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A COMMON PATHOPHYSIOLOGY FOR SUDDEN COT DEATH AND SLEEP APNOEA. "THE VACUUM-GLOSSOPTOSIS SYNDROME"

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ABSTRACT

Several congenital and acquired conditions, characterized by upper airway narrowing, may result in respiratory, cardiac, and sleep disturbances. In all these conditions the leading clinical feature is the occurrence of cyclic obstructive apnoea, mainly during sleep. The common pathogenic mechanism for the airway occlusion seems to be a backward displacement of the tongue and mandible, favoured by the muscle relaxation which occurs during sleep and by gravity in the supine position. A constant factor determining the glossoptosis is the pharyngeal vacuum occurring in these conditions as a result of inspiratory efforts in face of a narrowed upper airway. The response to this type of obstruction is age-dependent, since only in early infancy may these apnoeic spells be life-threatening.

A similar pathophysiology is suggested for sudden cot death, which could be considered as a peculiar presentation of this "vacuum-glossoptosis syndrome". This hypothesis could explain why sudden cot death is often associated with naso-pharyngitis and occurs always in infancy, almost invariably during sleep.

Key words: Sudden death, apnoea, sleep, airway obstruction, hypoventilation, respiratory loading, neonatal respiration, polygraphic studies.

INTRODUCTION

Sudden Infant Death Syndrome (SIDS) represents the most important cause of infant mortality beyond the perinatal period (1,2). The aetiology of SIDS is still unknown but epidemiological studies (2-6) have consistently shown that: (i) it is more frequent during winter months, (ii) it occurs nearly always during sleep, (iii) peak risk for this type of death is between two and four months of life, (iv) inflammatory changes of the upper respiratory tract are found at autopsy in about 50% of the victims.

Recently a relationship between SIDS and prolonged sleep-apnoeas has been postulated by some investigators and the causative factor has been identified as a central defect in the control of respiration (7-9). Nevertheless, other authors believe that a respiratory arrest of peripheral origin (i.e., upper airway obstruction) is the cause of unexpected cot deaths (1,6,10-12).

In infants with choanal atresia we have observed that the life-threatening episodes of upper airway obstruction are caused by glossoptosis, favoured by a high negative intrathoracic pressure (13). This same pathogenic mechanism seems to be responsible for the sleep-apnoea occurring in adults and children affected by various forms of upper airway stenosis. However, the ability to respond properly and remove the obstruction appears to be age-related, since only infants may fail to do so and die from asphyxia.

On the basis of these considerations, the purpose of this paper is to suggest for SIDS a mechanism similar to the one causing death in choanal atresia and compatible with all the epidemiological features mentioned above.

RESPONSE TO UPPER AIRWAY OBSTRUCTION IN ADULTS AND CHILDREN: (HYPERSOMNIA-SLEEP APNOEA SYNDROME)

A cyclic breathing pattern with frequent and prolonged nocturnal apnoeas, causing sleep deprivation and explaining the day-time somnolence, has been revealed by continuous respiratory monitoring in obese patients (Pickwickian syndrome) (14). These apnoeic spells may result in alveolar hypoventilation leading to hypercapnia, hypoxia and pulmonary hypertension which in turn causes "cor pulmonale". In opposition to the hypothesis that the sleep-apnoeas of the obese patient are due to a primary disorder of the respiratory centers, recent investigation has shown that cyclic obstruction of the

upper airway can explain these episodes of respiratory arrest. In two Pickwickian patients, serial X-ray of head and neck showed that during sleep the air column between the base of the tongue and the pharyngeal wall was interrupted (15). During obstructive sleep-apnoea in these patients, the pharyngeal walls progressively collapsed while the ineffective respiratory attempts determined a strong intrathoracic depression. In agreement with these findings, a 3 year-old Pickwickian girl had episodes of apnoea that were again explained on the basis of a recurrent upper airway occlusion from glossoptosis (16).

A similar clinical picture, reported as the "hypersomnia sleep-apnoea syndrome", has also been described in non-obese patients (17,18), in acquired micrognathia (19,20) and in laryngeal stenosis (21). Some of these patients were just heavy snorers before any other symptoms appeared. In all these conditions polygraphic studies have shown that the cyclic episodes of sleep-apnoea are caused nearly always by recurrent upper airway obstruction. In fact, during these episodes, while no air flow is detected, large swings of intrathoracic pressure are recorded, meaning respiratory efforts in face of an obstructed upper airway. Weight reduction in the obese patients or tracheostomy in the others produce a dramatic clinical improvement. In all these situations sedation or anaesthesia can be very dangerous, since they may precipitate a severe obstructive episode.

In children these conditions are rather uncommon (16,18, 20). The most frequent cause of a similar cardio-respiratory syndrome in this age group is the upper airway stenosis caused by hyperthrophic tonsils and adenoids (22-27). An example of this condition was observed by us in a 15 month-old boy who had a history of feeding difficulties, recurrent bronchopneumonia, snoring, somnolence and failure to thrive. In this patient glossoptosis, occurring in the supine position, caused episodes of sleep-apnoea that were spontaneously relieved by arousal, vigorous shaking of the head, "searching for air" and screaming. These episodes were prevented with the use of a naso-pharyngeal tube which, equalizing the pharyngeal pressure to the atmospheric pressure, prevented the pharyngeal vacuum and the consequent glossoptosis (27).

This type of obstruction at the level of the oro-pharynx is well known to occur in the unconscious state during anaesthesia when, because of the muscle relaxation, the mandible and the tongue tend to slide backwards. As a consequence, the

dorsum of the tongue and the soft palate adhere to the posterior pharyngeal wall and completely obstruct the airway. Head extension, elevation of the mandible, insertion of an oro-pharyngeal or naso-pharyngeal airway are all measures adopted by the anaesthesiologist to prevent this obstruction.

It seems very likely that in all these conditions respiratory efforts in the presence of a narrowed airway determine a progressive pharyngeal depression and as a final result, a complete upper airway obstruction from glossoptosis. Subsequent inspiratory attempts are equivalent to the Muller's manoeuvre (inspiration against a closed glottis).

RESPONSE TO UPPER AIRWAY OBSTRUCTION IN INFANTS

A) Clinical Observations. In early life cardio-respiratory disorders similar to the ones described above are seen in infants with the Pierre-Robin Syndrome (congenital micrognathia, cleft palate and glossoptosis). In this anomaly the tongue slides back, mainly in the supine position and during sleeping or feeding, and causes episodes of complete upper airway obstruction. As a result respiratory distress, cyanotic spells and feeding difficulties usually occur in these babies, whereas "cor pulmonale" has been seldom reported (28). However, what strikes in this syndrome is the occurrence of sudden cot death in a certain number of the affected infants. While older patients with acquired micrognathia can wake up and reverse the obstruction by shaking their head in such violent way that they sometimes fall out of bed (20), many young infants with the Pierre-Robin Syndrome cannot reestablish an adequate airway and may die asphyxiated.

Babies born with choanal atresia have respiratory and feeding disturbances similar to those of babies with the Pierre-Robin syndrome and, like these patients, may die suddenly from upper airway obstruction. The apnoeic spells observed in infants with choanal atresia or stenosis share a common pathogenic mechanism with those occurring in congenital micrognathia: the apnoea is due to a complete upper airway occlusion caused by a posterior displacement of the tongue (13). The factor determining this glossoptosis is a strongly negative intrathoracic pressure, which is a consequence of the strenuous inspiratory efforts these babies make to overcome the increased resistance to the airflow. This increase may be caused by the supine position, sleeping, feeding or other factors alone or in various combinations. These episodes can be terminated by breaking the seal between the tongue and the

palate with a suitable device (one mother used the handle of a spoon), but usually the baby is capable of reestablishing a patent airway by crying frequently and thus moving the tongue forwards. The use of a naso-pharyngeal tube in the Pierre-Robin syndrome or of an oral airway in choanal atresia, preventing the pharyngeal vacuum, can avoid glossoptosis and the associated life-threatening spells (13). Naso-pharingitis in infants causes a temporary increase of the airflow resistance, thus mimicking the situation found in congenital choanal atresia or stenosis.

In conclusion, all the acquired conditions so far described as the "sleep-apnoea syndrome", together with the congenital anomalies considered in this chapter, could be grouped under a "vacuum-glossoptosis syndrome" since in all these instances the pharyngeal vacuum is a constant causative factor, whereas the sleeping status in infancy is not essential for the apnoea to occur. The obstructive mechanism is identical for all ages. However, the response to these apnoeic spells can be totally inadequate in infancy and death may occur as a result.

B) Experimental Findings. Like adults, normal infants during quiet or non-REM sleep respond to nasal occlusion with respiratory efforts which, increasing the negative intrathoracic pressure, cause a progressive increase in the tidal volume that compensates for the initial hypoventilation (29). Conversely, during active or REM sleep the infant's response to digital nasal occlusion (30) or elastic respiratory loads (29) is also characterized by an increased intrathoracic pressure, followed this time by a progressive fall in the tidal volume and ventilation. In some infants these respiratory efforts during sleep may be even followed by no volume changes at all (29). This sleep-apnoea as a response to nasal obstruction occurs more frequently in older infants (i.e., 44% of a group of 6 week-old infants) than in newborns (17%) (12).

The decrease in the tidal volume and the apnoea as a response to upper airway obstruction have been explained as the result of an intercostal-phrenic inhibitory reflex triggered in REM sleep by the distortion of the rib cage which follows vigorous inspiratory efforts (29). However, in normal infants, similarly to what has been reported in Pickwickians, during these episodes of inappropriate compensation to a respiratory load, a complete obliteration of the air shadow that normally exists between the soft palate and the base of the skull has been demonstrated by X-ray (1). This last ob-

servation seems to indicate that the pathogenesis of sleep-apnoea in the above experiments, is obstructive and similar to the one reported in babies with bilateral choanal atresia, whose respiratory problems are obviously reproduced by the experimental nasal occlusion. Babies with this anomaly when an oral airway is inserted, have a constant and adequate air flow; when the oral airway is removed, they respond with strong inspiratory efforts. The consequent increase of the negative intrathoracic pressure is associated with decreasing airflow and tidal volume. The intrathoracic pressure can reach values as low as -80 cm H_2O, while no airflow is recorded. Oral inspection during these apnoeic spells shows that the tongue is firmly adherent to the posterior portion of the palate (13).

In summary, there is good evidence showing that in some normal infants, more frequently after the first month of life and during REM sleep, there is an inappropriate response to raised airflow resistance, which may lead to obstructive apnoea, caused by glossoptosis. These apnoeic spells, like those of patients with choanal atresia or stenosis, may endanger life because some infants are unable to remove the obstruction. Crying and thus moving the tongue forwards seems to be the only way for an infant in this situation to spontaneously restore respiration (31).

HYPOTHESIS ON SUDDEN COT DEATH

In some normal infants a posterior displacement of the tongue and soft palate may occur because of the muscle relaxation during sleep especially in the supine position. As a result there is a narrowing of the naso-pharingeal airway between the velum and the posterior wall of the pharynx, with an increase in the airflow resistance. Abnormal factors which temporarily decrease the airway size (e.g., mucosal congestion or inflammation, excess of secretions, plugging from mucus or exudate, etc.) can produce an equivalent situation. The infant will then respond by making stronger inspiratory attempts to maintain a constant tidal volume. The resulting increase of the negative intrathoracic pressure, in the absence of an adequate naso and oro-pharyngeal airway, can cause a fall of the pharyngeal pressure to a sub-atmospheric level, unless the infant starts crying and thrusts his tongue down and forwards to open the oral passage. If the pharyngeal pressure is sufficiently low, the tongue and the soft palate will be aspirated backwards causing an additional increase of the airflow resi-

stance and a decrease in the tidal volume. The ensuing more vigorous inspiratory efforts will produce a stronger pharyngeal depression, which will account for a sealing of the tongue to the hard palate (closure of the glosso-palatal flap valve). The displacement of the tongue backwards and upwards will cause also the adherence of the soft palate to the posterior pharyngeal wall (closure of the velo-pharyngeal flap valve). The effect of this complete upper airway obstruction will be the disappearance of any airflow inspite of an increasingly negative intrathoracic pressure. In this situation further inspiratory action can only perpetuate the pharyngeal vacuum and thus the adherence of the two above mentioned valves. In infancy this vicious cycle can cause asphyxia and may be lethal, since many normal babies are unable to remove the obstruction unlike adults and older children, who, in a similar situation, always wake up with a feeling of suffocation and reestablish a patent airway.

IMPLICATIONS

Further research and clinical observation may prove or disprove this hypothesis, however, on the basis of the available evidence, it seems reasonable to avoid the supine position during sleep and to adopt the practice of the prone placement in the first months of life. For the same reason during this period of time all cases of rhino-pharyngitis and of upper airway narrowing from any cause should not be underestimated, but considered a risk and the obstruction properly treated.

Indrawings of soft parts of the neck and thoracic cage and, on inspection of the oral cavity, an obvious aspiration of the tongue backwards, are signs of an abnormally increased negative endothoracic pressure. In this event even the use of a naso-pharyngeal tube should be considered in order to ensure a sufficient airway.

Sleeping infants sucking dummies do not respond to nasal occlusion with signs of pharyngeal obstruction because they manage to keep their oral airway patent (12). Therefore, the use of a pacifier or of other oral devices with a large, rigid guard designed to avoid falling out of the mouth during sleep, could probably prevent the seal of the glosso-palatal valve, thus breaking the death cycle above described.

REFERENCES

1. Cross KW, Lewis SR. Upper respiratory obstruction and Cot death. Arch. Dis. Child. 46: 211, 1971.

2. Working party for early childhood Deaths in Newcastle: Newcastle survey of deaths in early childhood 1974/76 with special reference to sudden unexpected deaths. Arch. Dis. Child. 52: 828, 1977.

3. Beckwith JB. The sudden infant death syndrome. Curr. Probl. Pediatr. 3: 29, 1973.

4. Ministry of Health. Enquiry into sudden death in infancy. Reports on Public Health and Medical Subjects. 113, H.M.S.O., London, 1965.

5. Steinschneider A. Nasopharyngitis and the sudden infant death syndrome. Pediatrics 60: 531, 1977.

6. Tonkin S. Sudden infant death syndrome: hypothesis of causation. ibid 55: 650, 1975.

7. Guilleminault C, Ariagno R, Souquet M, Dement WC. Abnormal polygraphic findings in near-miss sudden infant death. Lancet I: 1326, 1976.

8. Steinschneider A. Prolonged sleep apnea and respiratory instability: a discriminative study. Pediatrics 59: 962, 1977.

9. Shannon DC, Kelly DH, O'Connel KN. Abnormal regulation of ventilation in infants at risk for sudden-infant-death syndrome. New Eng. J Med. 297: 747, 1977.

10. Shaw EB. Sudden unexpected death in infancy syndrome. Am. J. Dis. Child. 119: 416, 1970.

11. Beckwith JB, Bergman AB. The sudden death syndrome of infancy. Hosp. Prac. 2: 44, 1967.

12. Swift PGF, Emery JL. Clinical observations on response to nasal occlusion in infancy. Arch. Dis. Child. 48: 947, 1973.

13. Cozzi F. Glossoptosis as cause of apnoeic spells in infants with choanal atresia. Lancet 2: 830, 1977.

14. Gastaut H, Tassinari CA, Duron B. Polygraphic study of the episodic diurnal and nocturnal (hypnic and respiratory) manifestations of the Pickwick syndrome. Brain Res. 2: 167, 1966.

15. Smirne S, Comi G. Etude sériographique des apnées obstructives des pickwickiens. Rev. Electroencephalogr. Neurophysiol. Clin. 61: 126, 1976.

16. Simpser MD, Strieder DJ, Wohl ME et al. Sleep apnea in a child with the Pickwickian syndrome. Pediatrics 60: 290, 1977.

17. Lugaresi E, Coccagna G, Mantovani M et al.Hypersomnia with periodic breathing: periodic apneas and alveolar hypoventilation during sleep. Bull. Physiopathol. Respir. 8: 1103, 1972.

18. Guilleminault C, Eldridge FL, Dement WC. Une anomalie du système nerveux central peut-elle être responsable de troubles hémodynamiques? Nouv. Presse Med. 4: 1343, 1975.

19. Tammeling GJ, Blokzijl EJ, Boonstra S et al. Micrognathia, hypersomnia, and periodic breathing. Bull. Physiopathol. Respir. 8: 1229, 1972.

20. Coccagna G, Di Donato G, Verucchi P et al. Hypersomnia with periodic apneas in acquired micrognathia. A bird-like face syndrome. Arch. Neurol. 33: 769, 1976.

21. Coccagna G, Mantovani M, Brignani F et al. Continuous recording of the pulmonary and sistemic arterial pressure during sleep in syndromes of hypersomnia with periodic breathing. Bull. Physiopathol. Respir. 8: 1217, 1972.

22. Kravath RE, Pollak CP, Borowiecki B. Hypoventilation during sleep in children who have lumphoid airway obstruction treated by nasopharyngeal tube and T and A. Pediatrics 59: 865, 1977.

23. Menashe VD, Farehi C, Miller MJ. Hypoventilation and cor pulmonale due to chronic upper airway obstruction. Pediatrics 67: 198, 1965.

24. Ainger LE. Large tonsils and adenoids in small children with cor pulmonale. Br. Heart. J. 30: 356, 1968.

25. Macartney FJ, Panday J, Scott O. Cor pulmonale as a result of chronic naso-pharyngeal obstruction due to hypertrophied tonsils and adenoids.Arch. Dis. Child. 44: 585, 1969.

26. Cayler GG, Johnson EE, Lewis BE et al. Heart failure due to enlarged tonsils and adenoids. Amer. J. Dis. Child. 118: 708, 1969.

27. Cardi E, Cozzi F. Unpublished.

28. Cogswell JJ, Easton DM. Cor pulmonale in the Pierre Robin syndrome.
Arch. Dis. Child. 49: 905, 1974.

29. Knill R, Andrews W, Bryan AC, Bryan MH. Respiratory load compensation in infants.
J. Appl. Physiol. 40: 357, 1976.

30. Purcell M. Response in the newborn to raised upper airway resistance. Arch. Dis. Child. 51: 602, 1976.

31. Andran GM, Kemp FH. The nasal and cervical airway in sleep in the neonatal period. Am. J. Roentgenol. Radium Ther. Nucl. Med. 108: 537, 1970.