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MINI REVIEW

COMPARATIVE ASPECTS OF IODINE CONSERVATION IN MAMMALS

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Abstract—1. Comparative aspects of iodine conservation in mammals were studied on the basis of published data on kidney and thyroid weights and function.
2. Very small mammals possessed an efficient reabsorption of iodide to compensate for the high glomerular filtration rate (GFR).
3. Humans and mammals of a similar and larger size had "lost" the ability to reabsorb iodide efficiently.
4. Very large mammals are protected against renal loss of iodide due to the relatively low GFR.
5. Thyroid weights in relation to body weight were highest in humans suggesting that humans and other mammals of a similar size are especially susceptible to iodine deficiency.

INTRODUCTION

Occurrence of iodine deficiency (ID) is theoretically possible in all mammals living in areas with a low iodine content in soil and drinking water, however humans seem to be especially susceptible to low iodine intake, since ID affects about 20% of the world population (Hetzel, 1987).

This raises the question whether other mammals possess mechanisms which protect against ID? This question was addressed by comparing thyroid weight (TW) with kidney weight (KW) in different mammals and comparing these data with data concerning the renal iodide clearance (C_i) and GFR.

MATERIALS AND METHODS

Data were collected from a series of studies of C_i in different mammals. Both values from anesthetized animals and values measured during physiological conditions were obtained. Values of GFR were also collected, preferably from studies where C_i was also measured.

C_i and GFR were depicted graphically according to the allometrical method of scaling renal function parameters (Adolph, 1949; Edwards, 1975), in which:

$$y = aM^b, \quad (1)$$

where M is expressed in kg, a is the value of y for a theoretical animal of 1 kg, b is also a constant, being 1 if y is directly proportional to the mass (M), approximately 0.67 if y is proportional to the surface area and 0.75 if y is proportional to the metabolic rate (Edwards, 1975).

Values of TW and KW were also collected from different mammals and depicted graphically as a function of body weight (body wt).

RESULTS

Scaling of GFR and C_i

C_i values from mammals such as mice, rats, rabbits and humans (Wayne *et al.*, 1964; Bricker and Hlad, 1955; Wollman and Reed, 1959; Brown, 1956; Halmi *et al.*, 1958; Vadstrup, 1989) were depicted graphically (Fig. 1) and compared to the regression line of GFR values from different mammals (Edwards, 1975). It can be seen, that the regression line of C_i values fits to a b values close to 1, indicating proportionality between C_i and body wt, whereas the regression line of GFR has a b value of 0.72 (Edwards, 1975) indicating proportionality between GFR and the surface area or metabolic rate of the mammal.

This difference between GFR and C_i as a function of body wt can also be expressed as a decreasing excretion fraction of iodide (EF_i) ($EF_i = C_i/GFR$) with decreasing body wt, as shown in Table 1. EF_i decreases from 0.33 in humans to 0.01 in mice (unanesthetized mammals).

A circadian rhythm in C_i has been observed in several mammals (Isler, 1959; Pallardo *et al.*, 1976; Oddie *et al.*, 1964; Vadstrup, 1989) and values of the fast and slow phase of GFR, C_i and EF_i are shown in Table 1.

Comparison between KW and TW

The ratio KW/BW increases from 20 to 1200 in mammals with a body wt of 2×10^{-2} to 10^4 kg, whereas TW/BW shows a biphasic pattern with the highest value in humans and low values in both small

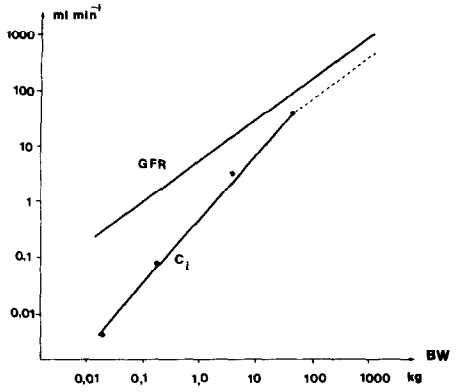

Fig. 1. Comparison between GFR and BW and between C_i and body wt based on values from Table 1. The upper regression line is drawn according to Edwards (1975). The formula is $y = aM^b$ where y = GFR and M is body wt in kg. The values of a and b are for GFR 5.4 and 0.72 (Edwards, 1975). The lower regression line is calculated on basis of data from mice, rats, rabbits and humans. The formula is $y = 0.43\ M^{1.1}$.

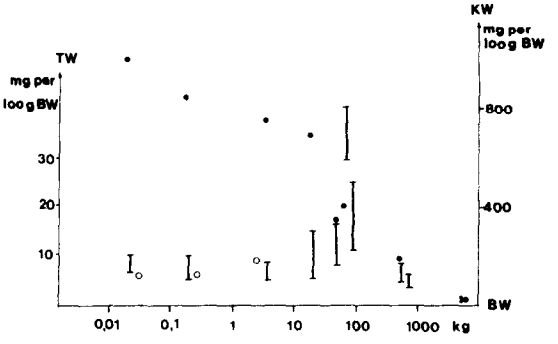

Fig. 2. Comparison between TW and TW per 100 g body wt. The values of TW are from mammals without known iodine deficiency, the normal range of TW is indicated. The KW values are indicated as mean values (●). A few data on TW from birds are also shown (○) (Morris, 1951; Newcomer, 1967). The mammalian values are from mice, rats, rabbits, dogs, sheep, humans, pigs, horses, cows and elephants (Wollman and Reed, 1959; Groth, 1968; Puntriano and Meites, 1951; Laurberg, 1980; Appleton, 1951, Altman, 1972; Brody, 1945).

mammals and very large mammals. Only values from mammals without known iodine deficiency have been used for this comparison (Groth, 1968; Puntriano and Meites, 1951; Laurberg, 1980; Appleton, 1951; Altman and Dittmer, 1972; Brody, 1945; Wollman and Reed, 1959).

DISCUSSION

Iodine conservation in mammals depends on the balance between the thyroid clearance of iodide (TC_i) and the renal clearance of iodide (C_i) (Ermans, 1986). TC_i and C_i are almost equal in humans and C_i is independent of the concentration of iodide in blood (Wayne *et al.*, 1964; Bricker and Hlad, 1955; Wesson, 1969). EF_i is about 0.33 in humans and relatively constant during physiological and pathophysiological conditions (maximal range 0.2–0.8) (Wayne *et al.*, 1964; Bricker and Hlad, 1955). During conditions of low iodide intake C_i is unchanged whereas TC_i may increase with a factor of 5–6 (Ermans, 1986) thereby reducing the compulsory loss of iodide from about 50% to about 15%.

The kidneys are consequently the weak link in iodide conservation and since TC_i is in the same order of magnitude when expressed per mg thyroid in different mammals (Taurog, 1986) one would expect that the size of the thyroid in relation to body wt would reflect indirectly the effectiveness of the kidneys as far as iodide reabsorption is concerned.

Looking at very small mammals like mice, in which GFR is about 20-fold higher/unit of body wt than in humans, one would expect a thyroid size also 20-fold higher/unit of body wt as compared with man, if C_i/GFR was about 0.33 as in humans. This has not been observed (Fig. 2) and TW/BW is also much lower in mice than in humans, indicating a very efficient reabsorption of iodide in the kidneys, also consistent with actually measured values (Table 1).

In very large mammals KW/BW is much lower than in humans and these mammals have consequently very small problems with iodine conservation, which is also reflected by a small KW/BW ratio in these mammals, as well as a small TW/BW ratio.

If the renal reabsorption of iodide was similar in all mammals, one would expect to find proportionality between TW/body wt and KW/body wt. This was observed for mammals with a larger body wt than humans, however in smaller mammals TW/BW decreases and the only explanation possible is an

Table 1. GFR and C_i values from unanesthetized mammals during fast and slow phases of the circadian rhythm

		Fast phase			Slow phase		
	Weight (kg)	C_i (ml/min)	GFR (ml/min)	EF_i	C_i (ml/min)	GFR (ml/min)	EF_i
Mouse*	0.025	0.005	0.5	0.01	—	—	—
Rat†	0.2	0.07	0.8	0.09	0.023	0.8	0.03
Rabbit‡	4	4.2	19	0.22	2.0	19	0.11
Man§	75	40	120	0.33	24	115	0.21

The data were obtained from *Isler (1959); Edwards (1975); †Pallardo *et al.* (1976); ‡Vadstrup (1989); §Wayne *et al.* (1964); Bricker and Hlad (1955); Oddie *et al.* (1964). The circadian variation in GFR is not known for rabbits and the same GFR value was used for both phases.

Table 2. Range of GFR, C_i and EF_i values in different mammals

	C_i (ml/min)	GFR (ml/min)	EF_i
Rat* (0.1 kg)	0.002–0.2	0.6	0.003–0.3
Rabbit† (3–4 kg)	0.02–6.5	6–23	0.002–0.3
Dog‡ (10–20 kg)	0.008–27	24–70	0.003–0.8
Man§ (60–70 kg)	10–60	50–150	0.2–0.8

The data were obtained from both unanesthetized and anesthetized mammals. *Halmi *et al.* (1958); †Vadstrup (1989); ‡Walzer and Rahill (1965); §Wayne *et al.* (1964); Bricker and Hlad (1955).

increasingly effective renal reabsorption of iodide, since TC_i/mg thyroid is not very different from one mammal to another (Taurog, 1986).

It is not possible to say whether this increase in reabsorption of iodide from about 33% in humans to 1% in mice is due to structural changes in the kidneys or due to a change from a passive to an active transport of iodide in the kidney tubules. An active transport of iodide as found in the thyroid has not been observed in the kidneys, but the reabsorption of iodide in small mammals is closely related to the reabsorption of NaCl and saltloading in small mammals, which may influence the reabsorption of iodide (Halmi *et al.*, 1958; Wayne *et al.*, 1964; Walzer and Rahill, 1965). Values of minimal and maximal reabsorption of iodide are indicated for some experimental animals and man in Table 2.

In summary it can be concluded that humans seem to have "lost" the mechanism of effective renal reabsorption of iodide, present in smaller mammals. Larger mammals are protected against renal loss of iodide due to their relatively low KW and GFR. TW/body wt depicts these differences in renal handling of iodide between different mammals and these findings may explain why humans and probably also other mammals with a similar renal function have special problems with iodine conservation.

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