Reduced Metabolic Rate in Acute Uremic Rats: Interrelations between Bilateral Nephrectomy and Anesthesia

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Dear Sir,

The bilaterally nephrectomized rat is a frequently employed experimental model in uremia research. According to our previous investigations [8], the metabolic rate of such animals is severely reduced independently of body temperature and blood pH. Reduced oxidative metabolism may influence secondarily other metabolic data studied in these rats. Since many experiments in acute uremia have to be performed under anesthesia, and our previous results were obtained in awake rats only, we investigated whether or not anesthesia induces a further reduction of the metabolic rate in acute uremia.

Results

Oxygen consumption is reduced about 20–30% in anesthetized non uremic rats. It is reduced about 50–60% in the uremic animals. Uremic rats are still conscious during this period and their activity is not essentially reduced. According to previous investigations [8, 9] in such uremic rats plasma urea is in the range of 400–600 mg/dl, arterial blood pH between 7.1 and 7.2 [9]. The metabolic rate of these uremic rats is not reduced further by anesthesia of both types (table I). In anesthetized uremic rats pO_2 was 102 ± 8.1 mm Hg, pCO_2 34.4 ± 6.5 mm Hg ($n = 14$). In non uremic anesthetized animals the corresponding values for pO_2 were

Materials and Methods

Male Sprague-Dawley rats weighing either 120–200 or 300–400 g were employed (Animal Breeding Institute of the University of Vienna). About 42–46 h after bilateral nephrectomy – controls being sham operated – the animals were divided into further groups, receiving the following substances per 100 g body weight: (1) 100 mg urethane in 0.5 ml 0.9% sodium chloride solution; (2) 8 mg pentobarbital sodium in the same solvent, and (3) the solvent alone. The anesthetics were obtained from Serva, Heidelberg. All solutions were applied intraperitoneally. Two hours later oxygen consumption was measured by employing a diaferometer (Kipp & Zonen, Delft). At least 3 h before measurement the animals were placed at a heated desk so that the rectal body temperature remained above 36 °C. In anesthetized animals a catheter was placed into the trachea; in some of the rats a second one was inserted into a carotid artery from which blood was collected anaerobically for blood gas analysis (apparatus

from Radiometer, Copenhagen). More details about the methods used were described previously [8, 9].

Table I. Whole-body oxygen consumption in normal and bilaterally nephrectomized rats (42–46 h after surgery): influence of anesthesia

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Means $\pm$ SD; number of animals in parentheses. For calculations t tests were employed. ' p < 0.01 versus conscious control rats.

2 p > 0.05 versus conscious uremic animals; p < 0.01 versus corresponding control group.

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95.6 $\pm$ 4.0 mm Hg and 40.1 $\pm$ 3.7 mm Hg for pCO₂ (n = 10). Blood gas values of smaller and larger rats, as well as of those receiving urethane or pentobarbital sodium, respectively, were pooled as there was no obvious difference between these groups. The differences between uremic and non uremic animals as indicated above are significant (t test, p < 0.01).

Discussion

The etiology of reduced whole-body oxygen consumption in anesthetized non uremic animals is still under discussion. Nevertheless, this phenomenon is regularly found in small animals but not in larger species [1–3, 5–7, 10]. A specific action at the cellular level is supposed by some authors [6,10]. Others assume unspecific effects such as reduced work for respiration and reduced transport of oxygen to the cells [1–3]. The mechanism of uremic hypometabolism is not clarified either. Thus, the fact that anesthesia does not reduce the metabolic rate in acute uremic rats any further is poorly understood. The following conclusions, however, may be drawn from the present results: (1) Less locomotion is not the main cause of reduced oxygen consumption in uremic rats. (2) Uremic rats certainly need additional energy turnover for compensatory hyperventilation as demonstrated by increased pO₂ and decreased pCO₂ in arterial blood.

Consequently, oxidative metabolism of tissues other than respiratory muscles may be even more severely reduced than might be supposed from whole-body oxygen consumption.

Blood gas analysis in awake rats was not performed. Our pO₂ and pCO₂ values in anesthetized control rats are, however, in a similar range as reported in normal conscious rats by different authors [4]. In conscious uremic rats less hyperventilation than in anesthetized uremics can hardly be assumed.

To summarize, for the interpretation of experimental results in acute uremic rats a severe reduction of oxidative metabolism has always to be considered. Anesthesia (urethane, pentobarbital sodium), however, does not further aggravate this condition.

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