Letter to the Editor

Bedtime levothyroxine administration is an attractive option for children with hypothyroidism

Sir,

Levothyroxine is traditionally administered before breakfast in the morning as its absorption is greater on an empty stomach as compared to a non-fasting state.¹ Current recommendations suggest that levothyroxine should be taken one half to one hour before breakfast and at least four hours before or after taking drugs that are known to interfere with absorption. However, distancing the administration of levothyroxine from food intake or interacting drugs may be inconvenient for patients with unpredictable or variable morning schedules and hence compliance with standard recommendations may be problematic.² The morning schedules are even tighter in children due to the school timings with most schools beginning at 8 AM and children often having to leave for school by 7:30 AM. Thus, maintaining the desired time gap between morning levothyroxine intake and the breakfast meal is often difficult for parents of children with hypothyroidism.

In this regard, an alternative schedule for levothyroxine administration that avoids the morning hours is desirable for children with hypothyroidism. The study by Radhakrishnan et al, in the November-December issue of *IJCP* is therefore an interesting read.³ The authors have shown that it is possible to maintain an euthyroid state in children with hypothyroidism by administering levothyroxine at bedtime instead of before morning breakfast thus offering a choice and convenience to parents of these children. The study is also important in terms of scarce data on alternative schedules of levothyroxine administration in children, this being only the second study on such topic.⁴ Even in adults, the available studies are few and their results are varied.²

While two studies in adults showed clear benefits of bedtime administration demonstrating lower serum thyroid stimulating hormone (TSH) and higher serum thyroxine (T4) concentrations similar to the present study, the results of other studies were inconsistent possibly due to a number of variables that included dietary differences, use of potentially interacting medications and the variable time intervals between levothyroxine administration and food intake.² However, patients did indicate a preference for bedtime administration.^{2,5} Similar preference for alternative schedules has been seen in studies on children with hypothyroidism.⁵ Bedtime administration of

levothyroxine is therefore a viable choice for maintaining euthyroidism in children with hypothyroidism.

Other than convenience and choice, there are several medical reasons for shifting the levothyroxine intake from morning to bedtime. The absorption of levothyroxine is enhanced by a lower gastric pH probably by an alteration in the ionization of the levothyroxine sodium salt in an acidic environment.² As the gastric acid secretion is greater in the evening than in the morning and is at its circadian peak during the nighttime hours, it is reasonable to assume that the absorption and hence the efficacy of levothyroxine may be better if given at bedtime. The increase in serum T4 levels in the present study as well as in other studies is probably a reflection of better absorption of the bedtime dosing.^{2,3}

A better bioavailability of levothyroxine after bedtime administration and decreased gastrointestinal movement during night time also contribute to better serum T4 levels as discussed in the present study.³ Opposite effects i.e. increase in serum TSH and decrease in serum free T4 and triiodothyronine levels were observed in one study when patients on bedtime administration were switched to the morning schedule.⁵ Additionally, the timing of levothyroxine administration has been shown to have no effect on the TSH circadian rhythm in different studies.² The improvement in quality of life (QOL) scores of patients in the previous studies appears to be an additional advantage of the bedtime schedule.²

The morning administration of thyroxine in a fasting state is an established tenet in endocrinology practice especially while treating children with hypothyroidism. Challenging such a major doctrine is not easy. The authors should to be commended for their concept and a successful execution of the study.

Future studies on this topic in children should include the additional estimation of serum transaminases for monitoring the tissue effects of hypothyroidism, and QOL scores. Also, children with congenital and acquired hypothyroidism should be studied differently due to different implications of treatment especially below four years of age when the brain growth may still be incomplete. To conclude, the available data on bedtime thyroxine administration holds a promise and offers an attractive option for maintaining a euthyroid state in children with hypothyroidism.

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