Phrenic-Recurrent Nerve Anastomosis in Animal Models with Unilateral Cutting of the Recurrent Nerve

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Abstract In our experimental study, the aim was to recover vocal cord physiology in cutting of recurrent laryngeal nerve, thus phrenic-recurrent nerve transposition was planned in rabbits. Experiments were performed on 10 experimental and 10 control rabbits. The right recurrent nerve was cut in the control group, while in the experiment group, the right recurrent nerve was cut. Then, a right phrenic-recurrent nerve end-to-end anastomosis was performed and the results were evaluated. After the 3rd postoperative week, videolaryngoscopy (VLS) and intramuscular electromyography (EMG) could not be evaluated in 1 rabbit from the experimental group which had died during anesthesia. In eight of the nine rabbits in the experiment which underwent VLS and EMG, activity was

recorded in the right vocal cords. On light microscopic examination, atrophy was not detected in the vocal cord muscles of 9 rabbits among the 10 in the experiment group, while all rabbits in the control group and 1 rabbit in the experiment group were diagnosed with vocal cord atrophy. A success rate of approximately 90% was obtained based on the pathologic examination. We believe that the method can be used in patients without any contraindications, considering the complications of tracheostomy and the quality of life.

Keywords Laryngeal reinnervation · Recurrent nerve · Vocal cord paralysis · Vocal cord palsy · Phrenic nerve · Nerve transposition

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Introduction

Cutting of the recurrent nerve is a serious complication in thyroid surgery. Bilateral nerve cutting causes even more serious danger. In these patients, tracheostomy is required and along with tracheostomy-related social problems, serious systemic complications might also be observed [1, 2]. If we manage to recover vocal cord movement through nerve transposition in patients with recurrent nerve palsy, we can protect them against many life-threatening complications. Therefore, our experimental study aimed to recover vocal cord movement by performing phrenic nerve and recurrent nerve anastomosis and transferred the nerve impulse from the phrenic nerve to the recurrent nerve.

Materials and Methods

After obtaining the consent of the ethical board, two groups (experimental and control) were formed. There were a total of 20 New Zealand white rabbits (10 in each group). The operation was performed under general anesthesia (ketamine [90 mg/kg], and xylazine [3 mg/kg]). Following the cleaning of the operative area, skin flaps were created by making a skin incision with a Kocher's collar incision. In the midline, the pretracheal muscles were retracted laterally. The right recurrent nerve was identified and cut below the inferior level of the thyroid gland. In the control group, after the right recurrent nerve was cut, the layers were anatomically closed after hemostasis was assured, and the operation was ended. In the experimental group, after cutting the right recurrent nerve, the right phrenic nerve was identified on the anterior surface of the anterior scalene muscle and was cut above the sternoclavicular junction. An end-to-end anastomosis was made with 10/0 polypropylene between the proximal part of the right phrenic nerve and the distal part of the right recurrent nerve. Thus, a nerve transposition was made between the phrenic and recurrent nerves. An impulse was conducted through the phrenic nerve to the posterior cricoarytenoid muscle.

On the 1st pre- and post-operative days, videoendoscopic vocal cord examinations were performed. After the 3rd postoperative week (between the 23rd and 25th days), a videoendoscopic vocal cord examination, determination of vocal cord denervation and re-innervation with electromyography (EMG) [3], and microscopic examination of the vocal cords after sacrifice were performed. The videoendoscopic and EMG examinations were carried out under general anesthesia with ketamine (Figs. 1 and 2).

Fig. 1 Phrenic(1) and recurrent(2) nerves

Results

Surgical examination All rabbits were in good condition in the pre-operative period. On the 1st post-operative day, all the rabbits were active and in good condition with no complications at the incision sites. After the 3rd post-operative week, before the videoendoscopic and EMG examinations, one rabbit in the experiment group was observed to be moving slowly; however, no complications were noted at the incision site. The other rabbits were

Fig. 2 Nerve transposition is seen

healthy and had normal incisions. No complications were detected, such as wound infections or hematomas.

Otorhinolaryngologic examination Videolaryngoendoscopy was performed under anesthesia with ketamine during spontaneous respirations. All of the rabbits were subjected to a videolaryngoscopic examination to evaluate their cord activity on the 1st pre- and post-operative days and in the 3rd post-operative week. In the pre-operative examination, all rabbits were observed to have normal activity of the vocal cords bilaterally. During the examination on the 1st post-operative day in the experimental and control groups, the right vocal cords were fixed and the left cord activities were normal. In the examination performed in the 3rd post-operative week, in the experimental group the left cords were active with minimal activity in the right cords in eight rabbits and complete fixation of the right cord in one rabbit. In one rabbit in the experimental group in poor condition, vocal cord activity could not be evaluated and the rabbit died during anesthesia. In the examination performed in the 3rd post-operative week in the control group, it was observed that the right cords of all the rabbits were fixed and all had normal left cord activity.

One rabbit in the experimental group was in poor condition and died during the videoendoscopic examination; thus, the EMG could not be performed, but only a pathologic examination could be performed.

Intramuscular EMG examination: Nine rabbits in the experiment group and 10 rabbits in the control group were examined 3 weeks after the procedure using a concentric needle electrode at both vocal cords. The examination was made under ketamine anesthesia. The vocal cords were reached through the cricothyroid membrane. A Medelec Sapphire 4ME was used in the EMG examination. Examinations of healthy left vocal muscles and symptomatic right vocal muscles were recorded as video and trace.

In one rabbit in the experimental group, intense denervation activity was obtained from the right vocal muscles, while no motor units of regeneration were observed; this observation was accepted as total denervation. In the left vocal muscles of this rabbit, normal motor unit activities were observed synchronous with respirations.

In the other eight rabbits in the experimental group, the EMG recording on the left vocal muscles was found within normal limits. Along with denervation activities on symptomatic right vocal muscles, there was the presence of motor unit discharges synchronous with respirations. The findings were evaluated as regeneration.

In all 10 rabbits in the control group, intensive total denervation potentials were observed in symptomatic right vocal muscles. There was no motor unit activity synchronous with respirations in any of these muscles. However,

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Fig. 3 Normal activity

normal motor unit activities synchronous with respiration were observed in the left vocal muscles (Figs. 3, 4 and 5).

Pathologic Examination

The rabbits were sacrificed after the videolaryngoendoscopic examination and EMG, and subjected to neck dissection. Tissues were fixed in 10% buffer formalin and buried in paraffin to be examined under the light microscope with H&E staining. Muscle tissue changes in the experimental and control groups were histologically-

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Fig. 4 Post-operative activity (experiment group)

Fig. 5 Total denervation

evaluated by comparing the right hemilarynx at the experiment site. Of the muscle tissue changes, atrophy was detected in only one case in the experimental group (10%) in the right hemilarynx, and it was later established that the anastomosis in this case was not functional. No right vocal cord muscle atrophy was detected in the other nine rabbits in the experiment group. In all cases in the control group, atrophy was observed in the right hemilarynx. No atrophy was detected in the left hemilarynx in the experimental and control groups (Figs. 6, 7 and 8).

Discussion

Of the complications of the thyroidectomy procedure, cutting of the recurrent nerve was examined in our study and our experimental study aimed to treat this complication.

Fig. 6 No muscle atrophy was detected in the anastomosis group

Fig. 7 A microscopic image of the anastomosis area and suture site in the anastomosis group

The major anatomic function of the diaphragm is to separate the thoracic and abdominal cavities. The major physiologic function of the diaphragm is ventilation [4]. Prognosis is good in unilateral paralysis, especially in the absence of underlying neurological or pulmonary process [5]. Paralysis of the right or left hemidiaphragms does not significantly affect respiratory function. Clinically, respiratory distress is minimal in adults; however, patients may have complaints of chest pain and a non-productive cough. Bilateral diaphragmatic paralysis is tolerated in normal adults. The activity of the accessory respiratory muscles is evident in patients with bilateral paralysis. In infants and young children, however, unilateral paralysis might cause serious respiratory dysfunction; bilateral paralysis may be fatal in infants and children [6].

The only real abductor muscle of the vocal cords is the posterior cricoarytenoid muscle. The recurrent laryngeal nerve innervates all of the intrinsic muscles of the larynx,

Fig. 8 Muscle atrophy is observed in the control group

except the cricothyroid muscle [7]. Cutting of the recurrent nerve is a serious complication, as it leads to vocal cord paralysis. The ipsilateral vocal cord is fixed in the paramedian position [8]. The vocal cords should be evaluated pre-operatively. This evaluation helps identify the pre-operative presence of vocal cord paralysis or its post-operative development. The recurrent laryngeal nerve should be routinely identified during thyroidectomy or parathyroidectomy. Bilateral recurrent nerve cutting is very dangerous as it might cause respiratory obstruction. Both paralyzed vocal cords are slightly in the abducted position [8]. The patients develop stridor. In vocal cord paralysis, maintenance of the airway forms the basis of treatment. Bilateral vocal cord paralysis will require tracheostomy to maintain a stable airway. Tracheostomy may also be needed in unilateral paralysis. In permanent unilateral vocal cord paralysis, the paralyzed vocal cord can be injected with Teflon [9]. Some studies have been conducted to ensure the re-innervation of the larynx. Tucker's nerve-muscle flap prepared with the sternohyoid was implanted in the larynx [9–11]. Chen and et al performed a study in humans. In this study; clinically, it may be safe and available for cutting phrenic nerve off at the level of the subclavian vein [12].

During total thyroidectomy, as all of the arteries and veins feeding the thyroid will be cut, it might be very difficult to determine whether the incised structure is a vein or a recurrent nerve. If suspected structures are cut because they are assumed to be arteries, the presence or absence of lumens should be ascertained in the cut ends and if there is no lumen, the possibility of cutting a recurrent nerve should be considered; if the incised structure is ascertained to be a nerve, then primary suturing should be performed [13]. When a cut recurrent nerve is identified, primary suturing cannot be performed if the laryngeal end is identified while the other end is not. Our nerve transposition experiment was designed to be used in such cases. In our experimentation, a model of unilateral recurrent nerve paralysis was created and diaphragmatic stimuli were directed to vocal cords by nerve transposition. By stimuli conducted to the vocal cords, denervated muscles were re-innervated and actively participated in respiration. In our experimentation, nerve anastomosis is made in an end-to-end formation. On the 1st post-operative day of anastomosis, no vocal cord activity was identified; nevertheless, in the examinations performed in the 3rd week, vocal cord activities and re-innervation potentials were detected on EMG. With a success rate of 90%, no pathologic atrophy was observed in the larynx. Following the cutting of the recurrent nerve, our nerve transposition experiment successfully restored the larynx physiology.

Consequently, as previous experiments and our experimental studies suggest, right phrenic-to-right recurrent nerve

anastomosis can be performed on patients with bilateral recurrent nerve cutting if there are no contraindications.

The patient who planned to operation must be consulted with thoracic surgeon and liver surgeon preoperatively.

Unilateral recurrent nerve palsy may not need therapy. Nerve transposition is major operation. We do not advise this operation for unilateral recurrent palsy. Whereas bilateral recurrent nerve palsy is serious problem. Tracheostomy is serious condition. Tracheostomy has social and medical problems. We aim that to save the patient to the tracheostomy and to recover of the laryngeal functions. If the patient has not any contraindication, nerve transposition may be performed.

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