CASE REPORT

The lady who presented as a "sleep emergency"

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Abstract

The case of a 74 years old hypertensive and obese lady is reported. She had repeated hospitalizations following episodes of left ventricular failure A polysomnographic study confirmed the diagnosis of obesity hypoventilation syndrome. This condition is briefly reviewed.

Keywords: obesity hypoventilation syndrome, hypertension, atrial fibrillation, bilevel positive airway pressure therapy

Case history

A 74 years old lady, who had been a homemaker, presented to the emergency room with progressive shortness of breath resulting into acute respiratory distress over one day. She had been having shortness of breath since last six years; initially occurring on moderate exertion that would be relieved after resting for a while. There were no particular seasonal variations. Her breathlessness would increase with exposure to dust and smoke. Breathlessness had been gradually increasing in grade and frequency over the years; lately she would be breathless even after walking a few steps. Since the last six months, her breathlessness would increase on lying supine. Her symptoms progressed despite therapy with inhaled medication. She was bed bound for the last two weeks. She also complained of having cough with scanty, mucoid sputum at times, since three years. There was swelling of feet since six months.

She had experienced excessive daytime sleepiness since six months. She was noted to be a snorer by her family. She would wake up multiple times each night, occasionally with a choking or gasping sensation. She denied any nasal congestion or obstruction. She had been putting on weight since the last twelve years. On admission she weighed 90 kg and she was 156 cm in height.

She was hypertensive since 20 years and was on anti-hypertensive medication. There was no history of diabetes mellitus or thyroid dysfunction.

There was history of exposure to bio-mass fuel in the remote past. She had been hospitalized 5 yrs ago with breathlessness and anxiousness; a coronary angiography (CAG), that was then conducted, was normal; she had then been treated as hypertensive emergency.

She had been hospitalized six months ago, as well, with sudden onset shortness of breath. A 2-D ECHO had then revealed no RWMA; LV ejection fraction of 60%, concentric LV hypertrophy, mild aortic regurgitation; the aortic leaflets were thickened; the Troponin-I test was negative. The BNP value was 1200 (N<125); D-dimer 901 (N<278); CAG revealed non-critical CAD. Arterial blood gas (ABG) values revealed a paO_2 of 45 mmHg, and $paCO_2$ of 65 mmHg.

Three weeks ago, she was admitted to a local hospital, reportedly for "accelerated hypertension with LV dysfunction". She was managed conservatively with diuretics and oxygen therapy; however, she continued to be breathless, turned drowsy and unresponsive. She was therefore transferred to a referral hospital four days

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later for what was documented as "atrial fibrillation (AF) with CO_2 narcosis".

In the referral hospital, she was found to be breathless, conscious, drowsy, but arousable. Her pulse was approximately 139/min, irregularly irregular; respiratory rate 34/min, BP 110/83 mmHg; JVP was normal, edema was present. There was no icterus, pallor, clubbing. Chest auscultation revealed vesicular breath sounds with bilateral basal crackles. The CVS, CNS and abdomen examination were normal. The baseline investigations were as follows:

Hemoglobin: 11.3 g/dL, TLC: 8500/mm^3, DLC: P73, L24, M2, E1, blood culture: sterile, BUN: 11 mg/dl (10-50). The CK-MB was 23 (0.6-7.25); CPK: 47 (21-215), creatinine : 0.6 mg/dL(0.6-1.2), D-Dimer (semi-quantitative): 4.0 (0-0.5)µq/mL FEU, chloride : 96meq/l (93-108), potassium : 4.30 mg/dl (3.5-5.5). HBSAg, HCV and HIV were negative. SGPT: 57 IU (30-65). The albumin level : 2.8 g/dl (3.4-5); A/G ratio : 1.1; alkaline phosphatase: 182 IU (50-136); SGOT : 16 (15-37); bilirubin : 0.39 mg/dl (0-0.8); GGT :179 (5-85); globulin: 2.6 g/dl (2-4.1); LDH : 235 (230-460); NT Pro BNP; 2482 (0-125).The procalcitonin level was 0.073 (0-0.5 ng/mL), PT (INR) : 0.86 (0-1.4), free T4 : 1.34 (0.93-1.71), free T3 : 2.34 (2-4.4), TSH : 1.040 (0.27-4.2), troponin T : <0.010 (0-0.03), urinalysis: NAD, urine C/S : sterile. The ABG was suggestive of acute on chronic respiratory academia. She was intubated and mechanically ventilated. The period of ventilation was brief (48 hr) following which she was extubated. She was discharged on 8th day on inhaled LABA-ICS on controlled oxygen, ramipril, torsemide, aspirin, pantoprazole, diltiazem.

She was re-admitted to hospital after 14 days with progressively increasing shortness of breath and sleepiness. Her pulse was 124/min, irregularly irregular, RR 32/min, afebrile, BP 140/100 mmHg, sPO2: 88% on room air; 90-92% on 2 LPM O_2. Chest examination revealed bilateral vesicular breath sounds. Investigations showed Hb 12.2gm/dL, TLC 10,600, DLC P65, L30, E2, M3, platelets: 1,04,000/mm^3, urea: 45mg/dl, creatinine: 0.7 mg/dl, glucose : 88mg/dl, Na : 128meq/L, K: 4.3meq/L, Chest X-ray (Fig 1) showed cardiomegaly, ECG recorded atrial fibrillation (Fig 2). ABG: (FiO_2- 0.21): paO_2 24mmHg, pCO_2 60mmHg, pH 7.39, HCO_3 36meq/L, sPO_2 42%. On the second day ABG (on FiO2- 0.25) showed a paO2 56, pCO2 61, pH 7.34, HCO_3 32meq/L, sPO_2 84%. Bilevel positive airway pressure therapy was administered with

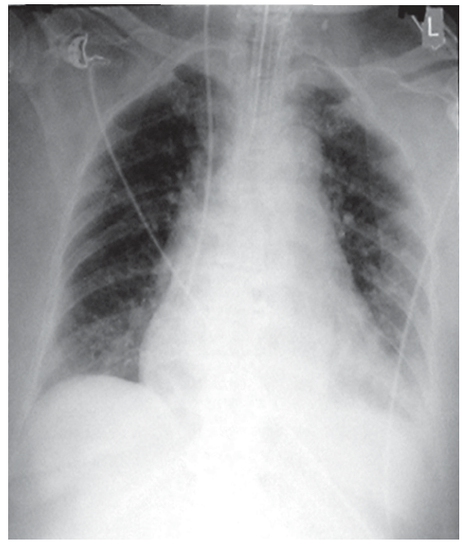

Figure 1: Chest X-ray showing cardiomegaly

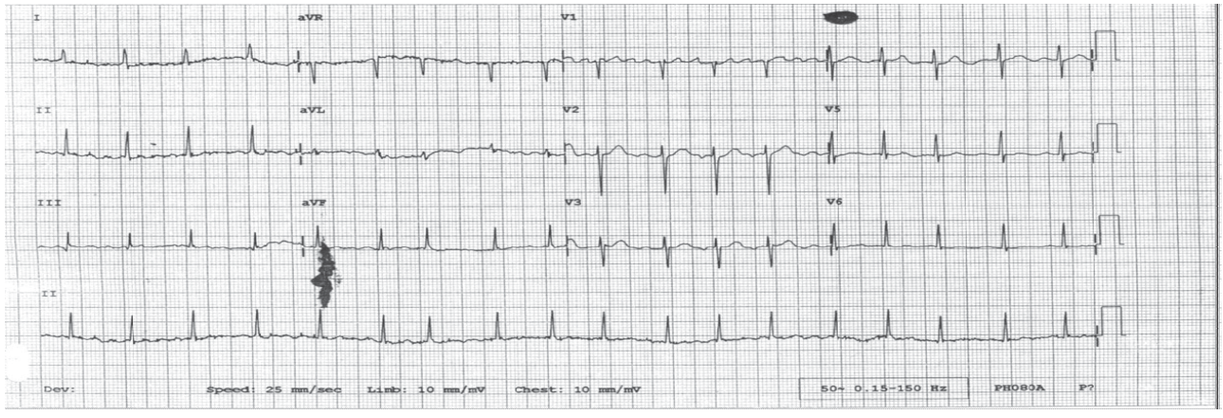

Figure 2: ECG showing atrial fibrillation

IPAP/EPAP:12/6cm and then 18/8 cm. She desaturated during sleep on FiO_2 0.28; therefore BiPAP was adjusted to 20/10cm on FiO_2 0.28. She slept well with sPO_2 90%, BP 150/94 mmHg, pulse 90/min, expirated tidal volume 240 ml. On the third day she was more comfortable. Her BP was 150/100 mmHg, sPO2 on FiO2 0.24: 94%. The ABG on room air was pH 7.437, PaO_2 47.5 mmHg, PCO_2 61.7 mmHg, HCO_3 41 meq/L. Bilevel PAP was adjusted to 24/10 cm. On the fifth day, her physical examination revealed a pulse rate of 82/min, BP 150/100 mmHg, RR 24-26/min, sPO_2 86% (FiO_2 0.21); her ABG on room air showed a pH of 7.438, pCO_2 55.4 mmHg, pO_2 45.8 mmHg, HCO_3 36.9 meq/L. She was being administered ramipril 5 mg od, torsemide 20 mg, aspirin 150 mg, pantoprazole 40 mg, enoxaparin 0.4 ml OD, diltiazem 60 mg TID; bilevel PAP was administered at pressure levels of 26/10 cm. On day 7, ABG showed pH 7.45, $paCO_2$ 54.6 mmHg, paO_2 52.3 mmHg, HCO_3 37.8, pulse 80/min, BP 140/90 mmHg, RR 22/min, spO_2 92%. A polysomnography was done and bilevel PAP adjusted to 26/12cm. (Figs 3-5)

On the fifteenth day following hospitalization, she was found to be afebrile; her pulse rate was 90/min, BP 160/90, RR 24, spO_2 82%; ABG: pH 7.45, pCO_2 47.8, pO_2 50.8, HCO_3 32.8. She was discharged on home ventilation and domiciliary oxygen therapy. Future plans for pulmonary rehabilitation and bariatric surgery were outlined for consideration.

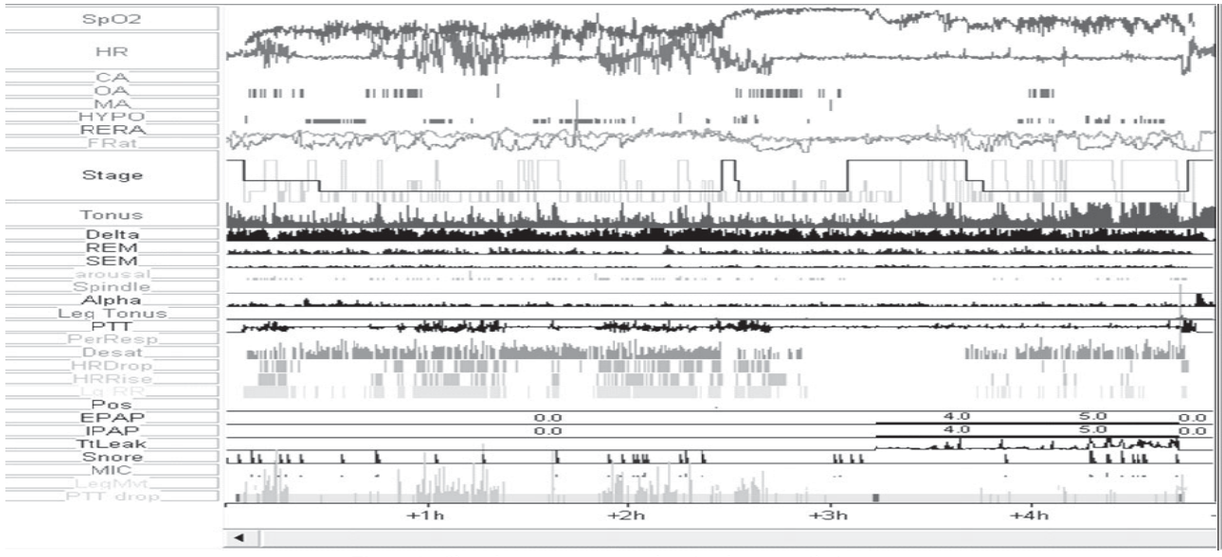

Figure 3: Sleep hypnogram trace showing hypoventilation

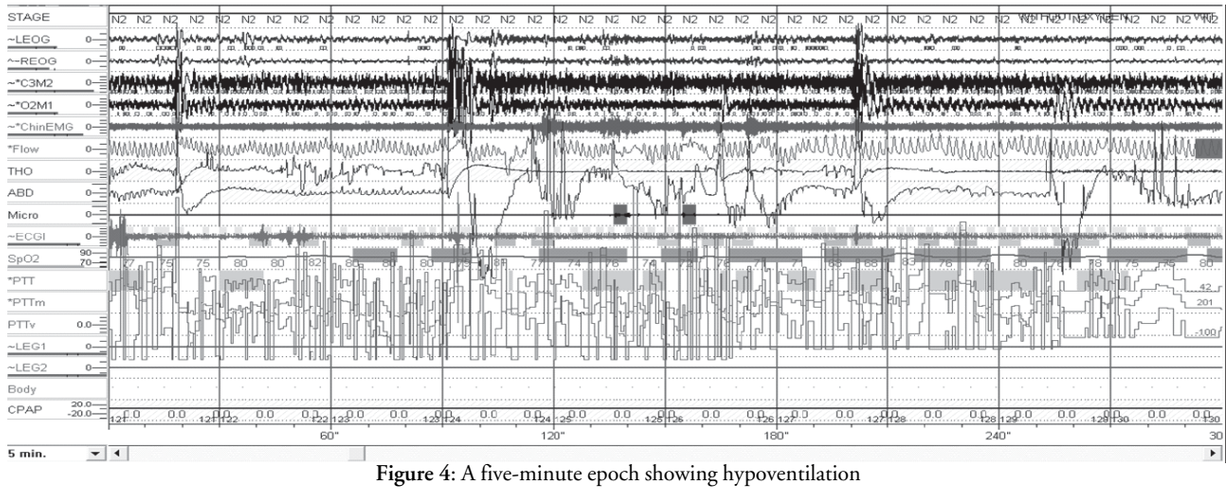

Figure 4: A five-minute epoch showing hypoventilation

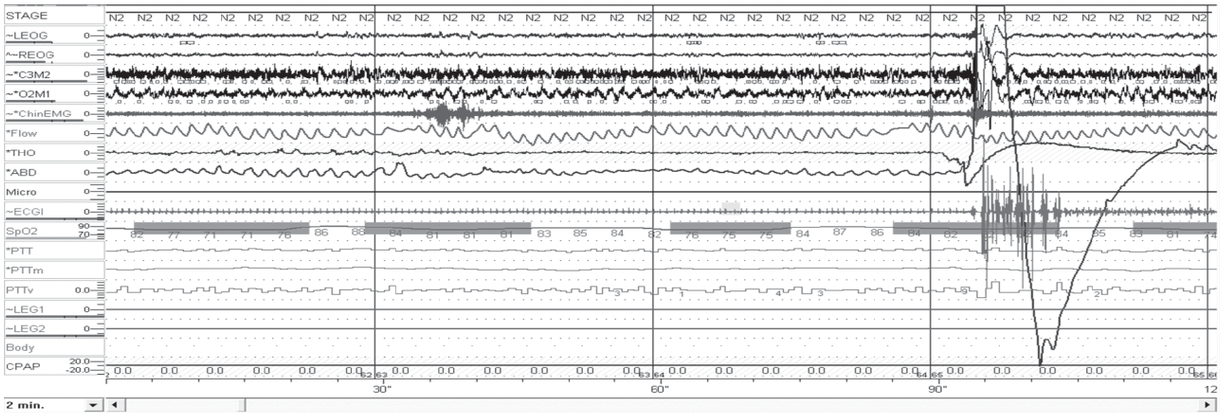

Figure 5: A two-minute epoch showing periods of reduction in airflow with de-saturation (hypoventilation)

Final diagnosis

Obesity hypoventilation syndrome, OSA, hypertension, diastolic dysfunction, atrial fibrillation, chronic respiratory failure type-II on home NIV with domiciliary oxygen therapy

Discussion

Most patients of obesity hypoventilation syndrome are first recognized while presenting to the ICU as acute-on-chronic respiratory failure[1]. This patient also was earlier being treated in isolation as "chronic asthma/COPD", "hypertension", "recurrent LVF". Inability to address the primary problem had led to a progressive deterioration in clinical status and quality of life, repeated emergency room visits and hospitalizations. Several conditions that present with hypercapnic respiratory failure, as outlined in Table-1, need to be considered in any such case.

The World Health Organization categorizes body mass index (BMI) values as follows. A BMI value of <18.5 is classified as underweight; 18.5-24.9-normal weight; 25.0-29.9-overweight; 30.0-34.9-class I obesity; 35.0-39.9-class II obesity; >40.0-class III obesity. The last category is often termed as severe or morbid obesity. Obesity hypoventilation syndrome is diagnosed only if the following three entities are present; obesity, chronic hypoventilation and sleep-disordered breathing. Chronic hypoventilation is described as awake daytime hypercapnia ($PaCO_2 \geq 45$ mm Hg and $PaO_2 \leq 70$ mm Hg); sleep disordered breathing (SDB) can manifest either as obstructive sleep apnea (apnea-hypopnea index $\geq$ 5 events/h, with or without sleep hypoventilation) present in 90% of cases, or non-obstructive sleep hypoventilation (apnea-hypopnea index $\geq$ 5 events/ h) in 10% of cases. Exclusion of other causes of hypercapnia is necessary before arriving at a diagnosis of OHS. These conditions include severe obstructive airways disease, severe interstitial lung disease, severe chest-wall disorders (eg, kyphoscoliosis), severe hypothyroidism, neuro-muscular disease, and congenital central hypoventilation syndrome.

The prevalence of OHS amongst patients of OSA who have a BMI of $\geq$ 30 has been found to vary between 9% and 20%[2]. Hypercapnia with OSA is unlikely to develop in patients with BMI $\leq$ 30 kg/m^2. In 90% of patients with OHS, the underlying cause of SDB is OSA.

Table 1: Conditions presenting with hypercapnic respiratory failure

Chronic obstructive pulmonary disease
Emphysema
Chronic bronchitis
Neuromuscular disorders
Amyotrophic lateral sclerosis
Muscular dystrophies - Duchenne and Becker dystrophies
Diaphragm paralysis
Guillain-Barré syndrome
Myasthenia gravis
Chest wall deformities
Kyphoscoliosis
Fibrothorax
Thoracoplasty
Central respiratory drive depression
Drugs - Narcotics, benzodiazepines, barbiturates
Neurologic disorders - Encephalitis, brainstem disease, trauma, poliomyelitis, multiple sclerosis
Primary alveolar hypoventilation
Obesity hypoventilation syndrome (OHS)

The remaining 10% have hypoventilation during sleep which is non-obstructive in nature (rise in $paCO_2$ during sleep of >10 above wake or significant de-saturations with AHI < 5). It has also been seen that 75% of OHS patients with very severe OSA are responders to positive airway pressure (PAP) therapy; 25% of them respond poorly. So there is a spectrum within the population of patients with OHS. In an analysis of 757 patients with OHS it was observed that the age ranged from 42-61 years, 60% were males, BMI was 35-56[2]. The mean pCO2 was 53, paO2 56, serum bicarbonate 32. The AHI ranged from 20-100, oxygen nadir during sleep was 59%-76%, percentage of time of sleep spent with SpO2 ≤ 90% was 46%-56%.The Epworth Sleepiness Score was 12-16. Among those with a serum bicarbonate 27 mEq/L, obesity hypoventilation syndrome (OHS) is present in 50% of the patients. Very severe OSA (AHI 100 events/h or SpO_2 nadir during sleep less than 60%) increases the prevalence of OHS to 76%.[3] The percentage of sleep time spent with spO2 <80% is significantly more amongst patients with OHS than in those with OSA[4].

Sleep can bring about blunting of physiologic parameters like cortical inputs, respiratory center sensitivity, chemoreceptor sensitivity etc (Fig 6).

The pathophysiologic factors for the causation of OHS are outlined in Table 2. There is a defective central drive. This blunted response to hypercapnia, which may be corrected by PAP therapy is hypothesized to arise from obesity, genetic predisposition, sleep-disordered breathing, and leptin resistance[1,8-14]. In most patients with OSA, the hyperventilation that occurs after an apnea eliminates all CO_2 accumulated during the apnea. If during one sleep cycle, the hyperventilation that occurs between the apnea episodes is not adequate or the ventilatory response to the accumulated CO2 is blunted, it might result into an increase in PaCO2 during sleep. The kidneys can retain small amounts of bicarbonate to buffer the decrease in pH. However, in case the rate of excretion of this small amount of bicarbonate that has accumulated is low, the patient will have a net gain of bicarbonate. This would, in turn, lead to retention of some CO2 during wakefulness to compensate for the accumulation of bicarbonate. Thus, the simultaneous occurrence of a decreased response to CO2 and a slow rate of bicarbonate excretion has been hypothesized to pave the way for a blunted respiratory drive for the next sleep cycle[7]

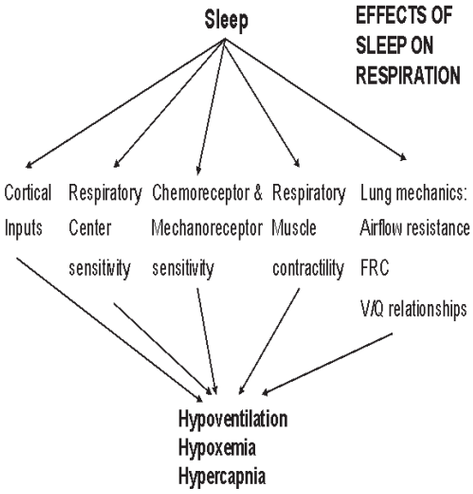

Figure 6: Effects of sleep on respiration

Table 2: Pathophysiologic factors for the causation of OHS

Excessive load on respiratory system
Upper airway resistance
Respiratory system mechanics
Respiratory muscles
Ventilation-perfusion mismatching
Pulmonary edema
Low lung volumes/atelectasis
Impaired central response to hypercapnia & hypoxemia
Sleep disordered breathing
Impaired neuro-humoral response (leptin resistance)

Therapy

Bi-level PAP should be strongly considered in all patients who fail CPAP, patients with OHS who experience acute-on-chronic respiratory failure, and in patients who have OHS without OSA. Improvement in symptoms and blood gases is directly related to adherence to therapy, and maximum improvement in blood gases can be achieved as early as 2 to 4 weeks. Because it does not have the ability to recognize hypo-ventilation and hypoxemia, auto-adjusting PAP technology cannot be recommended in patients with OHS. Bi-level PAP should be instituted if the patient is intolerant of higher CPAP pressure (15 cm H_2O) that may be required to resolve apneas or if hypoxemia is persistent despite adequate resolution of obstructive respiratory events during the titration study. During bilevel PAP titration, the inspiratory PAP (IPAP) should be at least 8 to 10 cm H_2O above the expiratory PAP (EPAP) in order to effectively increase ventilation.

In the minority of patients with OHS who do not have OSA, EPAP can be set at 5 cm H2O and IPAP can be titrated to improve ventilation[5].

The most common reason for persistent hypercapnia in patients with OHS is lack of adherence to PAP therapy[1]. If there is any evidence of optimal adherence by objective monitoring of PAP devices, other possibilities need to be entertained, such as inadequate PAP titration, CPAP failure, other causes of hypercapnia such as COPD, or metabolic alkalosis due to high doses of loop diuretics[1].

The mechanism of action of PAP therapy is multifaceted. EPAP stabilizes the upper airway, keeps atelectatic peripheral lung units open and reduces cardiovascular consequences of SDB. IPAP improves sleep-linked hypoventilation by enhancing the tidal volume. Standard guidelines for initiation and adjustment of bi-level PAP should be followed. High concentrations of oxygen can often worsen hypercapnia by decreasing minute ventilation in patients with untreated OHS. Supplemental oxygen should be added only when pressure support levels have been optimized and yet the spO2 remains ≤ 90% for 5-10 minutes or more. As in this patient, other complicating issues like diastolic dysfunction, airflow obstruction (asthma/ COPD), atrial fibrillation and hypertension should be addressed simultaneously. Weight reduction measures should be instituted[6].

Conclusions

OHS can present as a sleep emergency. Untreated OHS is associated with an increased use of healthcare resources and with a high morbidity and mortality. A high index of suspicion can lead to early recognition of the syndrome and initiation of appropriate therapy. Non-invasive ventilation (NIV) considerably improves survival, physiological parameters, symptoms of chronic hypercapnic respiratory failure, quality of life, and decreases use of health resources.

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