Deterioration of gas exchange in subjects with an increase in body mass index at an altitude of 2,240 m above sea level

Deterioro del intercambio gaseoso en sujetos con incremento del índice de masa corporal a una altitud de 2,240 metros sobre el nivel del mar

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Abstract

Introduction: Alterations of gas exchange (GE) have been recognized in morbid obesity; however, it is not known how their behavior would be as the body mass index (BMI) increases. **Objective:** The objective of the study was to know the behavior of GE at the level of Mexico City in the development of morbid obesity. **Materials and methods:** Through analytical design, subjects matched by gender and age were studied from four different groups of BMI (kg/m²), normal (18.5-24.9), overweight (25-29.9), obesity (30-39.9), and morbid obesity (≥ 40). Their pathological and demographic antecedents, arterial blood gas and simple spirometry variables were obtained. The variables were shown according to their sample characteristic. The differences between groups were made using one-way ANOVA with Bonferroni adjustment, as well as Pearson's correlation for the related variables. Statistical significance was considered with $p < 0.05$. **Results:** 560 subjects were studied in four groups. The average age was 49 ± 11 years old. The highest frequency of diabetes mellitus (34.29%), arterial hypertension (50%), and hyperlipidemia (36.43%) was in the obesity group, and being snoring (73.57%) in morbid obesity. There were differences from the normal group versus morbid obesity: PaCO₂ 31.37 ± 2.08 versus 38.14 ± 5.10 mmHg; PaO₂ 68.28 ± 6.06 versus 59.86 ± 9.28 mmHg; and SaO₂ 93.51 ± 1.93 versus $89.71 \pm 5.37\%$, all with $p = 0.0001$ the IMC-PaCO₂ correlation: 0.497, and IMC-PaO₂: -0.365, $p = 0.0001$, respectively. **Conclusions:** At the altitude of Mexico City and BMI > 30 kg/m², the variables related to GE and simple spirometry begin to deteriorate are evident with BMI > 40 kg/m².

Key words: Obesity. Altitude. Pulmonary circulation. Obesity-hypoventilation syndrome. Mexico.

Resumen

Introducción: Las alteraciones del intercambio gaseoso se han reconocido en la obesidad mórbida; sin embargo, no se conoce su comportamiento conforme se incrementa el índice de masa corporal. **Objetivo:** Conocer el comportamiento del intercambio gaseoso a la altura de la Ciudad de México en el desarrollo de obesidad mórbida. **Métodos:** Mediante un diseño transversal analítico se estudió a sujetos pareados por género y edad de cuatro grupos diferentes de índice de masa

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Date of reception: 30-12-2019

Date of acceptance: 12-04-2020

DOI: 10.24875/ACME.M21000171

Available online: 25-05-2021

Arch Cardiol Mex (Eng). 2021;91(1):7-15

www.archivoscardiologia.com

corporal (kg/m^2): normal (18.5-24.9), sobrepeso (25-29.9), obesidad (30-39.9) y obesidad mórbida (≥ 40). Se obtuvieron sus antecedentes patológicos y demográficos, variables de gasometría arterial y espirometría simple. Las variables se determinaron de acuerdo con las características de la muestra; las diferencias entre grupos se realizaron mediante Anova de una vía con ajuste de Bonferroni, así como la correlación de Pearson para las variables relacionadas. Una $p < 0.05$ se consideró con significación estadística. **Resultados:** Se estudió a 560 pacientes en cuatro grupos. La edad promedio fue de 49 ± 11 años. La mayor frecuencia de diabetes mellitus (34.29%), hipertensión arterial (50%) e hiperlipidemia (36.43%) se registró en el grupo de obesidad, y la de roncadur (73.57%) en la obesidad mórbida. Se identificaron diferencias desde el grupo normal respecto de la obesidad mórbida: PaCO_2 31.37 ± 2.08 vs. 38.14 ± 5.10 mmHg; PaO_2 68.28 ± 6.06 vs. 59.86 ± 9.28 mmHg y SaO_2 93.51 ± 1.93 vs. $89.71 \pm 5.37\%$, todas con $p = 0.0001$. Correlación IMC- PaCO_2 : 0.497, e IMC- PaO_2 : -0.365, $p = 0.0001$, respectivamente. **Conclusiones:** A la altitud de la Ciudad de México y con índice de masa corporal $> 30 \text{ kg/m}^2$, las variables relacionadas con el intercambio gaseoso y espirometría simple comienzan a deteriorarse; son evidentes con IMC $> 40 \text{ kg/m}^2$.

Palabras clave: Obesidad. Altitud. Circulación pulmonar. Síndrome de obesidad-hipoventilación. México.

Introduction

Gas exchange (GE) refers to the flow of oxygen from the lungs to the bloodstream and removal of carbon dioxide from the blood to the lungs. In clinical practice, arterial blood gas test is the most common way to calculate it through variables of interest, such as arterial pressure of oxygen (PaO_2), arterial oxygen saturation (SaO_2), and arterial pressure of carbon dioxide (PaCO_2), and it evaluates lung function as a GE. Another way, more specific and specialized, consists of determining the diffusing capacity for carbon monoxide of the lung, which evaluates the transfer of oxygen from the alveolar space to the hemoglobin of erythrocytes in pulmonary capillaries. It is used in entities with suspected alveolocapillary involvement and it requires pulmonary function assessment equipment for calculating it^{1,2}.

Obesity is a chronic metabolic disease of considerably high prevalence in the world that affects the subject's quality of life and respiratory system function³⁻⁵. It can be classified (World Health Organization) according to indexes, such as the body mass index (BMI, kg/m^2), abdominal girth, and waist/hip index³.

In severe obesity (BMI $> 30 \text{ kg/m}^2$), fat deposits in the abdominal cavity, diaphragm, and rib cage; alterations in lung volumes and distensibility, oxygen consumption, and even in GE have been described⁵⁻¹¹. Their main manifestation is hypoxemia of varying degree, and their mechanism is related to the formation of arteriovenous shunts (Qs/Qt), in addition to alterations in the ventilation/perfusion ratio (V/Q) due to compression of the lung bases by fat and elevated intra-abdominal and intrathoracic pressure these subjects experience^{7-9,11}.

Lung function and GE alterations acquired greater importance when heart and lung involvement in severe obesity was pointed out, which was referred to as cardiorespiratory syndrome of obesity⁷, now known as obesity hypoventilation syndrome (OHS), which includes clinical variables obtained from arterial blood gas test and GE-related (defined by BMI $\geq 30 \text{ kg/m}^2$, chronic daytime hypercapnia [$\text{PaCO}_2 \geq 45$ mmHg, $\text{PaO}_2 < 70$ mmHg], values established above sea level, and related to sleep breathing disorders)^{4,12,13}.

The study of respiratory function alterations has almost always been carried out with different designs and objectives, but two groups are generally used, one control group and one with severely obese individuals; however, the consequences as individuals increase their BMI over time (natural evolution) are not known, given the difficulty for making the follow-up people with normal weight and who later evolve to morbid obesity.

Due to this, studying independent groups according to BMI category or groups with already established obesity or morbid obesity is preferred. In their research, D'Ávila et al.¹⁴ reported the behavior of expiratory flows (forced vital capacity [FVC] and forced expiratory volume in one second [FEV_1] of simple spirometry test according to BMI categories (independent groups), and as part of GE, only partial saturation of oxygen (SpO_2) was obtained.

The behavior of arterial blood gas variables linked to GE in relation to obesity natural evolution (BMI increase) at Mexico City's altitude is not known. Consequently, said behavior was studied in this work in four independent groups of subjects with BMI increase; furthermore, in these same groups, through simple spirometry variables (expiratory flows), pulmonary functional diagnosis of the prevailing respiratory function was assessed in each group of BMI increase.

Materials and Methods

The study was carried out at the Cardiopulmonary Physiology Laboratory of the Department of Pulmonary Hypertension and Right Heart of the High Specialty Medical Unit (UMAE – *Unidad Médica de Alta Especialidad*) of the Mexican Institute of Social Security (IMSS – *Instituto Mexicano del Seguro Social*) National Medical Center Siglo XXI Cardiology Hospital, from January 2012 to December 2018.

An analytical, cross-sectional design was used, with consecutive patients who met the inclusion criteria of the study and who were matched by age and gender being admitted.

Four groups of individuals native to and residents of Mexico City (2240 masl) were studied. Subjects were categorized in independent groups according to BMI^{3,4} (BMI, kg/m²) as normal (18.5-24.9), overweight (25-29.9), obesity (30-39.9), and morbid obesity (≥ 40).

Patients with no history of smoking, or clinical evidence of lung or heart disease within at least 12 months before the study and with a pathological history related to obesity, including systemic arterial hypertension (SAH), diabetes mellitus, sleep-related breathing disorders, or suspicion thereof by questioning about snoring reported by the spouse.

Respiratory function tests were used (simple spirometry), which were performed on the MasterLab-Body equipment Standard Version with Diffusion Option Jaeger Company Type, serial number 101,221-175,110, made in Germany. The equipment was calibrated daily, at the beginning of the working day.

Disposable syringes were used: blood samples were obtained with DL 1-mL disposable syringes (for insulin) and needle length of 13 mm, 27-G caliber (Mexico City). All subjects were in the sitting position at the same time the sample was obtained.

Regarding the equipment for blood sample analysis, arterial blood gases were analyzed on the GEM Premier 3000 model 5700 analyzer (Instrumentation Laboratory, Lexington, Massachusetts, USA). The equipment was calibrated every 24 h before its use.

A scale was used to determine weight and height: BAME scale Mod. DGN. 2412. Weight and height were obtained in the standing position. For the measurement of weight, all patients were asked to remove their clothing and were provided with a hospital gown at the time of being weighed.

A simple spirometry test was performed: by analysis of variables related to expiratory flows (FVC and FEV₁); a functional spirometric pattern indicative of normality,

pulmonary restriction or pulmonary obstruction was defined. Spirometric diagnosis was established according to the American Thoracic Society/European Respiratory Society^{15,16} (ATS/ERS) working group for simple spirometry standardization.

To grade pulmonary restriction severity, the FVC value was used as follows: FVC 70-79%, mild; FVC 60-69%, moderate; FVC 50-59%, moderate-severe; FVC 35-49%, and severe; < 35%, extremely severe. In turn, for pulmonary obstruction severity, FEV₁ was used as follows: FEV₁ > 80%, mild; FEV₁ 50-79%, moderate; FEV₁ 30-49%, severe; and < 30%, extremely severe.

Intervention

Once the individual was selected, he/she was weighed and BMI was calculated; informed consent was obtained and the arterial puncture technique was explained. Subsequently, the modified Allen test was carried out¹⁷; the artery that showed the best filling was chosen for puncture. In the sitting position and in a state of rest, with the previous asepsis and antisepsis of the right or left radial artery, the sample was obtained by puncture.

Once the blood sample was obtained, it was kept under anaerobiosis conditions until analysis. The time elapsed between sample collection and analysis did not exceed 3 min in any of the cases.

Simple spirometry was then carried out with A quality¹⁵ in its performance technique. At the end, patient demographic variables and medical history were recorded.

For statistical analysis, nominal and ordinal variables were reported with frequencies and percentages, and numerical variables, with averages and standard deviations. The difference between the four BMI groups (kg/m²) was established by one-way analysis of variance for independent groups with Bonferroni's adjustment; Pearson's correlation between variables related to GE, BMI, and simple spirometry was obtained. $p < 0.05$ was accepted as significant.

The required sample was calculated based on the study by D'Ávila et al.¹⁴. This study categorized the obesity groups according to BMI, and for the GE variable, arterial oxygen saturation (SaO₂) was used. Therefore, this parameter was used to perform the respective calculation with the formula for mean comparison; for a two-tailed test, an alpha (risk) value of 0.05 and 80% power was established. The calculated sample was 64 subjects per group, with a total of 256, and

Table 1. Study population occupation according to body mass index

Group (BMI, kg/m ²)	Normal (18.5-24.9)	Overweight (25-29.9)	Obesity (30-39.9)	Morbid Obesity (≥ 40)
Arts and crafts	28 (5%)	37 (6.61%)	39 (6.96%)	36 (6.43%)
Homemaking	31 (5.54%)	32 (5.71%)	32 (5.71%)	45 (8.04%)
Technicians	23 (4.11%)	30 (5.36%)	24 (4.29%)	19 (3.39%)
Professionals	26 (4.64%)	14 (2.5%)	17 (3.03%)	14 (2.5%)
Occupational medicine	15 (2.68%)	14 (2.5%)	16 (2.86%)	11 (1.96%)
Sales employees	17 (3.03%)	13 (2.32%)	12 (2.15%)	15 (2.68%)
Total	140 (25%)	140 (25%)	140 (25%)	140 (25%)

to carry out the matching by gender and age, the sample was doubled to a minimum value of 512.

Ethical aspects

The study was approved by the Research and Ethics Committee of the UMAE, Cardiology Hospital of the National Medical Center *Siglo XXI*, IMSS, with number R-2013-3604-4. Informed consent was obtained from each participant as well.

Results

Five hundred and sixty subjects, grouped according to BMI (kg/m²), were studied. Each group was made up of 140 patients matched by age and gender; each gender included 70 individuals. The types of activity of the people were distributed in different areas, which were more often related to homemaking and arts and crafts, as shown in [table 1](#). Average age of the entire group was 49 ± 11 years and was similar in each group matched by gender and BMI, as shown in [tables 2-4](#).

History of comorbidities recorded in this population was negative for the group of patients with normal BMI (10.5-24.9 kg/m²). Male:female ratio is shown after each percentage in parentheses of all preexisting conditions for each BMI increase group. Type II diabetes mellitus was recorded in six subjects of the overweight group (4.29%; 2:4); in 48 with obesity (34.29%; 20:28); and in 42 with morbid obesity (30%; 20:22). Type II diabetes mellitus was more common in the obesity and morbid obesity groups, without a clear gender predominance.

This previous behavior profile was replicated in the case of SAH: five in the overweight group (3.57%; 2:3); 70 in the obesity group (50%; 35:35); and 69 in the morbid obesity group (49.29%; 32:37).

History of hyperlipidemia was recorded in two subjects of the overweight group (1.43%; 1:1); in 51 with obesity (36.43%; 26:25); and in 46 with morbid obesity (32.86%; 25:21), a similar distribution to the former two.

History of snoring in the same respective groups had the following figures: three (2.14%; 1:2); 87 (62.14%; 43:44); and 103 (73.57%; 47:56). The combination of the two most common comorbidities (SAH and snoring) in the normal BMI and overweight groups was negative; for obesity, 55 (39.29%; 28:27), and for morbid obesity, 52 (37.14%; 21:31), with a slight predominance of the female gender; and of the individuals who had all four comorbidities, 29 were found in the obesity group (20.71%; 15:14) and 22 in the morbid obesity group (15.71%; 12:10), without gender difference.

GE observed differences according to BMI groups are recorded in [table 2](#) as total group, and according to female and male genders in [tables 3 and 4](#), respectively.

In GE, variables' differences were observed as BMI increased; statistical evidence pointed at the obesity and morbid obesity groups; these values, from normal BMI to morbid obesity, were: Hb 13.92 ± 1.45 versus 16.24 ± 1.83 g/dL, $p = 0.0001$; PaCO₂ 31.37 ± 2.08 versus 38.14 ± 5.10 mmHg, $p = 0.0001$; with a pH of 7.41 ± 0.02 versus 7.39 ± 0.25 , $p = \text{NS}$; in addition to a decrease in PaO₂ of 68.28 ± 6.06 versus 59.86 ± 9.28 mmHg and in SaO₂ of 93.51 ± 1.93 versus $89.71 \pm 5.37\%$, $p = 0.0001$. Behavior of the changes with regard to the female and male gender is similar to that of the entire group and, in addition, neither were significant differences identified between genders at each one of the BMI categories.

The respiratory function diagnostic profiles obtained by simple spirometry are shown in [tables 2-4](#). In healthy patients, both males and females, the pattern was

Table 2. Differences in gas exchange and simple spirometry pattern according to body mass index in both genders

Variables (BMI, kg/m ²)	Normal (18.50-24.99) (n = 140)	Overweight (25-29.99) (n = 140)	Obesity (30-39.99) (n = 140)	Morbid obesity (≥ 40) (n = 140)	p
Age	49.85 $\pm$ 11.78	49.72 $\pm$ 11.92	49.81 $\pm$ 11.78	49.82 $\pm$ 11.85	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = NS
BMI, kg/m ²	22.88 $\pm$ 1.51	27.38 $\pm$ 1.35	33.42 $\pm$ 2.82	46.19 $\pm$ 6.69	1 vs. 2 = 0.0001 1vs.3 = 0.0001 1vs.4 = 0.0001
pH	7.41 $\pm$ 0.02	7.42 $\pm$ 0.02	7.42 $\pm$ 0.03	7.39 $\pm$ 0.25	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = NS
PaO ₂ , mmHg	68.28 $\pm$ 6.06	67.54 $\pm$ 9.33	65.53 $\pm$ 9.27	59.86 $\pm$ 9.28	1 vs. 2 = NS 1 vs. 3 = 0.046 1 vs. 4 = 0.0001
PaCO ₂ , mmHg	31.37 $\pm$ 2.08	32.86 $\pm$ 4.21	34.79 $\pm$ 4.38	38.14 $\pm$ 5.10	1 vs. 2 = 0.0001 1 vs. 3 = 0.0001 1 vs. 4 = 0.0001
SaO ₂ , mmHg	93.51 $\pm$ 1.93	93.03 $\pm$ 3.36	92.22 $\pm$ 4.72	89.71 $\pm$ 5.37	1vs.2 = NS 1 vs.3 = 0.049 1vs.4 = 0.0001
Hb, g/dL	13.92 $\pm$ 1.45	13.97 $\pm$ 1.73	14.82 $\pm$ 1.71	16.24 $\pm$ 1.83	1 vs. 2 = NS 1 vs. 3 = 0.0001 1 vs. 4 = 0.0001
Spirometry diagnostic pattern	Normal 140 (100%)	Restriction 1 (0.72%)	Restriction 9 (6.43%)	Restriction 97 (69.29%)	

BMI: Body Mass Index; pH: potential of hydrogen; PaO₂: arterial pressure of oxygen; PaCO₂: arterial pressure of carbon dioxide; SaO₂: arterial saturation of oxygen; Hb: hemoglobin.

normal in 140 (100%); in the subjects with overweight, only one individual (1.43%) of the female gender had a consistent pattern of mild lung restriction, and the rest were normal; in the obesity group, in male subjects, 3 of them (4.29%) showed mild, moderate, and moderate to severe lung restriction, respectively; in female patients, 6 (8.57%), one had mild, four had moderate, and one more had moderate-severe restriction; the rest were classified as normal. In the group with morbid obesity, overall respiratory function (%) and male:female ratio were established as follows: normal 40 (28.57%; 18:22); mild restriction 35 (25%; 18:17); moderate restriction 36 (25.71%; 19:17); moderate-severe restriction 20 (14.29%; 11:9); severe restriction 6 (4.29%; 3:3); and mild obstruction 3 (2.14%; 1:2).

The recorded BMI-arterial blood gas test variables correlations related to GE were: BMI-PaCO₂ ratio: 0.497, p = 0.0001; BMI-PaO₂ ratio: -0.365, p = 0.0001; BMI-hemoglobin (Hb) ratio: 0.309, p = 0.0001; and PaO₂-PaCO₂ ratio: -0.607, p = 0.0001.

The correlations of BMI and variables related to simple spirometry test expiratory flows were: BMI-FEV₁

ratio: -0.391, p = 0.0001; BMI-FVC ratio: -0.489, p = 0.0001.

The correlations of variables related to simple spirometry test expiratory flows and those of arterial blood gas test associated with GE were: PaCO₂-FEV₁ ratio: -0.331, p = 0.0001; PaO₂-FEV₁ ratio: 0.478, p = 0.0001; PaO₂-FVC ratio: 0.503, p = 0.0001; and PaCO₂-FVC ratio: -0.346, p = 0.0001.

Discussion

This work focused on the behavior of arterial blood gas variables related to GE; however, by including patient known history of comorbidities and not intervening on GE, identifying the behavior of patients comorbidities according to the BMI, as well as the variables related to the simple spirometry test (expiratory flows), was also possible.

This behavior does not directly refer to the time for the development from the obesity of an individual with normal BMI to morbid obesity, since it would be necessary for another type of design to be used, it would

Table 3. Differences in gas exchange and simple spirometry pattern according to body mass index in female subjects

Variables (BMI, kg/m ²)	Normal (18.50-24.99) (n = 70)	Overweight (25-29.99) (n = 70)	Obesity (30-39.99) (n = 70)	Morbid obesity (≥ 40) (n = 70)	p
Age	49.81 ± 11.84	49.79 ± 11.86	49.84 ± 11.76	49.84 ± 11.84	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = NS
BMI, kg/m ²	22.85 ± 1.47	27.48 ± 1.32	33.35 ± 2.87	46.04 ± 7.03	1 vs. 2 = 0.0001 1 vs. 3 = 0.0001 1 vs. 4 = 0.0001
pH	7.42 ± 0.02	7.42 ± 0.02	7.43 ± 0.03	7.37 ± 0.36	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = NS
PaO ₂ , mmHg	67.43 ± 6.10	67.91 ± 9.46	65.87 ± 10.46	61.71 ± 10.14	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = 0.003
PaCO ₂ , mmHg	31.36 ± 2.05	33.36 ± 4.38	34.31 ± 4.46	37.04 ± 5.65	1 vs. 2 = NS 1 vs. 3 = 0.0001 1 vs. 4 = 0.0001
SaO ₂ , %	93.31 ± 2.14	93.19 ± 3.21	92 ± 5.98	90.47 ± 5.21	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = 0.001
Hb, g/dl	13.34 ± 1.49	13.77 ± 1.43	14.73 ± 1.87	16.06 ± 1.81	1 vs. 2 = NS 1 vs. 3 = 0.0001 1 vs. 4 = 0.0001
Spirometry diagnostic pattern	Normal 140 (100%)	Restriction 1 (0.72%)	Restriction 3 (2.14%)	Restriction 46 (32.86%)	

BMI: Body Mass Index; pH: potential of hydrogen; PaO₂: arterial pressure of oxygen; PaCO₂: arterial pressure of carbon dioxide; SaO₂: arterial saturation of oxygen; Hb: hemoglobin.

require a very long time and the sample size would have to be enormous.

This study is the first to characterize, based on an independent group design, how could the “natural evolution” of GE, expiratory flows and comorbidities of subjects with BMI values ranging from normal to morbid obesity be (a “natural evolution” constructed with the aforementioned methodological limitations, but valid for these purposes).

The protocol assumed that obesity is the metabolic disease with the highest prevalence in Western countries and that it is linked to high morbidity and mortality associated with cardiovascular disorders, type II diabetes mellitus, hyperlipidemia, some cancers, osteoarticular disorders, metabolic syndrome, and respiratory function disorders^{4,6,18}.

There is an estimate of 1600 million overweight (BMI ≥ 25 kg/m²) adults in the world, with 25% corresponding to obese individuals (BMI ≥ 30 kg/m²). In the USA, between the years 1960 and 2000, average BMI increased by around 12%. From 1986 to 2000, the prevalence of adults with BMI ≥ 40 kg/m² was quadrupled¹⁹⁻²².

Mexico ranks second with regard to prevalence of adult obesity in the world; in comparative terms, it is 10 times higher than that of Japan and Korea. In the child population, it ranks fourth in the world, only surpassed by Greece, USA and Italy²³. Overweight and obesity have become a serious health, social, and economic problem. For these reasons, the problem of obesity has been widely diffused in the world, and social programs have been designed in Mexico to counteract its harmful effects^{18,24}.

This work used a population sample of men and women with normal BMI, healthy, and with a history of known heterogeneous diseases related to BMI increase. Age of the overall group ranged between the fifth and sixth decades of life. As previously noted, comorbidities start since the appearance of overweight (BMI > 25 kg/m²) to a lesser extent for all them, and increase in the groups of obesity and morbid obesity; moreover, they increase even to the point of having two to four comorbidities in the latter two groups.

In the work by Bouloukaki et al.²⁵, 6716 patients of both genders, diagnosed with sleep apnea, with

Table 4. Differences in gas exchange and simple spirometry pattern according to body mass index in male subjects

Variables (BMI, kg/m ²)	Normal (18.50-24.99) (n = 70)	Overweight (25-29.99) (n = 70)	Obesity (30-39.99) (n = 70)	Morbid obesity (≥ 40) (n = 70)	p
Age	49.89 ± 11.80	49.66 ± 12.07	49.77 ± 11.89	49.80 ± 11.84	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = NS
BMI, kg/m ²	22.91 ± 1.56	27.27 ± 1.37	33.61 ± 2.79	46.34 ± 6.37	1 vs. 2 = 0.0001 1 vs. 3 = 0.0001 1 vs. 4 = 0.0001
pH	7.41 ± 0.02	7.42 ± 0.02	7.43 ± 0.03	7.41 ± 0.03	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = NS
PaO ₂ , mm Hg	69.13 ± 5.95	67.16 ± 9.27	65.19 ± 7.98	58.01 ± 8.02	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = 0.0001
PaCO ₂ , mm Hg	31.39 ± 2.11	34.37 ± 4	35.27 ± 4.27	38.89 ± 4.04	1 vs. 2 = 0.0001 1 vs. 3 = 0.0001 1 vs. 4 = 0.0001
SaO ₂ , mm Hg	93.70 ± 1.69	92.87 ± 3.52	92.44 ± 3	88.95 ± 5.45	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = 0.0001
Hb, g/dL	14.01 ± 1.39	14.16 ± 1.98	14.91 ± 1.54	16.41 ± 1.25	1 vs. 2 = NS 1 vs. 3 = NS 1 vs. 4 = 0.0001
Spirometry diagnostic pattern	Normal 140 (100%)	Normal 140 (100%)	Restriction 6 (4.29%)	Restriction 51 (36.43%)	

BMI: Body Mass Index; pH: potential of hydrogen; PaO₂: arterial pressure of oxygen; PaCO₂: arterial pressure of carbon dioxide; SaO₂: arterial saturation of oxygen; Hb: hemoglobin.

adjunctive symptoms, and prevalence of cardiovascular disease were studied; 66% corresponded to obese subjects, and average age was 52 years. Women were shown to be more likely to show cardiovascular disease and to refer fewer sleep apnea symptoms than the male population. In the work of the authors, with a smaller sample size, it is possible to observe a certain predominance of comorbidities in the female gender in the group with obesity.

Comorbidities increase as BMI increases, until obesity is reached, but, interestingly, they are not more numerous than those identified in morbid obesity. This is likely due to the fact that, with this high BMI, morbidity, and hospital admissions did increase²⁶, and thus they are no longer seen in usual clinical practice, or that these subjects can be included in specific research protocols, such as this one.

As for GE-related arterial blood gas test variables, PaO₂ and SaO₂ decrease and PaCO₂ increase start to show deterioration in the overweight group (BMI, 25-29.9 kg/m²), and become quite evident in the obesity group (BMI 30 kg/m²), with these findings supporting

the implementation of programs against obesity since subjects start showing evidence of overweight^{18,24}.

The type of hypoxemia that occurs in this obesity scenario is functional and, by decreasing BMI, it improves^{7,8,10}. The described mechanism is the effect of a V/Q anomaly and a pulmonary arteriovenous shunt¹¹. It is possible to define its reversibility and shows that hypoxemia is due to obesity by means of the deep breathing maneuver⁵.

Unlike the findings of this work for SaO₂, in those of D'Ávila et al.¹⁴, the observed changes were shown at BMI values ≥ 51 kg/m² (morbid obesity), although it should be noted that their recorded changes in SaO₂ were ~ 95%, that is, normal values at sea level and for Mexico City's altitude^{27,28}. The authors' values for PaO₂ and SaO₂ showed a clear GE deterioration starting from a BMI > 30 kg/m² (obesity group), which is observed even before morbid obesity is reached, unlike the observations previously reported by D'Ávila et al.¹⁴, and as it occurs in severe obesity^{5,7,8,11}, according to other specialists, without being able to specify that in reality it starts occurring since obesity (as noted in this work),

given that only groups with morbid obesity (BMI > 40 kg/m²) were studied. This earlier presentation of deterioration in these arterial blood gas variables appears to be related not only to BMI increase, but also to altitude.

GE values obtained at sea level have been regularly extrapolated to various levels of altitude, which is wrong. Mexico City's altitude is 2240 masl, as it has been already pointed out, barometric pressure gradually decreases as height above sea level increases²⁷⁻³⁰. Oxygen pressure in inspired air (PIO₂) and pressure of alveolar oxygen (PAO₂) is directly proportional to barometric pressure, and therefore both and PaO₂ progressively decrease as altitude increases (hypobaric hypoxia). Values with normal BMI show the above, and those that occur in obesity and morbid obesity seem to also depend on the altitude where the BMI increase occurs.

To exemplify how inaccurate using GE-related arterial blood gas variables obtained at sea level and extrapolated to other altitudes (e.g., Mexico City) can be, the values established for the diagnosis of OHS are shown: BMI ≥ 30 kg/m², chronic daytime hypercapnia (PaCO₂ ≥ 45 mmHg), and PaO₂ < 70 mmHg, values determined at sea level^{5,12,13}, where the cutoff value for PaO₂ is 70 mmHg. At Mexico City's altitude (2240 masl), normal value would be ~ 67 mmHg, and something similar occurs for PaCO₂ and, according to the aforementioned, instead of 30 kg/m², perhaps BMI should be > 40 kg/m² to complement the diagnosis. This work points at the need to rethink these diagnostic criteria at Mexican capital's altitude.

Furthermore, at Mexico City's altitude, when would supplemental oxygen be indicated in these obese patients with hypoxemia? According to this country's clinical practice guidelines³⁰ for chronic obstructive pulmonary disease (COPD), usual indication is long-term home oxygen therapy with a PaO₂ < 55 mmHg, or SaO₂ < 88%, or with PaO₂ of 56-60 mmHg in the presence of polyglobulin (hematocrit > 55%), Cor pulmonale, or pulmonary hypertension. The effect of supplemental oxygen is observed in improved survival, exercise tolerance, sleep, and intellectual capacity at Stage IV COPD³¹.

Is it actually right using this cutoff point in this group of patients? The indication for the use of oxygen in hypoxemia is safe, given that it has been shown to modify survival in COPD^{32,33}, actually, which are SaO₂ or PaCO₂ cutoff points at this altitude? And, would their use really confer a benefit in obese or morbidly obese subjects (alone or in conjunction with established

measures for weight loss) such as that referred to for COPD, given the almost always functional behavior of hypoxemia?

In obesity, variables related to expiratory flows calculated by simple spirometry can be normal or suggest a restrictive process due to a reduction in FEV₁ and FVC^{34,35}. In addition, FVC reduction can be severe in obese individuals, which has demonstrated that BMI is associated with FEV₁/FVC ratio³⁶. On the other hand, in severe obesity (BMI > 62 kg/m²), an airflow limitation (mean expiratory flow rate), and a reduction in FEV₁/FVC ratio have been demonstrated³⁷.

The impact of BMI increase (obesity) on simple spirometry test variables was indicative of pulmonary restriction starting from morbid obesity (BMI > 40 kg/m²). In contrast with the results of the authors, in the work by D'Ávila et al.¹⁴, alterations in spirometric variables were evident starting from a BMI > 51 kg/m². These differences appear to be related to height, since it generally was 1.61 ± 0.10 versus 1.65 ± 0.08 m of the reference in the authors' analysis, in addition to the fact that the population is smaller than others, and the reference values for spirometry test appear to differ^{15,16}.

The GE-related arterial blood gas, simple spirometry and BMI variables have a good correlation, as it has been observed in works carried out at sea level¹⁴; however, in this study, this relationship was moderate, which may indicate that there are other variables that influence this correlation and that were not anticipated in this study, or that the effect with the highest correlation between variables is due to the higher BMI observed in these subjects at sea level.

An important limitation of this protocol for being able to construct the natural evolution of GE deterioration as BMI increases is precisely its methodological design. Given that obtaining a population sample in which weight gradually increases and shows the spectrum of systemic damage and, therefore, respiratory system damage, is not possible in a restricted time, selecting independent and gender- and age-adjusted groups was decided.

Despite the limitations that were found with this design, the posed question was answered, and it allowed restrictions in the diagnosis of OHS and cardiorespiratory syndrome of obesity at Mexico City's altitude to be recognized.

Conclusions

In individuals with a BMI > 30 kg/m² (obesity) and at Mexico City's altitude, GE-related variables, and those

related to simple spirometry-diagnosed pulmonary restriction, were observed to start to deteriorate. In both, these changes are evident with BMI > 40 kg/m² (morbid obesity).

With a BMI > 25 kg/m² (overweight), comorbidities are already present, and the frequency of comorbidities increased in the obesity group; however, this frequency was not higher in the group of morbid obesity.

Funding

None.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

References

- Hughes JM. Assessing gas exchange. *Chron Respir Dis*. 2007;4(4):205-14.
- Vázquez-García JC, Gochicoa-Rangel L, Del Río-Hidalgo RF, Cid-Juárez S, Silva-Cerón M, Miguel-Reyes JL, et al. Prueba de difusión pulmonar de monóxido de carbono con técnica de una sola respiración (DLCOsb). Recomendaciones y procedimiento. *Neumol Cir Torax*. 2016;75(2):161-72.
- Moreno D. Definición y clasificación de la obesidad. *Rev Med Clin Condes*. 2012;23(2):124-28.
- Díaz-Domínguez E, Rosas-Peralta M, Santos-Martínez LE, Rodríguez-Almendros NA, Magaña-Serrano JA, Pérez-Rodríguez G. Síndrome de obesidad hipoventilación e hipertensión pulmonar. Una asociación poco conocida en México. *Rev Med Inst Mex Seguro Soc*. 2018;56(1):72-83.
- Santos-Martínez LE, Martínez-Guerra ML, Bautista E, Castillo F, Castañón-Mejía A, Pulido-Zamudio T, et al. Impacto de la maniobra de inspiración profunda en el intercambio gaseoso del sujeto con obesidad severa e hipertensión arterial pulmonar asociada a síndrome de Eisenmenger. *Arch Cardiol Méx*. 2008;78(3):265-72.
- Ramos P-de Lucas JM, Rodríguez-González-Moro JM, Rubio-Socorro Y. Obesidad y función pulmonar. *Arch Bronconeumol*. 2004;40 (Supl 5):27-37.
- Martínez-Guerra ML, Fernández-Bonetti BP, Lupi-Herrera E, Rotberg T, Elizalde A. Cambios respiratorios en la obesidad. Estudio de 26 casos clínicos y funcionales. *Arch Inst Cardiol Méx*. 1975;4:12-21.
- Martínez-Guerra ML, Fernández-Bonetti BP, Sandoval-Zárate J, Lupi-Herrera E. Los efectos de la posición corporal sobre la función mecánica del pulmón en el obeso. *Arch Inst Cardiol Méx*. 1981;51:565-70.
- Kutcha KF. Pathophysiologic changes of obesity. *Anesthesiology Clin N Am*. 2005;23:421-29.
- Parameswaran K, Todd DC, Soth M. Altered respiratory physiology in obesity. *Can Respir J*. 2006;13:203-10.
- Martínez-Guerra ML, Fernández-Bonetti BP, Sandoval-Zárate J, Lupi-Herrera E. El cortocircuito veno-arterial en la obesidad, su dependencia del volumen pulmonar. *Arch Inst Cardiol Méx*. 1981;51:365-70.
- Masa JF, Pépin JL, Borel JC, Mokhlesi B, Murphy PB, Sánchez-Quiroga PB. Obesity hypoventilation syndrome. *Eur Respir Rev*. 2019;28(1):1-14.
- Bacelar-de Athayde RA, Bandeira de Oliveira-Filho JR, Lorenzi-Filho G, Rodrigues-Genta P. Obesity hypoventilation syndrome: a current review. *J Bras Pneumol*. 2018;44(6):510-18.
- D'Ávila-Melo SA, Aragão-de Melo V, Soter de Menezes-Filho R, Fábio Almeida-Santos F. Effects of progressive increase in body weight on lung function in six groups of body mass index. *Rev Assoc Med Bras*. 2011;57(5):499-505.
- Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am J Respir Crit Care Med*. 2019;200(8):e70-e88.
- Pérez-Padilla R, Valdivia G, Muño A, López MV, Márquez MN. Spirometric reference values in 5 large Latin American cities for subjects aged 40 years or over. *Arch Bronconeumol*. 2006;42(7):317-25.
- Allen EV. Thromboangiitis obliterans: Methods of diagnosis of chronic occlusive arterial lesions distal to the wrist with illustrative cases. *Am J Med Sci*. 1929;178:237-44.
- Barroso-Camiade C. La obesidad, un problema de salud pública. *Esp publ*. 2012;15(33):200-15.
- Prentice A, Webb F. Obesity amidst poverty. *Int J Epidemiol*. 2006;35(1):24-30.
- McTigue K, Larson JC, Valoski A, Burke G, Kotchen J, Lewis CE, et al. Mortality and cardiac and vascular outcomes in extremely obese women. *JAMA*. 2006;296:296(1):79-86.
- Freedman DS, Khan LK, Serdula MK, Galuska DA, Dietz WH. Trend and correlates of class 3 obesity in the United States from 1990 through 2000. *JAMA*. 2002;288(14): 1758-61.
- Sturm R. Increases in clinically severe obesity in the United States, 1986-2000. *Arch Intern Med*. 2003;163(18):2146-8.
- Dávila-Torres J, González-Izquierdo JJ, Barrera-Cruz A. Panorama de la obesidad en México. *Rev Med Inst Mex Seguro Soc*. 2015;53(2):240-9.
- Barquera-Cervera S, Campos-Nonato I, Rojas R, Rivera J. Obesidad en México: epidemiología y políticas de salud para su control y prevención. *Gac Med Mex*. 2010;146:397-407.
- Bouloukaki I, Mermigkis C, Markakis M, Pataka A, Alexaki I, Erimidou C, et al. Cardiovascular effect and symptom profile of obstructive sleep apnea: Does sex matter? *J Clin Sleep Med*. 2019;15(12):1737-45.
- Cox ZL, Lai P, Lewis CM, Lindenfeld J. Body mass index and all-cause readmissions following acute heart failure hospitalization. *Int J Obes (Lond)*. 2019. doi: 10.1038/s41366-019-0518-6.
- Martínez-Guerra ML, Fernández-Bonetti BP, Balvanera-Abreu A, Correa R, Elizalde-Ramos A, Soni-Cassani J. Valores normales de algunas medidas de la función respiratoria en la ciudad de México. *Prensa Méd Mex*. 1973;38(1-2):1-5.
- Pérez-Martínez SO, Pérez-Padilla JR. Valores gasométricos en sujetos sanos reportados en la población mexicana: revisión y análisis. *Rev Inv Clin*. 1992; 44(3):353-362.
- Lizardi-García D, Pérez-Padilla JR. Las altitudes sobre el nivel del mar en México: Principales poblaciones, carreteras, vías férreas, montañas y viajes aéreos. Guía para los neumólogos y sus pacientes. *Neumol Cir Torax*. 1993; 52(1):7-14.
- Vázquez-García JC, Pérez-Padilla JR. Valores gasométricos estimados para las principales poblaciones y sitios a mayor altitud en México. *Rev Inst Nal Enf Resp Mex*. 2000;13(1):06-13.
- Vázquez-García JC, Hernández-Zenteno RJ, Pérez-Padilla JR, Cano-Salas MC, Fernández-Vega M, Salas-Hernández J, et al. Guía de Práctica Clínica Mexicana para el diagnóstico y tratamiento de la enfermedad pulmonar obstructiva crónica. *Neumol Cir Torax*. 2019;78 (supl. 1):s1-s76.
- Agrawal R, Moghtader S, Ayyala U, Bandi V, Sharafkhaneh A. Update on management of stable chronic obstructive pulmonary disease. *J Thorac Dis*. 2019;11(Suppl 14):S1800-S09.
- Nocturnal oxygen therapy trial group. Continuous or nocturnal oxygen therapy in hypoxemic chronic lung disease: a clinical trial. *Ann Intern Med*. 1980;93:391-8.
- Beuther DA, Sutherland ER. Obesity and pulmonary function testing. *J Allergy Clin Immunol*. 2005;115:1100-01.
- Collins L, Hoberly PD, Walker JF, Fletcher EC, Peiris AN. The effect of body fat distribution on pulmonary function tests. *Chest*. 1995;107:1298-302.
- Lazarus R, Sparrow D, Weiss ST. Effects of obesity and fat distribution on ventilatory function. *Chest*. 1997;111:891-8.
- Biring MS, Lewis MI, Liu JT, Moshenifar Z. Pulmonary physiologic changes of morbid obesity. *Am J Med Sci*. 1999;318:293-7.