Clinical scoring and biophysical evaluation of nasolabial skin barrier damage caused by rhinorrhea

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Background: An acute viral cold is a very common illness and is characterized by sneezing and a runny nose. Because of rhinorrhea and frequent use of handkerchiefs, the skin around the nose feels uncomfortably dry and flaky.

Objectives/Methods: To evaluate the nasolabial skin barrier impairment, 14 female volunteers with a common cold were recruited. Visually assessed clinical scoring and/or biophysical measurements – including transepidermal water loss, stratum corneum hydration, skin colour, squamometry, skin pH, and a skin surface lipid profile analysis – were carried out at the start of the cold, a second time when the severity of the cold symptoms was maximal, and finally when the volunteers felt healthy again and stopped using handkerchiefs.

Results and Conclusions: Transepidermal water loss assessments showed significantly higher measurements on the maximum outcome of the nasal cold compared with the time-point when the symptoms of the cold had disappeared. This was in accordance with skin colour chroma a* measurements and the visually assessed skin erythema and scaliness scores, indicating that the superficial nasolabial skin barrier was inferior at the maximum of a nasal cold in comparison with the skin condition when volunteers were fully recovered.

Key words: biophysical measurements; common nasal cold; hydrolipidic film; nasolabial skin barrier; quantitative squamometry; visual scoring. © Blackwell Munksgaard, 2008.

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Suffering from an acute viral cold – caused by rhinoviruses or coronaviruses – probably is the most common illness known (1). A common cold usually is mild and self-limiting. Apart from an overall discomfort, cold symptoms are sneezing, serous nasal secretion, and obstruction of nasal breathing caused by the swelling and inflammation of the sinus membranes (2). These symptoms occur 2–3 days after the infection and usually last for 7–10 days (1). In acute viral rhinitis, only the symptoms can be treated and common over-the-counter medication for a cold may already be effective (3). When suffering from a cold, frequent rubbing of the nasolabial skin with handkerchiefs can provoke skin irritation, which – at first – heals difficultly because the skin reacts by an inflammatory response leading to hyperkeratotic scaly areas. These clinical symptoms of a mechanically

induced dermatitis probably are caused by removal of the superficial hydrolipidic layer and disturbance of the barrier function in the upper part of the stratum corneum (SC).

Therefore, the aim of the present study was to obtain more information on the damage of the skin situated directly under the nose and on the outer lower edges of the nostrils when suffering from a common cold. Apart from photo documentation and visual assessment of the skin around the nose, non-invasive biophysical measurements, i.e. transepidermal water loss (TEWL), SC hydration, apparent skin pH, and colour measurements were performed. These assessments were followed by squamometric measurements and a high-performance thin-layer chromatographic (HPTLC) analysis of the nasolabial skin surface lipids (SSLs). Consequently, the

biophysical assessments carried out will help in understanding the typical skin symptoms of a common cold and the effects of mechanical damage induced by handkerchiefs on the nasolabial skin regions.

Materials and Methods

Volunteers and experimental study design

From a number of previously recruited healthy female volunteers (Fitzpatrick scale phototype II or III), 14 participants (mean age 24 ± 5 years, range 19–36 years old) with an acute viral cold entered the study and signed informed consent. Chronic nasopharyngitis and allergic rhinitis were excluded from the study. The volunteers had no skin pathologies and were willing to follow up study restrictions. No medication was allowed. Exclusion criteria were summarized in an information letter. Study approval was obtained from the local Ethics Commission of the University Hospital Brussels (Jette, Belgium). The study was conducted between October and the end of March. Upon recruitment, all subjects received paper handkerchiefs (not pretreated), wrapped in anonymous plastic foils (Procter & Gamble, Schwalbach am Taunus, Germany). Volunteers were instructed to use only these handkerchiefs for nose cleansing and not to reuse a single handkerchief. No lotions, creams, decorative cosmetics, and other skin care products in the face were allowed from the first symptoms of the cold until the end of the study. During the course of the cold, the subjects recorded in a diary their experiences, the amount of individual handkerchiefs used per day, and the number of days their cold continued. Three assessment points were scheduled: day onset: very first start of the cold symptoms; day max: culminating point of the viral cold, at least 3 days of hanky use; day recovery: completely recovered from the cold, at least 2 weeks after the last handkerchief use. Evaluations were always carried out at the same hour of the day to exclude influences of circadian rhythmicity (4, 5).

Skin evaluation and biophysical measurements

An overview of the different skin assessments carried out on the respective facial zones 1, 2, 3, and 4 (Fig. 1) as a function of the three evaluation points is given in Table 1. Room conditions for day max and day recovery were $20.4 \pm 0.4^\circ\text{C}$ and $20.5 \pm 0.4^\circ\text{C}$ (temperature) and $50.2 \pm 2.9\%$ and $47.8 \pm 2.8\%$ (relative humidity), respectively. After a premeasurement rest of at least 30 min in this climate-controlled room, visual grading was carried out. The 'specified symptom sum

Fig. 1. Facial measuring zones. Zone 1 is located on the nostrils, zone 2 is the nasolabial area under the nose, and zone 3 includes the filtrum (i.e. centre directly below the nose bridge). Cotton rolls (Celluron® Ø 10 mm, ref. 430182; Hartmann, Heidenheim, Germany) were used to close the nasal orifices, avoiding nasal air turbulences on the skin. As control site, zone 4 is the area above the nervus supraorbitalis on the forehead. Randomization of left and right side for test zone 4 was respected among the different volunteers.

score system' (0, absent; 4, extreme situation) was used to score the clinical assessments of skin erythema and dryness/scaliness (6, 7). Biophysical tools from Courage + Khazaka electronic (Köln, Germany) were the Tewameter TM210® measuring TEWL by the open gradient technique, the Corneometer CM825® (electrical capacitance) and the Skin pH meter PH900® (apparent skin pH). The Chromameter CR300® (Minolta, Osaka, Japan) was used for skin colour measurements. Quantitative squamometry making use of D-Squame® discs (Ø 2.2 cm; Cuderm Corporation, Dallas, TX, USA) was conducted according to the methodology previously described by our group (8). Nasolabial SSLs were collected from the hydrolipidic layer by two consecutive single tape strips (1 × 3 cm; Leukoflex™, Beiersdorf, Germany). HPTLC analysis of the latter SSLs was based on the extraction method and quantitative densitometry, as published by Weerheim and Ponc (9). Lipid standards, representative for SSLs (squalene, triglycerides, cholesterol, cholesterol esters, free fatty acids, and wax esters), were purchased from Sigma (St Louis, MO, USA) to set up calibration curves. To avoid interference with the biophysical tools, squamometry and SSL samplings were carried out after the skin measurements.

Table 1. Overview of the visual scoring (photo documentation) and biophysical measurements carried out on skin zones 1, 2, 3, and 4 on day onset, day max, and day recovery^a

Time	Skin site			
	Zone 1	Zone 2	Zone 3	Zone 4
Day onset	Visual scoring	Visual scoring	Visual scoring	
Day max	Visual scoring	Visual scoring TEWL Skin hydration pH of skin Skin colour Squamometry Tape stripping	Visual scoring Skin hydration pH of skin	TEWL Skin hydration pH of skin
Day recovery	Visual scoring	Visual scoring TEWL Skin hydration pH of skin Skin colour Squamometry Tape stripping	Visual scoring Skin hydration pH of skin	TEWL Skin hydration pH of skin

TEWL, transepidermal water loss.

^aOne single operator was responsible for all biophysical measurements. Another person – blinded from the biophysical data – was involved in the clinical scorings. Squamometry and tape stripping carried out on zone 2 were randomized, each on a different side of the upper lip.

Results

To make sure that no climatological influences were present during measurements and sample collection, outdoor changes in atmospheric pressure (P_{atm} mmHg), temperature ($T^{\circ}\text{C}$) and relative humidity (RH%) were recorded throughout the test period. Conditions measured on day max and day recovery were 760.7 ± 8.4 mmHg and 761.2 ± 7.6 mmHg, $7.8 \pm 3.1^{\circ}\text{C}$ and $7.1 \pm 3.5^{\circ}\text{C}$, $85.1 \pm 14.0\%$ and $77.4 \pm 18.5\%$, respectively. None of the parameters assessed yielded significant changes over time (parametric paired *t*-tests), meaning that the participating subjects suffering from a cold entered the study equally divided over the complete assessment period of the experiment. At the end of the experiment, the information collected from the individual diaries indicated that an average cold lasted for 4 days and that 30 paper handkerchiefs were used per day.

Figure 2 displays TEWL measurements as assessed on the nasolabial area (zone 2) and the forehead (zone 4). Significant differences for zone 2 (both left and right sides) were observed with higher values on day max compared with day recovery, indicating a decreased skin barrier function. TEWL values measured on zone 4 did not show significant differences between both assessment points underlying the observation that day recovery took place under the same meteorological conditions as day max. This means that no winter climate-induced skin changes occurred and that the observed perturbations at the level of the skin barrier were completely because of the complications of the nasal cold and the frequent use of paper handkerchiefs. The skin barrier

impairment observed for zone 2 on day max was also confirmed by the chromametrically assessed skin erythema values (chroma a^*), which were significantly higher for zone 2L (Table 2) compared with those of day recovery.

In Fig. 3, the visually assessed scoring of skin redness and dryness/scaliness is expressed as a percentage of the subjects having a score higher than 0

Fig. 2. Absolute transepidermal water loss (TEWL) measurements in g/hr m^2 (mean $\pm$ SD; $n = 14$) as recorded on zones 2L and 2R and on zone 4, on day max and day recovery. The values of the nasolabial area (zone 2) measured on day max were significantly higher than those on day recovery ($P < 0.05$, non-parametric Wilcoxon signed-rank test).

Table 2. Mean $\pm$ SD ($n = 14$) and statistical significance of skin hydration, apparent skin pH, and chroma a* measurements^a

Parameter	Zone	Time		Significance (<i>P</i> value)
		Day max	Day recovery	
Skin hydration (a.u.)	2L	41 $\pm$ 12	45 $\pm$ 7	NS (0.451)
	2R	41 $\pm$ 12	45 $\pm$ 8	NS (0.116)
	3	40 $\pm$ 14	42 $\pm$ 12	NS (0.087)
	4	47 $\pm$ 10	53 $\pm$ 10	<i>P</i> = 0.007
Apparent skin pH (a.u.)	2L	4.7 $\pm$ 0.4	4.7 $\pm$ 0.4	NS (0.551)
	2R	4.7 $\pm$ 0.2	4.7 $\pm$ 0.3	NS (0.208)
	3	4.7 $\pm$ 0.3	4.7 $\pm$ 0.3	NS (0.505)
	4	5.1 $\pm$ 0.4	5.0 $\pm$ 0.3	NS (0.480)
Chroma a* (a.u.)	2L	20.90 $\pm$ 1.74	19.77 $\pm$ 2.08	<i>P</i> = 0.019
	2R	20.72 $\pm$ 2.44	19.64 $\pm$ 2.07	NS (0.064)
Scoring D-Squames [®]	2	2.25	2.50	NS (0.078)
Chroma C* (a.u.)	2	11.58 $\pm$ 3.86	14.36 $\pm$ 2.67	<i>P</i> = 0.041

a.u., arbitrary units; L, left; NS, not significant; R, right; SD, standard deviation.

^aSquamometrical data are expressed in median values for the D-Squame[®] scorings and a.u. for the chroma C* measurements. Results are ranked by facial skin zones as recorded on day max and day recovery. Statistical evaluation by non-parametric Wilcoxon signed-rank test; significant difference *P* < 0.05.

(total absence of symptoms). The investigated zones displayed significantly more erythema and dryness/scaliness on day max compared with day recovery.

The results for skin hydration, apparent skin pH, and squamometrically evaluated skin scaliness are also given in Table 2. For SC hydration

and skin pH measurements, no differences were seen between both evaluation points, except for the hydration level of zone 4, which was significantly higher on day recovery. During the course of the cold, significant changes were observed for the chromametrically measured squamometric results (chroma C*). Although the volunteers declared themselves as being fully recovered from their cold on day recovery, the applied squamometric technique showed a significantly higher level of skin scaliness on day recovery compared with day max. The latter phenomenon confirms the appearance of hyperkeratotic scales in response to physiological skin healing.

Finally, lipid analysis results (data not shown) indicated that the non-polar lipid fractions extracted from the tape strips tended to be depleted at the culminating point of the cold, but no statistically significant differences could be detected compared with day recovery (non-parametric Wilcoxon signed-rank test).

Discussion

The majority of common colds are associated with nasal congestion and periods of serous nasal discharge (rhinorrhea), requiring frequent nose cleansing with handkerchiefs (1). When having a cold, the skin of the outer lower edges of the nostrils as well as the skin area below the outside of the nose holes and the centre directly below the nose bridge can be quite painful. Subsequently, these skin areas often display erythema and scaliness. It was hypothesized that this characteristic feature possibly is because of maceration of the skin from the serous nasal secretion and, more importantly, frequent rubbing with handkerchiefs. The present study results show that skin

Fig. 3. Visual assessment of the three perinasal zones on day onset, day max, and day recovery with the percentages of subjects ($n = 14$) displaying erythema (ery) and dryness/scaliness (dry) on the different assessment points. Significantly higher values were found on day max for all zones compared with day recovery (*P* < 0.01, non-parametric Wilcoxon signed-rank test).

erythema and visually scored scaliness are indeed the most characteristic skin symptoms of a nasal cold. Together with the disrupted and inferior nasolabial skin barrier, marked by increased TEWL measurements, this clinical feature aggravates the discomfort of patients suffering from a cold. As changes in season and climate are important variables to consider during this type of study, evaluation of zone 4 was included to create an internal control for each of the participating volunteers throughout the complete duration of the experiment. This test area on the forehead – superior to the nervus supraorbitalis – was selected because it provides stable and reproducible TEWL values on both sides of the forehead (10).

Because of the cold and the occurrence of a runny nose, many handkerchiefs were used. The consecutive wiping of the skin aggravated the mechanical dermatitis, finally leading to a disturbed hydrolipidic film and barrier function in the upper layers of the skin. Although the skin of the nasolabial area looked scaly and dry, the hydration values measured during the study showed no significant differences between day max and day recovery.

As experienced in the present study, people suffering from an ordinary acute cold consume so many handkerchiefs that the wiping actions on their own increase the abrasive damage of the nasolabial zone, finally leading to a disturbed barrier function. It seems that the quality of the paper material used for nose cleansing could play an important role and that soft handkerchiefs would cause less damage on the hydrolipidic film and the skin barrier when having a cold. Soft paper handkerchiefs might then fulfil a preventive role in minimizing the damaging effect of the skin barrier function of the nasolabial zone. Consequently, during innovative product development, the first focus should lay on creating soft paper handkerchiefs. Second, one can also introduce a protective layer that may replenish the deteriorated superficial lipid barrier film. Such a comparative study between a pretreated paper handkerchief and its untreated control tissue is currently being carried out in a large population of volunteers suffering from an acute viral cold (11).

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