Exercise calorimetry in sedentary patients: procedures based on short 3 min steps underestimate carbohydrate oxidation and overestimate lipid oxidation

S. Bordenave, S. Flavier, C. Fédou, J.F. Brun*, J. Mercier

Service central de physiologie clinique, unité d’exploration métabolique (CERAMM), CHU Montpellier, hôpital Lapeyronie et Inserm, équipe ERI 25 “Muscle et pathologies”, 34295 Montpellier cedex 05, France

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Abstract

Objectives. – Among exercise calorimetry tests designed for calculating the respective part of carbohydrates and lipids oxidized at exercise, some use 6 min steps and others use 3 min steps. Is this last method, which has been validated in healthy subjects, still accurate in very sedentary patients, who need more time to reach a steady state in respiratory gas exchanges?

Methods. – We compared data obtained with calorimetry (RER and indicators of substrate oxidation) performed on the 2nd–3rd min and the 5th–6th min of each step of a protocol using four 6-min submaximal steps in 17 sedentary subjects (mean age: 51 years) including seven type 2 diabetics and six obese persons.

Results. – Respiratory exchange ratio (RER) measured with the 3 min steps procedure are well correlated with the 6 min procedure in sedentary patients ($r = 0.928$). However, a Bland–Altman analysis indicated an average underestimation of RER with 3 min steps ($-0.0138$). Moreover, we observed an average underestimation of carbohydrate oxidation rates of 70.1 mg/min with the 3 min steps procedure. On the contrary, as to lipid oxidation, we measured an average overestimation of 16.2 mg/min. Furthermore, carbohydrate and lipid oxidation rates measured with the 3 min steps procedure are well correlated with the 6 min steps procedure. Moreover, there was an average overestimation of the point at cross over with 3 min steps (+3.29 Watts). For lipox max point (power at which the increase in lipid oxidation induced by the increasing workload reaches a maximum), we observed an average underestimation with 3 min steps ($-1.88$ Watt). Although the differences between respectively mean values in cross over point and lipox max point between the two protocols are weak, a Bland–Altman analysis indicated more relevant discrepancies in many subjects between the two protocols.

Conclusion. – In very sedentary patients undergoing such tests for targeting exercise prescription, the 3-min procedure appears to be too short for performing an accurate calorimetry and we rather recommend the protocol using 6-min steps.

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Résumé

Calorimétrie d’effort chez des patients sédentaires : les méthodes fondées sur des paliers courts de trois minutes sous-estiment l’oxydation des glucides et surestiment l’oxydation des lipides

Objectif. – Parmi les tests de calorimétrie utilisés pour calculer la part respective de l’oxydation des glucides et des lipides à l’exercice, certains utilisent des paliers de six minutes et d’autres utilisent des paliers de trois minutes. Cette dernière méthode, qui a été validée chez les sujets sains, reste-t-elle valable chez des patients très sédentaires, qui mettent plus de temps pour atteindre un état stable dans les échanges gazeux respiratoires ?

Méthodes. – Nous avons comparé les données obtenues par calorimétrie entre la deuxième et la troisième minute et entre la cinquième et la sixième minute de chaque palier à partir d’un protocole utilisant quatre paliers sous-maximaux de six minutes chez 17 sédentaires (âge moyen : 51 ans) incluant sept patients diabétiques de type 2 et six obèses.

Résultats. – Le quotient respiratoire (QR), mesuré avec la méthode utilisant des paliers de trois minutes, est bien corrélé avec la méthode utilisant des paliers de six minutes chez ces sédentaires ($r = 0.928$). Cependant, une analyse en Bland–Altman indique une sous-estimation moyenne du QR avec les paliers de trois minutes ($-0.014$). De plus, nous avons observé une sous-estimation moyenne des taux d’oxydation des glucides de 70,1 mg/min avec la méthode des paliers de trois minutes. Au contraire, pour l’oxydation des lipides, nous avons mesuré une
Over the last years, protocols for assessing the balance of substrate oxidation at exercise have been developed by several teams [1–3]. They help to determine the level of exercise at which lipid oxidation rates are maximal, and this metabolic parameter has been used for targeting endurance-training protocols in obese subjects [4,5]. Such training protocols targeted the intensity at maximal lipid oxidation rate have been shown to increase the ability to oxidize lipids at exercise and to decrease body fat mass. Therefore, this approach appears promising for the management of obesity [4,5] and type 2 diabetes [6]. Studies performed in both obese and diabetic patients have mostly used several steps of steady state of graded exercise lasting 6 mins steady state workloads. During the 5th and 6th minute of each step, a stable plateau of gas exchange is usually reached, allowing the use of the equations of calorimetry for calculating carbohydrate (CHO) and lipid oxidation rates.

However, another interesting protocol (the FATMAX procedure) has been proposed and validated in healthy subjects and moderately trained athletes [3]. This protocol uses shorter steps of only 3 mins, allowing thus a greater number of steps for determination of the power intensity at which lipid oxidation rate is maximal. While this technique appears promising in sports medicine, it is unclear whether it can also be used in sedentary patients such as obese or type 2 diabetics. In those patients, a longer time to obtain a steady state of gas exchanges is frequently observed, so that the 3 mins protocol, despite its attractiveness, can be questioned.

We thus aimed in this study at comparing results of indirect calorimetry performed between the 2nd and the 3rd minute and between the 5th and the 6th minute of several 6-min steps of graded submaximal exercise.

2. Methods

2.1. Study design and exercise protocol

We compared data obtained with indirect calorimetry performed on the 2nd-3rd minute and the 5th-6th minute of each step of an exercise protocol on an ergocycle using four 6-min-submaximal steps.

These data were obtained in 17 sedentary subjects (mean age 51 years ± 9.7) including seven type 2 diabetics and six obese subjects (Characteristics of subjects are shown in Table 1).

We used a 800S Datalink ergometric bicycle and the CPX Medical Graphic Cardio 2 analyzer, for breath by breath gas exchange analysis (VO₂, VCO₂, RER) and electrocardiographic supervision. Each test consisted in four 6-min steps, respectively, at 20%, 30%, 40%, 50% of predicted Wmax. Then, active recovery at 20% of predicted Wmax during 2 min was performed and then passive recovery during 3 min.

2.2. Carbohydrate and lipid oxidation analysis during exercise

We averaged VO₂ and VCO₂ measured every 30 s, as stated in the precedent paragraph, on the 2nd-3rd minute of each step. Carbohydrate and lipid oxidation rates were calculated using indirect calorimetry equations [7].

Carbohydrate(mg/min) = 4, 585VCO₂ – 3, 2255VO₂

In the same manner we averaged VO₂ and VCO₂ measured all 30 s on the 5th-6th minute of each step in order to calculate carbohydrate and lipid oxidation rates with the same procedure.

2.3. Cross over and maximal fat oxidation points

We calculated two parameters representative of the balance between fat and CHO oxidation at exercise with the 3 and 6 min-steps procedure: the cross over point of substrate utilization and the maximal fat oxidation point. According to the concept proposed by Brooks and Mercier [8], the cross over point of substrate utilization is defined as the power at which energy from CHO derived fuels predominates over energy from lipids.

Although the shift from fat to CHO during increasing intensity exercise occurs as a continuum, the cross over point can be identified when approximately 70% of the energy derives from CHO and 30% from lipids, since the oxidation of one gram of

### Table 1

<table>
<thead>
<tr>
<th>Anthropometric measurements</th>
<th>Sedentary diabetics (7)</th>
<th>Sedentary obese subjects (6)</th>
<th>Sedentary (4) No diabetics, IMC &lt; 30 kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years ± S.D.)</td>
<td>58 ± 11</td>
<td>48.8 ± 12.95</td>
<td>53.25 ± 9.67</td>
</tr>
<tr>
<td>Weight (kg ± S.D.)</td>
<td>95.87 ± 13.58</td>
<td>102 ± 29.17</td>
<td>65.12 ± 10.53</td>
</tr>
<tr>
<td>IMC (kg/m² ± S.D.)</td>
<td>32.4 ± 3.85</td>
<td>39 ± 11.86</td>
<td>25.3 ± 2.64</td>
</tr>
</tbody>
</table>
lipids provides approximately nine Kcal, while the oxidation of one gram of glucose provides only four Kcal [8]. The maximal fat oxidation rate point is the power at which the increase in lipid oxidation induced by the increasing workload reaches a maximum [1], which will then be followed by a decrease as CHO becomes the predominant fuel.

3. Statistics

Results are presented as mean ± S.D. of the mean. Agreement between the two procedures was tested on Bland–Altman plots [9–11] with the software “Method Validator” (copyright Ph Marquis, Metz). The Bland–Altman plot consists of an x-axis showing the mean of the results of the two methods (assumed true value) and a y-axis, which represents the absolute difference between the two methods (evaluation of the measurement error). The plot includes the line for the mean difference and the experimentally observed 2σ limits of the differences between the two methods (95% limits of agreement). The mean difference indicates if there is a general trend to overestimate or to underestimate the parameter. The 95% limits of agreement should be interpreted in comparison with a clinically acceptable difference between the two methods. If these 95% limits of agreement are clinically acceptable, methods could be used interchangeably.

4. Results

4.1. Respiratory exchange ratio

In these sedentary subjects, RER measured with the 3 min steps procedure are well correlated with those measured with the 6 min procedure ($r = 0.928$) (Fig. 1). However, a Bland-Altman analysis indicated an average underestimation of RER with 3 min steps (average underestimation of 0.0138). Among 69 RER measured, 28 presented a higher discrepancy than 0.02 (40.5%) between the two methods and seven an upper deviation than 0.04 (10%); this undervaluation being able to reach 0.10.

This underestimation was mostly observed for low values or RER.

4.2. Evaluation of CHO oxidation rates

In these sedentary subjects, carbohydrate oxidation rates obtained with the two methods are well correlated ($r = 0.974$). However there was an average underestimation of 70.1 mg/min of CHO oxidation with the method using the short 3 min steps (Fig. 2). Among 69 measurements of CHO oxidation, 10 (14.5%) exhibit a deviation greater than 200 mg/min with a maximum difference as high as 374 mg/min.

4.3. Evaluation of lipid oxidation rates

In sedentary patients, lipid oxidation rates are rather well correlated ($r = 0.907$). There is on the Bland-Altman plots an average over-estimation of 16.2 mg/min of these oxidations rates with the 3 min steps (Fig. 3). Among 69 points, 15 (21.7%) exhibited a discrepancy of more than 40 mg/min and 6 of more than 80 mg/min with a maximum variation than 114 mg/min.

4.4. Evaluation of cross over point

Cross over points calculated with the two methods are well correlated ($r = 0.981$). However there is an average overestimation of 3.29 Watts with the method using the short 3 min steps (Fig. 4). Among 17 cross over points calculated, 10 (58.8%) exhibited a deviation greater than 4 Watts with a maximum difference as high as 10 Watts (6.8% of average predicted Wmax).
4.5. Evaluation of lipox max point

In these sedentary subjects, lipox max points calculated with the two methods are well correlated ($r = 0.972$). However, there is an average underestimation of 1.88 Watts with the method using the short 3-min steps (Fig. 5). Among 17 lipox max points calculated, 6 (35%) exhibited a deviation greater than 4 Watts with a maximum difference as high as 8 Watts (5.5% of average predicted $W_{max}$).

5. Discussion

This study showed that, despite an average good correlation between values of CHO and lipid oxidation rates calculated with the 3 min and the 6 min procedure, there are unacceptable discrepancies in many sedentary subjects.

Exercise calorimetry is now a well-validated technique which has been compared many times with isotopic measurements of lipid and CHO oxidation [12]. When this approach is used with long duration steady state workloads, it is clear that the balance of substrates displays a plateau [13]. However, it often takes several minutes to obtain, for a given workload, this plateau of gas exchange and thus a plateau of CHO and lipid oxidation rates as calculated with calorimetric equations. Based on our studies on long duration steady state workloads [13], we selected the duration of 6 min for our graded exercise protocol because it appeared to be sufficient to obtain the plateau of balance of substrates. This duration has also been selected by Mc Rae in a previous study [14]. The team of Desprès [2] used a procedure somewhat different with steps whose duration was actually not fixed, and that lasted enough to obtain this steady state.

The validation study published by Achten et al. [3,15,16] demonstrates that 3 min is a sufficient duration in a large sample of healthy controls and athletes. However, this validation is restricted to this population and cannot give any conclusion about the validity of the 3-min procedure in sedentary patients. The results of our study indicate that in this case there are a large percentage of subjects in whom the use of 3 min instead of 6 min workloads will lead to rather different results in terms of RER, lipids and CHO oxidation rates, crossing over and lipox max point.

However, in the case of cross over point and lipox max point, the differences between the two protocols are weak when we only compared, respectively, the mean values of cross over point and lipox max point. Indeed, the mean values of cross over point differ only from 3.29 Watts between the two protocols, a Bland–Altman analysis allows to observe more relevant discrepancies in many subjects between the two protocols: among 17 cross over points calculated, 10 (58.8%) exhibited a deviation greater than 4 Watts with a maximum difference as high as 10 Watts (6.8% of average predicted $W_{max}$). In a similar manner, a Bland–Altman analysis shows a deviation greater than 4 Watts with a maximum difference as high as 8 Watts concerning lipox max points calculated in six subjects (5.5% of average predicted $W_{max}$). So, the usually
bell-shaped curve representing lipid oxidation in function of exercise intensity, allows visualizing that such differences may cause relevant variability in lipid oxidation rates. So, for the purpose of targeting exercise training at maximal lipid oxidation rate, in order to increase the ability to oxidize lipids at exercise and to decrease body fat mass, these differences are unacceptable.

Exercise calorimetry protocols employing 6-min workloads have been used for targeting endurance training in the obese [5] and diabetic patients [6]. Consistent with the initial assumptions that underlied the development of this procedure, preliminary data collected in our laboratory indicates that the lipid oxidation rate measured at 5–6 min of this graded exercise test closely predicts the lipid oxidation rate that could be measured over 45 min, i.e., the usual duration of endurance training sessions as recommended by current guidelines. For all these reasons, we think that the procedure based on 6-min steps is accurate for the purpose of targeting exercise training in sedentary patients.

The pathophysiological explanation of this loss of validity of the 3-min procedure in sedentary subjects is unclear. Regensteiner [17] evidenced that in persons with type 2 diabetes mellitus the change in the rate of VO2 in response to a constant-load exercise (measured by VO2-uptake kinetics) was slowed. They assumed that this abnormality may reflect either an impairment in heart responses to exercise, or a defect in skeletal muscle oxygen diffusion, or some degree of impairment in mitochondrial oxygen utilization. That study focused on diabetes, but sedentary subjects exhibiting insulin resistance can be expected to exhibit similar defects. A typical profile in Fig. 6 shows that the rise in VO2 in response to a transition from rest to exercise exhibits a progressive slope over 400 s.

Another study by Zanconato [18] may explain our findings on CO2, since it shows that if the changes of VO2 directly reflect the variations of consumption of O2 by tissues, the CO2 variations during exercise are influenced by a significant percentage of CO2 storing in tissues (presumably adipose tissue), a mechanism that may influence gas exchange kinetics in overweight subjects such as those of our study.

This does not rule out that the procedure based on 3-min steps developed by Achten provides relevant and useful information in athletes and is suitable for metabolic testing and training targeting in sport medicine.

Actually, each method has its own advantages. A test using 3-min steps allows to measure CHO and lipid oxidation at 8–10 different intensities, and thus to directly visualize the bell-shaped curve of lipid oxidation [15,16]. In this case, determination of the power intensity and the maximal flow rate to define the LIPOX max or FAT max is very easy and is performed visually. By contrast the 6-min procedure allows a lower number of steps and thus calculation of the LIPOX max is performed more indirectly by curve fitting. This later procedure has the advantage of smoothing the error on each measurement, but the power intensity and the flow rate are given by a model rather than directly measured. In some situations the shape of the curve may be somewhat different from the usual bell-shaped relationship and thus the value of the power intensity calculated should be considered with caution. This is mostly the case when, rather than a narrow peak, the curve of lipid oxidation displays a large plateau. In this case, a precise power intensity is given by the calculation but is probably meaningless, and it should be rather concluded that there is an optimal range rather than a point. Nevertheless, with the four or six steps allowed by the 6-min procedure, this conclusion is easy to drive from the observation of the shape of the curve. Therefore, in our opinion, there is no major advantage for the 3-min steps procedure and we think that 6-min steps procedure can be satisfactorily employed in patients training prescription.

6. Conclusion

In this study, we show that in very sedentary patients undergoing such tests for targeted prescription of physical activity, the 3 min procedure appears to be too short to reach a steady state. These findings lead us to recommend the use of the 6-min procedure rather than the 3-min procedure for the targeting of training in sedentary patients.

References


