International Journal of Pediatric Otorhinolaryngology 113 (2018) 208–212

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

Review Article

Descent of the human larynx: An unrecognized factor in airway distress in babies with cleft palate?

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ARTICLE INFO

Presented at the Craniofacial Society of Great Britain and Ireland, Newcastle UK, April 5–7th, 2017.

Keywords:
Laryngeal descent
Feeding in cleft palate
Timing of cleft palate repair
Robin sequence

ABSTRACT

The intranarial epiglottis, a feature of all newborn mammals, allows suckling and breathing to continue almost simultaneously by separating an oral food stream from a nasal airstream. In contrast to other mammals, the human larynx descends in the neck between birth and six months, extending the distance between the caudal aspect of the soft palate and the cephalic tip of the epiglottis. The mechanism of airway protection changes from a pattern in which an upright epiglottis is grasped by an intact palatopharyngeal sphincter to one in which the epiglottis folds down over the laryngeal aditus and the adducted vocal folds.

The comparative anatomy and anthropological literature describing laryngeal descent was reviewed. A series of MRI images were used to illustrate the normal descent of the human larynx, which take place in infants in the first six months of life. Based on this information, we hypothesize that a cleft palate, by interrupting the sphincter function of palatopharyngeus on a high neonatal epiglottis, precipitates a need for premature and rapid maturation of the neonate's airway protection pattern, particularly during feeding. This may explain why, even in the absence of Robin sequence, some babies with cleft palates suffer respiratory distress during feeding.

1. Introduction

Babies with clefts of the secondary palate can present with varying degrees of airway distress, especially during feeding. This is typically present in the Robin sequence of micrognathia, glossoptosis and respiratory distress, usually associated with a wide U-shaped palatal cleft [1–3]. Airway obstruction in Robin sequence occurs as a result of the tongue falling backwards into the pharynx. The presence of a cleft palate exacerbates this tendency since an intact velum would normally constrain posterior and superior displacement of the tongue base [4]. Sher described four patterns of resulting airway collapse that were seen on endoscopy, of which the most common was occlusion of the base of the tongue against the posterior pharyngeal wall [5]. Recent genetic studies have indicated that, at least in some patients, the Robin sequence is associated with various mutations of regulatory elements associated with *SOX9*, a gene of critical importance in chondrocyte differentiation in the early embryo [6–8]. It is thought that a deficiency of chondrocytes in Meckel's cartilage (derived from the first branchial arch) leads to the small mandible, which is the primary element in the sequence. The tongue is consequently positioned high and posterior in the developing oral cavity and obstructs medial migration and fusion of the palatal shelves.

An alternative (or perhaps complementary) hypothesis has been advanced by Abadie and colleagues [9]. They studied a large cohort of babies with Robin sequence and found a very high prevalence of disorders of rhythmic sucking, oropharyngeal co-ordination in relation to swallowing and breathing, specific abnormalities of oesophageal motility and co-ordination (including gastro-oesophageal reflux) and vagal control of cardiac activity. They postulated that the underlying cause of Robin sequence might be a developmental anomaly of brainstem neuronal networks that regulate feeding, swallowing, respiratory and cardiac reflexes. The craniofacial deformity is explained as being secondary to deficient stimulation of the functional matrix within which the embryonic mandible develops [10,11]. This latter hypothesis must be considered with some caution as an explanation of the Robin sequence since rhythmic jaw opening and swallowing movements are not seen in human embryos until after the time of palatal shelf fusion [12–14]. However, it is clear from the work of Abadie and others that a disorder of the control of sucking, swallowing and breathing contributes to airway distress in many patients with Robin sequence [9].

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https://doi.org/10.1016/j.ijporl.2018.07.052
Received 27 May 2018; Received in revised form 28 July 2018; Accepted 29 July 2018
Available online 31 July 2018

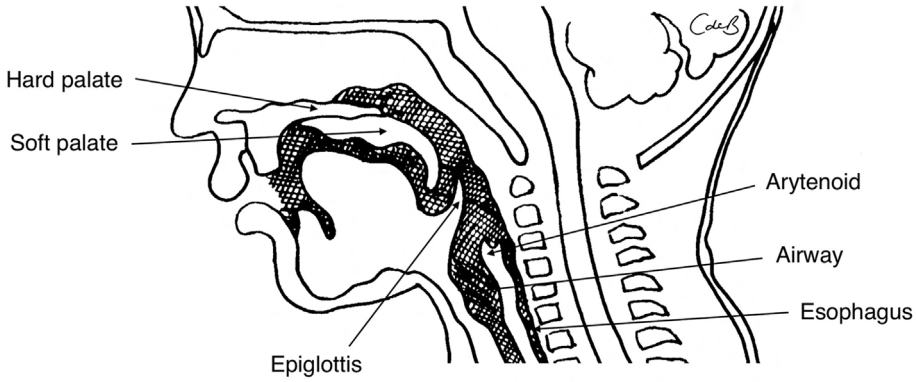

Fig. 1. Sketch of relevant cross sectional anatomy of the upper aerodigestive tract, corresponding to the sagittal MRI images in Fig. 2.

2. The theory of laryngeal descent

Not all babies with cleft palates who develop respiratory distress have micrognathia or typical features of Robin sequence. Some cases may be explained by neurologically-mediated disorganization of sucking, swallowing and breathing and others by loss of control of the tongue base by an intact velum as described by Malek [4]. However, another factor to be considered is the effect of a cleft palate on the adaptation of the infant to the normal descent of the larynx that takes place in the first six months of life [15–21]. This ancestral mammalian phenomenon is well described in anthropological and comparative anatomical literature but rarely alluded to in clinical accounts.

The typical position of a mammalian larynx is high in the neck with the epiglottis protruding into the nasopharynx and the aditus to the larynx protected from swallowed oral contents by the soft palate, particularly the palatopharyngeus muscle, which acts as a sphincter around the cranial end of the laryngeal complex [15,19,22]. This “intranarial” epiglottis is a feature of all newborn mammals and allows suckling and breathing to continue almost simultaneously, since the oral food stream and nasal air stream are separated (Fig. 1) [15,16,23]. This protective mechanism has been demonstrated in human infants by cineradiography during both breast and bottle feeding [16,24,25]. Between birth and around six months of postnatal life, the human larynx undergoes a significant descent in the neck, leaving the upper end of the epiglottis and the soft palate widely separated [17,20,21,26,27]. The epiglottis can no longer be grasped by the palatopharyngeal sphincter and now folds down over the arytenoid cartilages and the laryngeal aditus during swallowing [16]. The critical mechanism now protecting the airway is adduction of the vocal folds and this is not affected by the presence of a cleft palate.

3. Imaging evidence of laryngeal descent

Early studies describing the phenomenon of laryngeal descent were based upon anatomical observations [15,19,21]. Lieberman et al. studied cephalometric radiographs taken of children between birth and adulthood and showed clear skeletal evidence of descent of the hyolaryngeal complex [17]. Vorperian et al. used data from MRI scans of 63 children between birth and 6 years and 12 adults in order to model the growth and development of the vocal tract [27]. This study also indicated hyoid and laryngeal descent, mostly occurring in the first 18 months of life. An illustrative series of mid sagittal MRI scans of (non-cleft) infants between birth and 24 months of age is presented in Fig. 2. Images were acquired using 3D T1 weighted MRI of the brain and cervical spine. The investigations had been carried out for a variety of indications and were randomly selected based on age for the purposes of illustrating descent of the larynx. A line (yellow dashed) was dropped from the top of the arytenoid cartilage perpendicular to the posterior spinous line and the point where it intersected the cervical spine was observed. Progressive laryngeal descent relative to the bony landmarks of the C2 and C3 vertebrae is clearly demonstrated.

As regards a functional analysis, electromyographic techniques have been used to study the development of suck-swallow coordination in infancy [28–30]. While early radiological studies accurately described tongue and nipple or teat positions during feeding [24,25], ethical concerns about unnecessary radiation exposure have precluded further similar studies. Recently however, Elad and colleagues have used ultrasound to confirm the biomechanics of milk extraction during breastfeeding [31]. It is possible that this technology could be used to investigate the adaptation of feeding to the descent of the larynx in the first few months of life. Furthermore, recent advances in magnetic resonance imaging of cleft palate may provide useful information about the relationship of the velum and the larynx in infancy [32].

4. Clinical relevance

Some laryngeal descent probably occurs in most mammals, but the degree in humans is very marked [23,33–36] and produces a long, bifurcated supraglottic vocal tract with the soft palate acquiring a new function as a speech organ, controlling relative resonance and airflow between the oral and nasal cavities [18]. This descent of the larynx in the first few months of life explains why human infants do not have the ability to produce babbling sounds until approximately six months of age.

Descent of the larynx necessitates a change in the mechanism of airway protection from a pattern in which an upright epiglottis in the newborn is grasped by an intact palatopharyngeal sphincter to one in which the epiglottis folds down over the aditus to the larynx and the closing vocal folds. This also coincides with the transition from obligate nasal breathing in early infancy to the adult pattern of facultative nasal or oral breathing. It has been suggested that difficulties in adjusting to this transition may be a factor in sudden infant death syndrome, which peaks in incidence at approximately the same age that laryngeal descent is complete (4–6 months) [26,34].

Orofacial clefts are common in humans (around 1:700 live births world-wide) [37,38], but rarely reported in wild mammal populations [39,40] and only occasionally in captive primates [39,41–44] and domestic mammals [45–50]. Cleft palate in non-human mammals appears to carry a much higher mortality compared with humans and it is possible that this is at least partly due to the fact that human babies are pre-adapted to cope with loss of the palatopharyngeal-epiglottic-laryngeal sphincter mechanism as the larynx descends in early infancy.

4.1. Feeding

Normal infant feeding involves an intact, coordinated sequence of