, and one measurement with 4 mg and 8 mg, respectively. The parameters that were measured included the Medical Research Council (MRC) dyspnoea scale (grade 1 (not troubled by breathlessness except on strenuous exercise) to grade 5 (too breathless to leave the house, or breathless when dressing or undressing)),[2] and the Karnofsky score (score 100: able to work and no complaints to score 10: moribund).[3] Other measurements recorded were breathing frequency at rest and after light exercise (after a walk of about 400 metres at normal speed). Blood gases were also analysed at two time points. The time of intake of prednisone was usually around 06.30 am. All measurements were taken between 4 pm and 8 pm. The results of the measurements are shown in *table 2*. At measurement 3, after ingesting 8 mg of prednisone, shortness of breath was so severe that the patient was unable to exercise.

Due to the intensity of pain experienced by the patient during the first arterial puncture it was decided to undertake a venous puncture during the second blood test. Analysis of the results showed a clear difference in both the breathing frequency at rest and breathing frequency after light exercise. There were also clear differences on the dyspnoea scale. The small difference between the outcomes on the Karnofsky score were attributed to the patient's PMR symptoms, meaning she was unable to perform several activities, independent of prednisone.

Blood tests showed that there was a respiratory alkalosis after ingestion of 8 mg prednisone and a normal blood gas after ingestion of 2 mg. The use of arterial and venous blood should not produce any differences given that the pH and bicarbonate percentage are comparable.[4,5]

DISCUSSION

PMR symptoms may lead to a situation where patients require (maintenance) doses of prednisone for many years.[6] This is already known to be associated with numerous symptoms. However, the relationship between episodes of shortness of breath and prednisone has not been previously described in medical literature. But when we did a simplified search through the use of Google (and search with the terms prednisone and shortness of breath or breathing difficulties) this relationship is mentioned

Table 2. *Results of measurements*

	BF/min in rest	BF/min after light exercise	Grade shortness of breath (MRC dyspnoea scale)	Functional limitation (Karnofsky) (%)	Blood gases
Measurement 1 (intake 4 mg prednisone)	16	24	4	70	
Measurement 2 (intake 2 mg prednisone)	14	18	2	80	
Measurement 3 (intake 8 mg prednisone)	18	-	5	70	Arterial: pH 7.48; pCO_2 30; HCO_3 21.8; BE -0.3; pO_2 70; O_2 saturation 0.96
Measurement 4 (intake 2 mg prednisone)	14	18	2	80	Venous: pH 7.37; HCO_3 27.0
Measurement 5 (intake 2 mg prednisone)	14	20	2	80	

BE = base excess; BF = breathing frequency.

several times. We tried to objectify the relationship between episodes of shortness of breath and prednisone with the abovementioned N-of-1 study.
The most plausible explanation for the increase in respiratory rate is that prednisone may pass through the blood-brain barrier and stimulate the breathing centre. Another hypothesis was that the shortness of breath was due to hyperventilation induced by psychological effects. However, her breathlessness only developed several hours after the intake of prednisone and also disappeared after a few hours. So, in our opinion, this hypothesis is not plausible. A myopathy of the breathing muscles as a potential cause of the symptoms is also implausible, mainly because the complaints were episodic.

The above N-of-1 study shows that prednisone side effects should be considered when a patient presents with shortness of breath. Our case has demonstrated that it took numerous consultations before the cause of the symptom became clear. Furthermore, it took many, very expensive, additional examinations, which in retrospect were not necessary.

REFERENCES

1. van Balkom RH, van der Heijden HF, van Herwaarden CL, Dekhuijzen PN. Corticosteroid-induced myopathy of the respiratory muscles. Neth J Med. 1994 Sep;45(3):114-22.
2. Fletcher CM, Elmes PC, Fairbairn AS, Wood CH. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. Br Med J. 1959 Aug 29;2(5147):257-66.
3. Karnofsky DA, Barchenal JH. The clinical evaluation of chemotherapeutic agents in cancer. In: Macleod CM, editor. Evaluation of chemotherapeutic agents. New York: Columbia University Press; 1949. p. 191-205.
4. Kelly AM, McAlpine R, Kyle E. Venous pH can safely replace arterial pH in the initial evaluation of patients in the emergency department. Emerg Med J. 2001 Sep;18(5):340-2.
5. Kelly AM, McAlpine R, Kyle E. Agreement between bicarbonate measured on arterial and venous blood gases. Emerg Med Australas 2004. Oct;16(5-6):407-9.
6. Vos PAJM, Bijlsma JWJ, Derksen RHWM. Polymyalgia rheumatica and temporal arteritis. Ned Tijdschr Geneeskd. 2005 Aug 27;149(35):1932-7.