The Relationship between Central Adrenal Insufficiency and Sleep-Related Breathing Disorders in Children with Prader-Willi Syndrome

Roderick F. A. de Lind van Wijngaarden, Koen F. M. Joosten, Sandra van den Berg, Barto J. Otten, Frank H. de Jong, C. G. J. (Fred) Sweep, Al W. de Weerd and Anita C. S. Hokken-Koelega

Dutch Growth Research Foundation (R.F.A.d.L.v.W., A.C.S.H.-K.), 3016 AH Rotterdam, The Netherlands; Erasmus University Medical Center Rotterdam/Sophia Children’s Hospital, Department of Pediatrics, Subdivisions of Endocrinology (R.F.A.d.L.v.W., A.C.S.H.-K.) and Intensive Care (K.F.M.J., S.v.d.B.), 3015 GJ Rotterdam, The Netherlands; Radboud University Nijmegen Medical Center (B.J.O.), Department of Pediatrics, Subdivision of Endocrinology, 6525 GA Nijmegen, The Netherlands; Erasmus University Medical Center Rotterdam, Department of Internal Medicine (F.H.d.J.), Laboratory of Endocrinology, 3015 GE Rotterdam, The Netherlands; Radboud University Nijmegen Medical Center (C.G.J.S.), Department of Chemical Endocrinology, 6525 GA Nijmegen, The Netherlands; and Sleep Center SEIN (A.W.d.d.W.), 8025 BV Zwolle, The Netherlands

Address all correspondence and requests for reprints to: Roderick de Lind van Wijngaarden, Clinical Research Fellow, Dutch Growth Research Foundation, and Erasmus University Medical Center/Sophia Children’s Hospital, Westzeedijk 106, 3016 AH Rotterdam, The Netherlands. E-mail: r.delindvanwijngaarden(at)erasmusmc.nl.

Background: The annual death rate of patients with Prader-Willi syndrome (PWS) is high (3%). Many deaths of children are sudden and unexplained. Sleep apneas have been suggested to play a role in sudden deaths. Recently, we discovered that 60% of patients with PWS suffer from central adrenal insufficiency (CAI) during stress.

Objective: The aim was to study the relationship between CAI and sleep-related breathing disorders.

Design: In 20 children with PWS who underwent a metyrapone test (30 mg/kg at 2330 h), sleep-related breathing was evaluated by polysomnography before the metyrapone test. In addition, we recorded sleep-related breathing in 10 children with PWS during their metyrapone test. CAI was diagnosed when ACTH levels during the metyrapone test were below 33 pmol/liter at 0730 h. All tests were performed during healthy condition.

Setting: The study was conducted in a pediatric intensive care unit and specialized sleep center.

Results: Median (interquartile range) age was 8.4 yr (6.5–10.2). After metyrapone administration, median (interquartile range) central apnea index (number/hour) increased significantly from 2.2 (0.4–4.7) to 5.2 (1.5–7.9) (P = 0.007). The increase tended to be higher in children with CAI [2.8 (2.0–3.9) vs. 1.0 (–0.2 to 2.6); P = 0.09]. During polysomnography before the metyrapone test, sleep-related breathing was worse in children with CAI, who had a significantly higher central apnea index and tended to have a lower minimum oxygen saturation compared to those without CAI (P = 0.03 and P = 0.07).
Conclusions: In children with PWS, the central apnea index increased significantly after metyrapone administration, particularly in those with CAI during stress. In addition, children with CAI had a higher central apnea index compared to those without several months before the metyrapone test.