Aldosterone Excretion Rates in Children and Adults During Sleep
J. Howard Pratt, Judy Z. Miller, Naomi S. Fineberg, and Charles A. Parkinson

SUMMARY  The present study undertook to examine aldosterone excretion during sleep as an integrated measurement of aldosterone production. A 24-hour urine collection was divided into awake and sleep fractions. Urinary aldosterone and electrolyte excretion were measured in 26 healthy children (mean age, 8.9 ± 1.9 [SD] years) and 28 adults (mean age, 29.9 ± 9.5 years). Aldosterone excretion in children was 5.6 ± 3.9 (SD) μg/g creatinine during the awake period, which was significantly different from the 3.9 ± 4.1 μg/g creatinine value recorded during sleep (p < 0.002). In adults, awake aldosterone excretion was significantly greater than that during sleep; 4.9 ± 2.7 versus 3.2 ± 1.6 μg/g creatinine (p < 0.001). Sleep aldosterone excretion values were highly correlated with the corresponding 24-hour aldosterone excretion values (r = 0.85, p < 0.001) in children and in adults (r = 0.64, p < 0.001). Sleep aldosterone excretion was correlated with 24-hour potassium excretion (p < 0.02) only in children. Sleep aldosterone excretion correlated with neither sleep nor 24-hour sodium excretion in children or adults. Sleep electrolyte excretion rates were highly correlated with 24-hour excretion rates in both children and adults. Dexamethasone, 1 mg, administered the night before to suppress the normally high morning levels of endogenous adrenocorticotropic hormone, had no discernible effect on sleep aldosterone excretion. These results indicate that measurement of aldosterone excretion in an easily collected sleep urine sample provides a reliable index of aldosterone production in children and adults. (Hypertension 8: 154-158, 1986)

Key Words  • urinary aldosterone • urinary sodium • urinary potassium • sleep urine collections • children • adults

Aldosterone secretion is responsive to a variety of diurnal events when people are awake and physically active. Standing or sitting and physical exertion stimulate aldosterone production by increasing angiotensin II levels and are probably the major factors contributing to the circadian change in aldosterone production. At night, during sleep, aldosterone production is less affected by events of the awake period; thus, aldosterone excretion (AE) during sleep should serve as an accurate index of aldosterone production. Measurement of the sleep AE has considerable practical importance in that overnight urine collections are obtained simply and can be assumed to be complete, in contrast to 24-hour collections where compliance with the collection procedure is less likely to be maintained.

In the present study, we compared sleep AE with 24-hour AE in children and adults. The effects of dietary sodium and potassium (as reflected by their urinary excretion) and nocturnal secretion of adrenocorticotropic hormone (ACTH) on sleep AE also were studied.

Subjects and Methods
Normal healthy subjects, 26 children (14 girls and 12 boys; mean age, 8.9 ± 1.9 [SD] years) and 28 adults (14 men and 14 women; mean age, 29.9 ± 9.5 years), were selected from families that were already under study for effects of diet on blood pressure. These studies were approved by Indiana University Human Use Committee, and informed consent was obtained from each participant. No dietary intervention occurred during the observation period of the present study. Urine samples were collected in the home; the awake period urine collection began at 0600 to 0700 and finished just before the subject went to bed.

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The sleep urine samples were collected over the subsequent period of sleep recumbency.

The effect of endogenous ACTH on sleep AE was examined in an additional group of nine normal subjects (5 women and 4 men, aged 22–43 years). Awake and sleep urine samples were collected twice, and dexamethasone (1.0 mg p.o.) was given at 2300 on the second day.

Aldosterone was measured as the acid-labile or pH 1 conjugate. Briefly, urine was incubated for 36 hours at pH 1, which released aldosterone from its 18-glucuronide form. Radiolabeled aldosterone was added as a tracer for subsequent recovery determinations, and dichloromethane then was used for extraction. Periodic acid was added for oxidation of aldosterone to the lactone, and samples then were washed and dried under nitrogen, reconstituted in buffer, and assayed using a specific aldosterone lactone antiserum. The excretion rate of 17-hydroxycorticosteroids was measured according to the method of Silber and Porter. Sodium and potassium were measured on an IL 943 flame photometer (Instrumentation Laboratory, Lexington, MA, USA), and creatinine was measured on a Beckman-2 Creatinine Analyzer (Brea, CA, USA).

Sleep AE and 24-hour AE, as well as sleep sodium and potassium excretions and 24-hour electrolyte excretions, were examined for correlations using Pearson's two-tailed correlation coefficient (Systat; Systat System Inc., Evanston, IL, USA). When appropriate, the paired t test was used to examine for differences between groups. Excretion rates were determined based on creatinine excretion to eliminate errors due to any instances of incomplete urine collections. Values shown are means ± SD.

Results
Sleep AE was highly correlated with 24-hour AE in children (p < 0.001; Figure 1) and in adults (p < 0.001; Figure 2). The awake AE rates (Figure 3) were higher than AE rates during sleep: 5.2 ± 3.1 versus 3.3 ± 2.1 μg/g creatinine in children (p < 0.002), and 4.9 ± 2.7 versus 3.2 ± 1.6 μg/g creatinine in adults (p < 0.001). Although on average sleep AE correlated well with 24-hour AE, when sodium levels in adults were low, daytime AE and 24-hour AE were higher than nighttime AE. Examples of this finding can be seen in Table 1, which shows that three adult subjects with sodium excretion rates of less than 40 mM/24 hr had sleep AE rates that were lower and mostly unrepresentative of the corresponding awake (or 24-hr) AE. Conversely, when sodium intake was high, sleep and awake AE were usually similar. In children this effect of sodium intake was less apparent; in children the intake of potassium rather than that of sodium appeared to affect AE.

The 24-hour sodium excretion rates in children ranged from 95 to 308 mM/g creatinine, with a mean of 196 ± 56 mM/g creatinine, and adult values ranged from 31 to 234 mM/g creatinine, with a mean of 124 ± 5.5 mM/g creatinine. Sodium and potassium excretion during sleep were highly correlated with 24-hour sodium and potassium excretion in children (potassium: r = 0.69, sodium: r = 0.74; p < 0.001) and in adults (potassium and sodium: r = 0.74; p < 0.001). The only correlation of sleep AE with 24-hour electrolyte excretion was found in children: sleep AE and 24-hour excretion of potassium showed a correlation of 0.46 (p < 0.02; Figure 4).

As depicted in Figure 5, suppression of nocturnal ACTH secretion by dexamethasone decreased sleep AE slightly but not significantly. Although the sample size may not have been adequate to detect an effect of ACTH suppression on sleep AE, nonetheless, sleep AE was distinctly less dependent on ACTH than on cortisol, since dexamethasone clearly suppressed 17-hydroxycorticosteroid excretion.

Discussion
A circadian rhythm of aldosterone secretion, with higher secretion rates during the day, has been demonstrated by several investigative groups. Since recumbency usually eliminates the difference between awake and sleep secretion rates, maintenance of upright posture is a major factor in the cyclical secretion of aldosterone, an effect probably mediated by increases in angiotensin II. In the present study, the mean value for AE was also higher during the day. Differences between awake and sleep AE were also related to diet effects on angiotensin II in that sodium intake affected the diurnal differences in AE. When adults consumed a diet high in sodium, daytime and sleep AE values were similar. When sodium intake was low, awake AE was approximately twice the sleep value. Thus, dietary effects on angiotensin II levels appeared to combine with posture effects to exaggerate the circadian pattern of aldosterone secretion. Despite higher AE during the waking hours, sleep AE showed a high correlation with 24-hour AE in children and adults.

Although what appears in urine is representative of aldosterone secreted somewhat earlier, the time lag is small with the conjugate of aldosterone measured in this study. Bougas et al. found that aldosterone was converted to its pH 1 conjugate and excreted in urine within 3 hours. Thus, what was excreted during sleep was largely representative of aldosterone secreted during the night.

In children, but not in adults, dietary potassium (estimated from 24-hour urinary excretion of potassium) correlated with sleep AE, indicating that potassium was particularly influential in affecting aldosterone secretion in this age group. Since potassium is at least partially dependent on angiotensin II for its capacity to stimulate aldosterone secretion, the increased responsiveness to potassium observed in children may have resulted from the higher angiotensin II levels that are known to occur normally in the young.

Although sodium and potassium excretion during sleep showed a high correlation with 24-hour sodium and potassium excretion rates in children and adults.
FIGURE 1. Correlation of sleep aldosterone excretion rate with the 24-hour excretion rate of aldosterone in children. Excretion rates for the two periods were highly correlated, indicating that sleep excretion of aldosterone reflects overall aldosterone production.

FIGURE 2. Correlation of sleep aldosterone excretion rates with the 24-hour excretion of aldosterone in adults. As was observed in children, sleep aldosterone excretion was highly correlated with the 24-hour excretion rate.

(an observation that has been made previously13-16), we were unable to relate sleep AE with sleep sodium or potassium (or sodium/potassium) excretion. A larger sample size may be required to delineate such a relationship.

The effect of endogenous ACTH on aldosterone production has been considered secondary to that of angiotensin II and potassium, in part because aldosterone production increases primarily when ACTH is given acutely and shows only a transient increase in production when ACTH is administered chronically.17,18 During sleep, however, ACTH secretion, which changes from negligible levels at about midnight to maximal values during the early morning hours,19 conceivably could contribute to the maintenance of aldosterone production. This proved not to be
SLEEP ALDOSTERONE EXCRETION

**Figure 3.** Aldosterone excretion rates during the awake period and during sleep in children and adults. Aldosterone excretion was significantly lower during sleep in both children and adults.

**Figure 4.** Correlation of sleep aldosterone excretion with 24-hour excretion of potassium and sodium in children. Sleep aldosterone excretion was significantly correlated with potassium, but not sodium, excretion. This correlation of potassium excretion (a reflection of dietary potassium) with aldosterone production was not observed in adults. NS = not significant.

**Table 1.** Aldosterone Excretion Rates in Three Adults with Low Sodium Intake and Three Adults with High Sodium Intake

<table>
<thead>
<tr>
<th>Subject</th>
<th>Na⁺ excretion (mM/g Cr/24 hr)</th>
<th>Aldosterone excretion (μg/g Cr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31</td>
<td>8.1</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>9.2</td>
</tr>
<tr>
<td>3</td>
<td>34</td>
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<td>204</td>
<td>2.6</td>
</tr>
<tr>
<td>6</td>
<td>234</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Cr = creatinine.

The application of sleep AE to the diagnostic assessment of adrenal disorders, particularly primary aldosteronism, was not addressed in this study; however, we would anticipate that autonomous aldosterone production by adenomatous or hyperplastic adrenals would result in a relatively constant rate of aldosterone secretion throughout a 24-hour period. Differences between awake and sleep AE would, if anything, be less than those found in normal subjects. Patients with hyporeninemic hypoaldosteronism, a common clinical disorder of aldosterone production, would also be
expected to have similar awake and sleep AE. Angiotensin II concentration is low in this disorder and thus would contribute little to awake and sleep differences in AE.

In summary, our results indicate that sleep AE reliably estimates the 24-hour integrated rate of AE in normal subjects (children and adults). The ease and completeness of sleep-collected samples make the sleep AE an important alternative method for determining aldosterone production.

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References

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