Laryngeal Reinnervation Surgery – Results of a Selective Approach in an Animal Study

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Laryngeal reinnervation surgery is a difficult subject due to the fact that the recurrent laryngeal nerve (RLN) is responsible for both adductor and abductor laryngeal activity. Non-selective reinnervation procedures will result in laryngeal synkinesis with restoration of tonicity. Restoration of mobility requires selective reinnervation of the adductor and abductor branches with nerves with similar activity patterns as the initial abductor and adductor branches of the RLN.

Methods

Three surgical procedures, each performed in a group of 10 cats were compared. Group 1 underwent reanastomosis of a sectioned RLN; Group 2 underwent a selective reinnervation of only the abductor branch with a phrenic nerve (PN) transfer; Group 3 underwent an anastomosis between the abductor branch and the PN as well as an anastomosis between the adductor branch and the ansa hypoglossi (AH). The reinnervation was evaluated with videolaryngoscopy and electromyography of the vocalis and posterior cricoarytenoid muscles during quiet breathing and in respiratory distress after a 10 week period.

Results

Showed that RLN-RLN reanastomosis (Group 1) led to poor functional results caused by laryngeal synkinesis. The PN proved suitable for selective abductor reinnervation. Nine cats could be evaluated. During quiet breathing seven cats showed good, one moderate and one poor abduction; during respiratory distress eight cats had good abduction and one poor abduction; EMG showed no signs of synkinesis. Selective reinnervation with a PN-abductor anastomosis

and an AH-ad eight cats had a good abduction and one poor, but some synkinetic interaction was seen during respiratory distress: five had good, two had moderate and two had poor abduction.

Conclusion

RLN reanastomosis has poor functional results due to synkinesis. Selective reinnervation of adductor and abductor RLN branches results in good laryngeal abductor function as long as the donor nerves are not activated simultaneously.

Key Words

Nerve transposition/laryngeal EMG/synkinesis

INTRODUCTION

Recovery of laryngeal function after a recurrent laryngeal nerve (RLN) injury is an important clinical issue because of the highly coordinated activity required for proper functioning of respiration, swallowing and phonation at the crossroads of airway and digestive tract. Poor recovery of laryngeal function, with permanent immobility, or restricted mobility of the hemilarynx, often has been observed after surgical reinnervation attempts.^{1,2,3,4} Laryngeal synkinesis due to misdirected reinnervation is considered to be the cause of this poor functional result.

Misdirected reinnervation is a phenomenon that occurs after nerve damage. Regenerating nerve fibres sprout and may grow along paths to other denervated muscles than to the original target muscle. For the RLN, misdirection of regenerating

axons is facilitated by the intraneural topography. Abductor and adductor axons are intertwined and only divide into the subsequent branches close to their target muscles.⁵ Misdirected regeneration of these axons leads to inappropriate reinnervation of opposing muscle groups. The neural activity, which is adequate, thus causes simultaneous contraction (synkinesis) of adductors and abductors, resulting in inadequate mobility, immobility, or paradoxical movement of the larynx. Laryngeal paradoxical movement implies adduction during inspiration, abduction during phonation, or both.

The presence of synkinetic activity can be established by electromyography (EMG) as was performed by Siribodhi in 1963.¹ The incidence of synkinesis after RLN injury in humans is unknown⁶ and, in clinical practice, is probably grossly underestimated, especially in cases of total immobility after vocal cord paralysis. In animal experimental reinnervation studies,^{3, 4, 6} synkinesis varies between 66% and 88%.

Therefore, surgical attempts to achieve functional laryngeal reinnervation should be directed towards selective appropriate reinnervation and prevention of synkinesis. This can be achieved by reinnervating the adductor and abductor muscle groups separately using different nerve transfers for each muscle group.⁷⁻¹² The donor nerves have to have activity patterns comparable to the laryngeal function which they have to restore. For restoration of abduction a respiratory dependent activity during inspiration is required, as is found in the phrenic nerve (PN). However, unlike the inspiratory activity of the PN, no adequate donor nerve with appropriate activity is available for laryngeal adduction during phonation, swallowing, effort closure, vomiting and coughing. The often suggested ansa hypoglossi (AH) branches, for adductor reinnervation, displays a very weak inspiratory activity pattern, increasing during respiratory distress. There is also a slight increase in activity during swallowing, coughing and straining.^{1,3-14} However, recovery of rancity in the adductor

muscles without restoration of mobility is already considered an advantage for phonation.

To evaluate the feasibility of the selective reinnervation the abductor function results, three surgical reinnervation procedures were compared in a cat model. The procedures involved: (1) non-selective reconstruction of the cut RLN, (2) selective reinnervation of the PCA muscle with the PN and (3) combined selective reinnervation of the abductor with the PN nerve and the adductor muscles with the AH.

MATERIALS AND METHODS

The three surgical procedures were each performed in a group of 10 cats, under general anaesthesia with ketamine hydrochloride 20mg/kg intramuscularly and xylazine hydrochloride 0.5mg/kg subcutaneously.

Group 1 underwent reanastomosis of a sectioned RLN. The right RLN was sectioned at a distance of 2.0 cm from the cricothyroid joint. The ends were then reapproximated with a 10 x 0 microsuture (Ethilon, Ethicon Inc. Somerville, NJ) and fixed with fibrin glue (Tissucol, Austrian Institute for Haemoderivates GESmbh, Vienna Austria).

Fig.1

Selective abductor reinnervation procedure using the phrenic nerve, dorsal view of larynx.

In Group 2 (Fig. 1) a selective reinnervation on only the abductor branch with a phrenic (PN) nerve transfer was performed. The larynx was rotated 90° along its longitudinal axis. The inferior pharyngeal constrictor muscle was sectioned at the insertion on the inferior margin of the right thyroid lamina. A small inferior posterior part of the thyroid lamina was resected to expose the RLN adductor and abductor nerve branches. The abductor branch was preserved and the adductor branch was severed, the proximal adductor stump was buried in the PCA muscle and fixed with a 10 x 0 microsuture and fibrin glue. To exclude any influence of the ansa Galeni, although unlikely because of its allegedly sensory nature, it was also severed and its proximal stump buried and fixed in the right PCA muscle with fibrin glue. The two roots of the right PN were identified. Contrary to the situation in humans, resected just before it joined the other root. The right RLN was severed 2.0 cm caudal to the cricothyroid joint and the distal RLN stump was anastomosed to the proximal PN stump using a 10 x 0 microsuture and fibrin glue. Thus all reinnervating PN axons were directed towards

the PCA muscle, even those that followed the path of the adductor branch or the ansa Galeni.

Group 3 (Fig.2) underwent an anastomosis between the abductor branch and the PN as well as an anastomosis between the adductor branch and the AH. The procedure described above was performed. The right AH was then identified and followed to its sternohyoid branch. The sternohyoid branch was severed near the sternohyoid muscle. The proximal stump was then transferred and anastomosed to the distal adductor stump with a 10 x 0 microsuture and fibrin glue.

Reinnervation was evaluated after 10 weeks. The cats were anaesthetised just as for the surgical procedure and videolaryngoscopy and electromyography of the left and right vocalis and posterior cricoarytenoid muscles was performed during quiet breathing and in respiratory distress. The respiratory distress condition was induced by performing a tracheotomy, placing a tracheotomy tube (type Shiley 00 CFS; Mallinkrodt Medical, Irvine, CA, USA) and occluding the tube for one minute. The abductor movement of the right vocal fold was compared to the unaffected left side. The abductor function was classified as good if the right side was equal to the left side; moderate if the right side was about half that of the left side; and poor if the right side was less than half of the left side or immobile.

RESULTS

During quiet respiration (Fig.3) ten cats in group 1 could be evaluated; nine cats in group 2, one cat died of postoperative haemorrhage; and in group 3 nine were evaluated, in one cat iatrogenic damage to the right RLN occurred before performance of the PN-RLN anastomosis precluding successful anastomosis. In group 1 all cats had a poor abductor function. In group 2 seven cats showed a good abductor function, one moderate and one poor (this cat proved to be a surgical failure as the anastomosis had lost its continuity). In group 3 eight cats had a good

Fig.2

Combined selective abductor reinnervation with phrenic nerve AND adductor reinnervation with ansa hypoglossi, dorsal view of larynx.

Fig.3

Diagram to show laryngeal abductor function during quiet breathing.

function and one poor, in this cat reduced mobility of the cricoarytenoid joint was disclosed on palpation.

EMG recordings showed signs of synkinesis (simultaneous inspiratory activity) in both the right PCA and right vocalis muscles in all cats in group 1. No signs of synkinesis were seen in group 2 and good phrenic nerve activity with its clear inspiratory activity was found in the PCA muscle of eight of the nine cats. In group 3 EMG recordings showed phrenic nerve activity in all nine PCA muscles. A minor respiratory activity pattern was recorded in the right vocalis muscle in two cats, in all other cats the right vocalis was inactive

During the respiratory distress condition (Fig.4) nine cats were evaluated in group 1, in one cat the right RLN was damaged during the tracheotomy. Eight showed poor abductor

function and one moderate. In group 2 eight cats had good abduction and one poor abduction (the surgical failure). In group 3, nine cats were evaluated, five had good, two had moderate and two had poor abduction.

In respiratory distress EMG signs of synkinesis were seen in all cats in group 1, in none in group 2 and in all cats in group 3. In group 3 this is explained by the increased inspiratory activity in the ansa hypoglossi during respiratory distress.

DISCUSSION

Many unsuccessful efforts had been made to reinnervate the larynx by making anastomoses with several nerves to the distal RLN stump. Although unrecognised, these failures undoubtedly resulted from synkinesis. Synkinesis is probably the most common condition of a so-called laryngeal palsy that has been immobile

Fig.4

Diagram to show laryngeal abductor function during respiratory distress conditions.

for more than 6 months, as those who regularly perform laryngeal EMGs know. This, however, changed the concept of laryngeal reinnervation. Apparently, the aim without synkinesis. This can be achieved only by separate reinnervation of adductor and abductor muscle groups (selective reinnervation).

The present study has demonstrated that unilateral selective laryngeal abductor reinnervation with a PN transfer is a highly effective procedure to restore laryngeal abductor function in cats. These results strongly support the findings of Baldissera and co-workers.¹⁰ Although the excellent restoration of abduction achieved in cats cannot simply be translated to the human situation, we feel that the described technique hold promise for laryngeal reinnervation in humans as well.

Some facts should however be taken into

consideration. Firstly, in the present study the reinnervation surgery was performed immediately following the RLN section. Normally in patients there is a considerable delay between the time of the nerve injury and the moment that therapeutical intervention is taken into consideration. Secondly, there is the trade-off between the morbidity of sacrificing a PN nerve and the morbidity of a bilateral RLN nerve palsy. The morbidity of unilateral PN palsy is considered to be minor and transection of one PN is generally well tolerated without negative pulmonary side-effects¹⁵⁻¹⁸. This may be due to the fact that the diaphragm is not only innervated by the PN proper, but also by accessory phrenic nerves and thoracic branches¹⁷. Bilateral transection of the PN, however, is associated with a higher morbidity. Therefore, selective abductor laryngeal reinnervation with a PN transfer can only be performed unilaterally, or

bilaterally if only one PN is used, as has been described by Baldiserra and co-workers¹⁹. Considering the remarkably good restoration of laryngeal abduction in this study, a unilateral PN reinnervation might even result in a sufficient airway in bilateral RLN palsy.

The theroretical advantages of adductor muscle tonus and the favourable experience in reinnervation with ansa cervicalis branches in

unilateal laryngeal paralysis in humans to improve phonation²⁰, together with the minor additional morbidity of sacrificing an ansa cervicalis nerve branch, in our opinion, justifies further development of selective abductor and adductor reinnervation and its eventual use in humans. The results obtained with selective reinnervation are obviously much better than those which can be achieved by direct RLN neurorrhaphy which results in gross laryngeal function impairment due to synkinesis.

References

1. Hiroto I, Hirano M, Tomita H. (1968): Electromyographic investigations of human vocal cord paralysis, *Ann Otol Rhinol Laryngol* 77:296-304
2. Tashiro T. (1972): Experimental studies on the reinnervation of larynx after accurate neurorrhaphy, *Laryngoscope* 82:225-236.
3. Siribodhi C, Sundmaker W, Atkins JP, Bonner FJ, (1963): Electromyographic studies of laryngeal paralysis and regeneration of laryngeal motor nerves in dogs, *Laryngoscope* 73:148-164.
4. van Lith-Bijl JT, Mahieu HF, Stolk RJ, Tonnaer JADM, Groenhout C, Konings PNM, (1996): Laryngeal abductor function after laryngeal nerve injury in cats. *Arch Otolaryngol Head Neck Surg* 122:393-396.
5. Sunderland S, Swaney WE, (1952): The intraneural topography of the recurrent laryngeal nerve in man. *Anat Rec* 114: 411-426.
6. Crumley RL. (1979): Mechanisms of Synkinesis, *Laryngoscope* 89:1847-1854.
7. Mahieu HF, van Lith-Bijl JT, Groenhout C, Tonnaer JADM, de Wilde P, (1993): Selective laryngeal abductor reinnervation in cats using a phrenic nerve transfer and ORG 2766. *Arch Otolaryngol Head Neck Surg* 119:772-776.
8. van Lith-Bijl JT, Stolk RJ, Tonnaer JADM, Groenhout C, Konings PNM, Mahieu HF: Selective Laryngeal Reinnervation with Separate Phrenic and Ansa Cervicalis Nerve Transfers. *Arch Otolaryngol Head Neck Surg* submitted.
9. Rice DH. (1982): Laryngeal reinnervation, 1982. *Laryngoscope* 92:1049-1059.
10. Baldiserra F, Cantarella G, Marini G, Ottaviani F. (1986): Restoring abduction of paralyzed vocal cords in the cat using selective laryngeal reinnervation by phrenic motoneurons, *Laryngoscope* 96: 1399-1404.
11. Attali JP, Gioux M, Henry C, Urtassun A, Vital C, Traissac L. (1988): Vocal cord abduction rehabilitation by nervous selective anastomosis, *Laryngoscope* 98:398-401.
12. Marie JP, Ducastell T, Dehesdin D, Senant J. (1989): Selective reinnervation of the abductor and adductor muscles of the canine larynx after recurrent nerve paralysis, *Ann Otol Rhinol Laryngol* 98: 30-536.
13. Ellenbogen BG, Gerber TG, Coon RL, Toohill RJ, (1981): Accessory Muscle Activity and Respiration, *Otolaryngol Head Neck Surg* 89:370-375.
14. Fink BR. (1975): *The Human Larynx – A Functional Study*, Raven Press New York pp 56-120.
15. Fackler CD, Penet GE, Bedell GN, (1967): Effect of unilateral phrenic nerve section on lung function, *J Appl Physiol*, 23: 923-926.
16. Robertson J, (1979): A physiological approach to hemidiaphragm paralysis. *Crit Care Med*. 563-565.
17. Easton PA, Fleetham JA, DelaRocha A, Anthonisen NR, (1983): Respiratory function after paralysis of the right hemidiaphragm. *AM Rev Resp Dis*, 127: 125-128.
18. Kelly WD, (1950): Phrenic nerve paralysis, special consideration of the accessory phrenic nerve. *J Thoracic Surg*, 19: 923-928.
19. Baldiserra F, Cantarella G, Marini G, Ottaviani F, Tredici G, (1989): Recovery of inspiratory abduction of the paralysed vocal cords after bilateral reinnervation of the crico arytenoid muscles by one single branch of the phrenic nerve. *Laryngoscope*, 99: 1286-1292.
20. Crumley RL, Izdebski K, (1986): Voice quality following laryngeal reinnervation by ansa hypoglossi transfer. *Laryngoscope*, 96: 611-616.