The influence of heat and moisture exchangers on tracheal climate in laryngectomized individuals: toward optimal pulmonary rehabilitation

Scheenstra, R.J.

Publication date
2011

Citation for published version (APA):
CHAPTER 1

General introduction
Laryngeal cancer: epidemiology, treatment and prognosis

In The Netherlands, approximately 600 new cases of laryngeal cancer are diagnosed each year. Over the past 20 years, the incidence of laryngeal cancer has declined from 5.4 to 3.9 per 100,000 inhabitants. In the same period, the male-female ratio has fallen from 9:1 to less than 6:1, which is primarily caused by a decline in the incidence among the male population with an unchanged incidence among female (www.ikcnet.nl). Regardless of the treatment modality, early stage (Tis, T1, and T2) laryngeal carcinomas have an 80-90% probability of cure and more advanced tumours of about 60% [1].

For many years, total laryngectomy (TL) followed by radiotherapy (RT) was considered the standard treatment for advanced-stage (T3-4) laryngeal cancer. During the last two decades, curative treatment has shifted from traditional radical surgery to larynx-preserving strategies. Indeed, after (chemo) radiotherapy ((C) RT), larynx preservation can be achieved in a majority of cases [2-4], but it would be erroneous to consider TL as salvage therapy. Basically, organ-sacrificing surgery has been shown to achieve higher 5-year survival rates than (C) RT in advanced-staged (T4 stage-IV) larynx tumours [4;5]. Therefore (at least for the moment), TL is still the best approach to achieve loco regional control and survival in patients with transglottic tumours with extra-laryngeal extension. Furthermore, TL is the only curative treatment strategy in patients with recurrent or residual laryngeal cancer, who have been treated with primary (C) RT. Additionally, in some cases, TL has to be performed for functional reasons since (C) RT can cause severe local side-effects leading to an irreversible non-functioning larynx and recurrent aspiration pneumonias. Each year, approximately 150 patients undergo total laryngectomy (www.prismant.nl), with an estimated total number of 2000-3000 laryngectomized patients presently living in The Netherlands.

Rehabilitation of total laryngectomy

Due to relatively good 5-year survival rates (about 60%) [1;6-8], optimal post-operative long-term rehabilitation after total laryngectomy is as important as it is challenging. Ever since the first laryngectomy for cancer performed by Billroth in 1873 [9], literature on rehabilitation after TL has been dominated by efforts to restore oral communication. Over the last decades, prosthetic tracheoesophageal voice has considerably improved the results of vocal
rehabilitation after TL, and nowadays is considered the most successful method in this respect with success rates up to 90% [10-12]. A voice prosthesis is (per) operatively placed into a tracheoesophageal puncture. When the tracheostoma is occluded airtight, expiratory air passes through the voice prosthesis into the pharynx, which leads to sound-producing mucosal vibrations and, as a result, enables speech (Figure 1.1).

Figure 1.1 Patient before (1a) and after (1b) laryngectomy. Figure 1c illustrates digital closure of the HME valve to obtain air-tight occlusion needed for tracheoesophageal speech.

Now that post-laryngectomy voice restoration has reached quite acceptable voice and speech quality results in most patients [12;13], other postoperative consequences of the disconnection of the upper and lower respiratory tract after TL, such as the inevitable disturbances of the sense of smell (hyposmia/anosmia), and pulmonary consequences have become more important issues to be addressed [14-16]. This thesis focuses on the respiratory consequences and pulmonary rehabilitation after TL.

**Pulmonary rehabilitation in laryngectomized individuals**

The larynx has a central position in the respiratory tract, connecting the upper and lower airways. The upper respiratory tract protects the lower airways by providing a defence mechanism against aspiration and with respect to respiratory ‘climate’ by: 1) heating and humidifying the inspired air; 2) providing airway resistance; and 3) providing a defence mechanism against dust particles through mucociliary transport and local immunity of the mucosal
layer. This thesis focuses on the restoration of normal climate conditions in the trachea.

**Physiological principles of respiratory heat and water exchange**

During inspiration, air is warmed by turbulent convection, and simultaneously moistened due to evaporation from the mucosal respiratory epithelium. During the thermal energy consuming evaporation process, the mucosa is cooled down. This heating and moistening process is continued along the whole respiratory tract. The point where inhaled air has reached body temperature (37 °C) and is 100% saturated with water vapour (44 mgH₂O/L) [17;18], is referred to as the isothermal saturation boundary (ISB) [19;20]. During normal rest breathing, this situation is reached in the main bronchi a few centimetres below the carina. During the following expiration, air comes from the alveolar environment with climate conditions similar to those at the ISB. After the expired air has passed the ISB, it goes along the previously cooled mucosal respiratory epithelium. By turbulent convection, heat is now transferred back to the mucosa. The more air is cooled alongside the respiratory tract, the less water vapour it can contain. Water vapour is then released by condensation [18;19;21-23]. As a result, approximately 20-25% of the previously exchanged heat and moisture is returned to the respiratory epithelium [18;19]. The remaining heat and water is lost in the expired air (see Figure 1.2).

If the upper airways are bypassed (after TL or tracheotomy) inspired air passes a much shorter respiratory tract before reaching the peripheral airways during open stoma breathing. As a consequence, the ISB is shifted in the direction of the lower peripheral airways. Consequently, the part of respiratory tract with optimal temperature and humidity (caudal from the ISB) is reduced. This means that a longer part (cranial of the ISB) of the tracheal/bronchial mucosa is too dry and too cold, which may lead to hyperactivity of the mucous and goblet cells [62-64]. Hence, it is not surprising that laryngectomized patients report an increased sputum production [15]. Clinically, the extent of the increased mucous production is best noticed in the morning, when an accumulation of mucous has occurred during sleep, when there is little coughing and expectoration, which during daytime deliberately can be applied for clearing the airways. In addition to the increased mucous production, other pulmonary problems with a major impact on daily life and thus on overall quality of life may develop, for example increased spontaneous coughing, frequent forced expectoration, dyspnoea, and recurrent pulmonary infections [15].
Heat and moisture exchange in nasal breathing in normal individuals in rest in room environment. Shown are the temperature, absolute humidity (AH in mgH₂O/L) and relative humidity (RH in %) values during inspiration and expiration. Inspired air has normal climate conditions (23 °C, 10 mgH₂O/L, 40% RH). In the peripheral airways, the isothermal situation is reached (37 °C, 44 mgH₂O/L and 100% RH). Modified from Rathgeber et al [19] and Webb et al [24].

Heat and Moisture Exchangers (HMEs)

Before introduction into pulmonary rehabilitation for laryngectomized patients, Heat and Moisture Exchangers (HMEs) were already used in anaesthesiology (further called HME-A) during mechanical ventilation. As an HME-A is too large for convenient use in laryngectomized patients (Figure 1.3), they were redesigned in order to fit to the tracheostoma, for example by using a peristomal adhesive (Figure 1.3).

In the late eighties of the last century, HMEs have been introduced for use in laryngectomized patients. Consistent use of these medical devices has been proven to reduce pulmonary complaints significantly, and, as a consequence, also to improve quality of life [25-27]. Therefore, postoperative and 24/7 use of an HME is generally considered an essential part of improvement of pulmonary function in laryngectomized individuals [28]. As frequent use of HMEs in laryngectomized patients is associated with a relief in pulmonary complaints [25-27], it is generally accepted that these devices, at least partly, compensate for the lost air-conditioning function of the upper airways.
Figure 1.3 Standard HME used in anesthesiology (HME-A; left) (Ø 5 cm), revised version of the first HME developed for use in laryngectomized patients with integrated adhesive (Provox® Stomvent HME; Ø 2.5 cm). Notice the difference in size, shape and the possibility for digital occlusion of the HME.

**Physical principles of HMEs and specification of HME performance**

Nowadays, many different HMEs are commercially available for use in laryngectomized patients. These medical devices may vary in shape, size and type of media for attachment to the peri- or intrastomal area. In contrast, the heat and moistening function of all these HMEs are based on the same principle: condensation and evaporation of water to retain water from expired air (Figure 1.4). The basic material of such devices consists of foam or paper, sponge or another substance. In order to increase heat and water retaining
capacity, this material is impregnated with a hygroscopic chemical (such as magnesium, lithium or calcium chloride) [29;30].

During expiration, water vapour from the warm and humid air condenses on the HME material, which initially has a lower temperature than the warm expiratory air. In turn, this water evaporates into the air that is subsequently inspired [31;32]. The main purpose of an HME is to conserve expired water, and therefore reduce water loss. Water loss is considered the main HME characteristic, and is measured \textit{in vitro} under standardized laboratory conditions (specified as ISO standards\textsuperscript{1}).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{hme_principles.png}
\caption{Principles of heat and moistening exchanging of a passive HME device. During expiration, air coming from the peripheral airways is warm and humid. Due to the relatively cold HME device, water condensates on the foam of the HME which involves a release of heat (energy). Environment air that is to be inspired is relatively cold and dry. During the following inspiration, water from the HME foam is evaporated to the inspired air (coupled with heat withdrawal).}
\end{figure}

\textsuperscript{1} ISO (International Organization for Standardization) is the world’s largest developer and publisher of International Standards. Those used for HME devices (ISO9360-2:2001) are available at www.sis.se.
Under these standardized conditions, one of the regularly-used HMEs (Provox® Normal HME, Atos Medical, Sweden; further named R-HME) for laryngectomized individuals is reported to have a moisture output of 23.7 mgH₂O/L. Assuming that the exhaled air contains 44.1 mgH₂O/L, this suggests that the R-HME would add 20.4 mgH₂O/L to inspired air. However, the in vivo measurements show that the R-HME actually ‘only’ adds approximately 3.2 mgH₂O/L to the inspired air [33], which differs substantially from the in vitro specification. Although in vivo end-inspiratory values are studied and not the overall mean (as is assessed in the ISO norm) this cannot explain the large difference in HME effectiveness. Several additional factors may be responsible. First, in the ISO norm the inhaled air is room environmental dry and the exhaled air relatively warm (and humid) compared to our conditions. Secondly, in the in vivo study, the breathing frequency (16-18 per minute) is considerably higher than in test condition 1 of the ISO norm (10 per minute). Thirdly, and perhaps most importantly, during the in vivo measurements, the trachea itself also functions as a heat and moisture exchanger, so that they cannot be compared with laboratory test conditions at all. Although it is hard to differentiate to what extent each of the above mentioned considerations (i.e. humidity of the air, ‘breathing’ frequency, trachea ‘HME’ properties) account for the difference between laboratory and in vivo measurements, it does emphasize the additional value and necessity of in vivo climate assessment.

The HME effect on tracheal climate (temperature and humidity)
A few studies had investigated the in vivo HME effect on endotracheal climate in laryngectomized patients under room climate conditions. These studies are reviewed by Zuur et al [34]. In short, a relatively wide range of end-inspiratory humidity values (AHinsp) has been reported when compared to the range of end-inspiratory temperature values (Tinsp). The explanation for these findings is that accurate and reliable temperature sensors with fast response times, able to follow the whole breathing cycle of 3-4 s (ranging 0.1–0.4 s), were only available for temperature measurements. Humidity measurements are technically much more complicated. Firstly, response times of the humidity sensors used in the reviewed studies ranged from 0.25 to > 9 s. Not all of them were therefore fast enough to follow the breathing cycle. Secondly, as

---

2 Manufacturer’s specification (test condition 1 of ISO): an environmental temperature (inhaled air) of 23 °C with an absolute humidity of < 1 mgH₂O/L; exhaled air of 37 °C and 100% RH (44.1 mgH₂O/L); a tidal volume of 1000 ml; and a breathing frequency of 10/min.
humidity sensors are generally too large to fit in the tracheostoma, air has to be sampled from the respiratory tract and measured outside the body. In none of the reviewed studies, this transported air was prevented from cooling down in the sampling tube and heated (to at least body temperature), leading to immediate condensation of the transported air, and thus to an underestimation of the reported humidity values.

Obviously, *in vivo* humidity measurements in laryngectomized patients are technically challenging. As no commercial measurement system is available for this purpose, a purpose-built machine has been developed in a collaborative project between the Netherlands Cancer Institute and the Academic Medical Centre of the University of Amsterdam (the Airway Climate Explorer; ACE), for the assessment of endotracheal temperature and humidity in laryngectomized patients (Figure 1.5). The development and first validations have been described in detail previously and shown in Figure 1.5 [35].

**Figure 1.5** The Airway Climate Explorer. A small diameter (5 mm) sample catheter is proximally connected to a sensor house in which a fast humidity sensor is built. Both the sample catheter and the sensor house are internally heated to 40 °C in order to prevent condensation of water vapour within the sample catheter and/or sensor house [35].
The HME effect in different climate conditions

Measurements with the ACE at room temperature showed that breathing with an HME has lead to an increase in AHinsp (23.3 to 26.6 mgH$_2$O/L; difference +3.3 mgH$_2$O/L). End-inspiratory temperature, however, decreased (28.5 to 26.9 °C; difference -1.5 °C) with the presence of an HME [33].

Measuring endotracheal temperature and humidity in a cold and dry room (4.5 °C; 4.5 mgH$_2$O/L) showed that the first centimetre of the trachea at the level of the tracheostoma already warms and humidifies inspired air to 19.7 °C and 20.9 mgH$_2$O/L respectively during open stoma breathing [36]. Using an HME has an immediate beneficial effect: the end-inspiratory temperature is increased to 23.6 °C (+3.9 °C) and the end-inspiratory humidity to 25.1 mgH$_2$O/L (+4.2 mgH$_2$O/L). This finding corresponds for instance well with earlier observations by Natvig et al who found that in wintertime patients experienced less pulmonary problems and a significant increase in peak expiratory flow after a fortnight stay in a subtropical climate [37].

So far no data about endotracheal temperature and humidity in a warm and dry environment were available. Although it seems reasonable to recommend HMEs under any climatologically circumstance to protect the airways from direct contact with the ambient air, no evidence-based recommendations about the use of HMEs under such climate conditions could be given yet.

HME and airway resistance

The upper airways account for 50–75% of total airway resistance during quiet breathing in normal individuals, of which two third is caused by nasal resistance [38]. It has been suggested by several authors that a reduced resistance to expiration indirectly decreases arterial oxygen saturation by reduced expiratory lung volumes resulting in suboptimal pulmonary gas exchange [39-42]. To compensate for upper airway resistance, stoma filters with breathing resistance equal to that of the normal upper airways have been developed. However, a beneficial effect of these so-called high-breathing resistance HMEs on tissue oxygenation has not been unambiguously shown yet [43;44]. Therefore, the clinical advantage of high-breathing resistance HME devices – if any – is expected to be limited and clinically probably not very relevant.

Clinically of more importance is that a high-breathing resistance is experienced as uncomfortable breathing and it is thus not surprising that HMEs with a
somewhat lower breathing resistance show a better patient compliance: high breathing-resistance HME comparable to that of the upper respiratory tract (0.32 kPa.L/s) is judged as comfortable in 80% of the patients during rest but only in 50% of the patients during exercise, whereas 94% of the patients experienced comfortable breathing during exercise in presence of a lower breathing-resistance HME (0.12 kPa.L/s) [45]. This is not unexpected, as the normal upper respiratory tract resistance is variable, whereas the HME resistance is fixed and thus not capable of adapting to different physical exertion levels.

To avoid uncomfortable breathing with an HME, its breathing resistance thus must be limited in order to optimize patient compliance. However, HMEs will unavoidably have a noticeable resistance: a close interaction between the air stream and the material of the HME is required for an effective heat and moisture exchange. Therefore, an accurate balance between heat and moisture exchange and breathing resistance is required when designing an HME.

**Impact of HMEs on clearing the airways**

Productive cough is effective in clearing the airways of small particles in a hypersecretory state of the lower airways [46]. In healthy individuals, closure of the epiglottis is important to be able to develop sufficient intrapulmonary pressure, which is important for the initiation of an effective cough. The subsequent sudden opening of the glottis leads to a considerable high flow rate necessary for expectoration. Although most laryngectomized patients acquire a new coughing technique, the effectiveness of their cough is considerably less than in normal individuals [47;48]. Secondly and perhaps more importantly, laryngectomized patients lack the mucociliary clearance of the upper airways, so that recurrent pulmonary infections, forced expectoration to clear the lower airways, and frequent coughing are not uncommon among laryngectomized patients.

Frequent use of an HME decreases the necessity for clearing the airways [26;27]. This is unlikely to be caused by filtering of dust particles by the HME filter as a simple hygroscopic HME filter is designed with a relatively large pore size [29;49]. Therefore, these HMEs are rather inefficient barriers for microorganisms, even though some HMEs have been impregnated with a bactericide solution (for example chlorine hexidine) in an attempt to control bacterial colonization [50]. Vice versa, effective antimicrobial filters, usually
constructed with a pleated hydrophobic membrane, are ineffective moisture 
exchangers [29;51].

Nevertheless, an HME (without additional antimicrobial filter) has been shown 
to reduce pulmonary infections [27]. Empirical experience in the Netherlands 
Cancer Institute is that winter-time trachea-bronchitis in laryngectomized 
patients has become a rare clinical entity over the last decades since the frequent 
use of HME devices started. This reduction in recurrent pulmonary infections 
is believed to result from improved mucociliary respiratory epithelium due 
to improved endotracheal climate. First, the degree of mucociliary activity is 
related to both temperature and humidity as mucociliary mucosa has an optimal 
function at a temperature ranging between 35 and 40 °C and with relative 
humidity values over 50% [32;52-54]. Additionally, excessive loss of water 
through the respiratory tract in laryngectomized patients leads to an increased 
viscosity of the mucous layer, which in turn leads to a disturbed mucociliary 
function and eventually to a damaged mucociliary respiratory epithelium 
[53;55]. Therefore, improving endotracheal temperature and humidity in 
laryngectomized patients may improve tracheo-bronchial mucociliary activity 
[26;27].

Conclusion and outline of this thesis

Total laryngectomy (TL) still is an indispensable therapy for a substantial subset 
of patients with laryngeal cancer. Because of the relative good prognosis with 
an overall 5-year survival of about 60%, laryngectomized individuals may 
survive for several decades. Therefore, optimizing quality of life after TL is of 
great significance. Apart from the obvious relevance of voice rehabilitation, 
reduction of the inevitable pulmonary problems laryngectomized individuals are 
confronted with has been a challenge for many years. Regular use of HMEs is the 
most significant evidence-based treatment option for pulmonary rehabilitation 
in laryngectomized patients, and these medical devices have been proven to 
reduce pulmonary complaints significantly. It must be noted, however, that 
although decreased, pulmonary complaints are not yet fully eliminated. As 
already postulated by Zuur et al [33] based on their finding that the R-HME 
reduces the end-inspiratory temperature with 1.5 °C, further improving the 
heat and moistening capacity of an HME device may lead to a further reduction 
of the pulmonary complaints in laryngectomized patients and improvement
of quality of life. Therefore, ongoing development and improvement of the presently available HMEs is still warranted.

The main purpose of this thesis is to gain better insight in the working mechanism of HMEs and their effects on endotracheal temperature and humidity. These newly gained insights may contribute to the further development and improvement of these therapeutic devices.

The first step in improvement is to obtain target temperature and humidity values for HMEs. Such a study has been performed by Ingelstedt et al in the early fifties [56] in young and healthy individuals, but these may not be representative for most laryngectomized individuals (mostly elderly and heavy smokers). In Chapter 2 the ‘HME-capacity’ of the upper respiratory tract is addressed, and new target values are presented and discussed.

Although in vivo testing of HMEs is a necessity, as discussed above, it would be practical when these studies do not require a too large number of patients in view of the technical aspects of the methodology and the potential burden of such testing for patients. Therefore the (intra- and inter-patient) variations of endotracheal temperature and humidity measurements with the Airway Climate Explorer was carried out in order to estimate the required number of patients for in vivo studies. In Chapter 3, the results of repeated in vivo measurements of endotracheal temperature and humidity with and without HME are shown and discussed. Extended statistical modelling also offers interesting details about the working mechanism of an HME.

All clinical studies investigating HMEs so far were performed in either room or cold climate conditions. No data about endotracheal climate in laryngectomized individuals in a warm environment is available yet. Chapter 4 describes the HME effect on endotracheal climate in a warm and dry environment. Deviations in the breathing pattern at temperatures up to 38 °C are discussed.

In the following three chapters, the results of measurements with different HME devices are discussed. Chapter 5 focuses on an HME with lower breathing-resistance. Since the foam (the core material) of this HME is more porous in order to offer lower breathing resistance, the heat and moistening capacity is also expected to be lower. Moreover, the difference on breathing pattern due to the difference in breathing resistance is discussed.
Chapter 6 focuses on a newly developed HME with integrated virus and bacterial filter. This HME is covered with an electrostatic layer (the antimicrobial filter) to decrease the risks of airborne infections and to protect the airway from polluting particles (like dust or pollen). This chapter deals with the heat and moisture exchanging effect of this particular HME. Similarly important are the results of a short-term clinical study, in which laryngetomized individuals tested this new HME with antimicrobial filter.

In Chapter 7 the endotracheal temperature and humidity values of two new generation HMEs are shown, which were developed using the insight gained in our previous studies. They are compared to the present generation and an older version of HME devices (with corrugated paper as its basic material). Additionally, the results of a 3-week testing period are shown and discussed.

Chapter 8 is a general discussion of all results mentioned in the previous chapters, and provides recommendations for further HME development.