A new prototype nebulizer to optimize aerosol deposition into maxillary sinus and to limit lung deposition.

Sandra Le Guellec (1), Francis Dubois (2), Gilles Chantrel (3).
Laurent Charrouin (3), Stéphane Gatier (3), Laurent Vecellio (1).

Introduction

In rhinologic pathology, the intranasal route is the logical choice to administer topical medication. Various advantages are attributed to this delivery route; in particular, the relative non-invasiveness, the rapid onset therapeutic effect of low drug doses and minimal adverse effects (1). In clinical practice, nebulizers with nasal plugs are used to deliver topical treatment. The major part of drug (70 to 80%) is impacted into the nasal cavity, the other part is mainly deposited into the lungs (20%) (2). This can be a problem when the drug is not intended to reach the lungs. Indeed, drug used in clinical practice to treat rhinologic pathology could present a risk for lungs when delivered with nebulizers, such as essential oils, hypertonic formulations or drug with sulfites. Delivery of topical medications strictly into the nasal cavity using nasal nebulizers, is, therefore, a critical issue and a challenge.

A new nebulizer prototype, the ND-prototype (Atomisor, DTF, Saint-Etienne, France) was developed for nasal delivery to minimize penetration of aerosol in the pulmonary area, and to increase sinus penetration. NaF aerosol deposition with the ND-prototype was evaluated in vitro using an artificial model of nasal cavity and maxillary sinus (cast model) and evaluated in vivo with a scintigraphic study using Krypton 81m gas (Kr81m gas). In each study, influence of sound of 100-Hertz frequency (100Hz-sound) on the aerosol or gas deposition pattern was evaluated.

Material and methods

The in vitro study evaluated the aerosol deposition into the nasal cavity and sinus.

Two nebulizers - the NL11s/AOLH (Atomisor, DTF, Saint-Etienne, France - figure1) and the ND-prototype - were connected to the cast model and loaded with a 3%-NaF solution (n=3).

Nebulizations with the ND-prototype were performed with and without 100Hz-sound while nebulizations with NL11s/AOLH were performed with 100Hz-sound.

After 10 minutes, the cast model was dismantled and NaF mass deposited into the sinus and in the nasal cavity was assayed by an electrochemical method. NaF deposition was expressed in % of the loaded dose of NaF introduced into the nebulizer of both systems.

In vivo study (Figure 3)

Percentage (median values) of NaF aerosol deposited into the sinus and into the nasal cavity obtained after nebulization with the new ND-prototype with sound was higher in comparison to the NL11s/AOLH with sound: 0.30% in sinus (vs. 0.08%) and 2.11% in nasal cavity (vs. 1.74%).

During 100Hz-sounding nebulization, the ND-prototype allows improvement of sinus and nasal cavity aerosol deposition compared to the NL11s/AOLH nebulizer.

The influence of 100Hz-sound was also evaluated with this new ND-prototype. Modification of aerosol deposition pattern was observed when nebulizations were performed with or without sound: 0.18% in sinus and 4.17% in the nasal cavity without sound, and 0.30% and 2.11%, respectively, with sound.

The addition of 100Hz-sound during nebulization improves the aerosol maxillary sinus deposition.

Results

For the in vivo study, ventilation scintigraphies were performed with Kr81m gas in three healthy volunteers using the ND-prototype and NL11s/AOLH nebulizers, with and without 100Hz-sound.

Volunteers were placed in a seated position in front of a gamma imager FORBETM (Phillips). A nasal plug (atomisor, DTF) is connected on the NL11s/AOLH.

Patients inhaled with relaxed tidal breathing.

Scintigraphic images (128x128, 1 minute) of lungs and nasal cavity were acquired during delivery of Kr81m gas delivered from the nebulizer (8mCi-generator, 1l/min). Activity of Kr81m gas delivered total activity (defined as the amount of radioactivity that exited the device).

In vitro study (Figure 3)

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In vivo study

Figure 4A & 4B shows the distribution of Kr81m gas obtained when delivered with the NL11s/AOLH nebulizer: 2% to 13% of total radioactivity is detected in the nasal cavity and 87% to 98% into the lungs.

With the ND-prototype (Figure 4C & 4D), 7% to 34% of gas Kr81m was detected in pulmonary area and 66% to 93% was detected in nasal cavity.

Figure 5: Scintigraphic images (axial orientation) of Kr81m gas delivered from the nebulizer (8mCi-generator, 1l/min). Activity of Kr81m gas delivered total activity (defined as the amount of radioactivity that exited the device).

Figure 4: Scintigraphic images (128x128, 1 minute) of lungs and nasal cavity were acquired during delivery of Kr81m gas delivered from the nebulizer (8mCi-generator, 1l/min). Activity of Kr81m gas delivered total activity (defined as the amount of radioactivity that exited the device).

Conclusions

In vivo study demonstrates that the ND-prototype, a new nasal device, limits Kr81m gas penetration into the lung, which may limit the aerosol deposition into the lung.

As shown with both studies, the addition of 100Hz-sound during nasal nebulization improves the aerosol penetration and deposition into maxillary sinuses.

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