Assessment of sonic nebuliser performance to target maxillary sinuses.


Introduction

Intranasal nebulisation is used in mostly chronic sinonasal pathologies. Despite the lack of clinical evidence (1), nasal aerosols seem to be the best therapeutic option for topical drug delivery, in particular for antibiotic therapy. Indeed, nebulisers are more effective, compared with nasal sprays, to target ethmoid, middle meatus and maxillary sinuses (MS), anatomical infected sites presenting a therapeutic interest (2,3,4). Moreover, in CF patients, studies described MS as reservoirs for P. aeruginosa to proliferate and diversify in mucoid forms inducing chronic lung infections (5). Specific nasal nebulisers used transitions to improve the aerosol deposition in MS as the sonic NL11SN.

The objective was to quantify the deposition of antibiotic in nasal cavities & in MS, obtained with a sonic nasal nebuliser in an in vitro study (plastinated head model). The sonic nebuliser was also in vivo evaluated for intranasal administration in healthy volunteers.

IN VITRO STUDY

In vitro METHOD

The in vitro nasal model was a plastinated head which has an exterior access to MS allowing drug collection. Nasal nebulisations (n=1) of Gentamicine were performed with the NL11SN (sonic, with 100Hz sound), in comparison with classic nasal nebuliser, without sound to test the effect of sound on drug MS deposition. The gentamicin aerosol was collected from MS and quantified by FPIA.

In vitro RESULTS

In head model, the gentamicine aerosol deposited in the MS was significantly increased (fig.3) until a factor 3 when aerosol is administered with 100 Hz sound in comparison without sound (0.05).

IN VIVO STUDY

In vivo METHOD

Human volunteers were 7 non-smoking healthy male (21 to 36 years). Protocol was conducted in 2 steps: Nasal ventilation of Krypton gas with or without NL11SN and nasal sonic nebulisation of Tc-DTPA with NL11SN. For both steps images of nasal cavities and thorax were registered with γ-imager (STARPORT 400AC/T, GE). The 99mTc-DTPA aerosol deposition into NASAL cavities and in the LUNGS were determined in terms of total aerosol deposited (Siemens and ImageJ processing).

In vivo RESULTS

Krypton images (fig. 4) showed the penetration of the gas into the volunteers’ MS when 2nm Kr gas is administered with 100 Hz sound (0.05).

The 99mTc-DTPA aerosol was mainly deposited into the volunteers’ nasal cavities, as 73 ±10% vs. 27 ±10% into the lungs (0.05).

SINUS DRUG DEPOSITION

Q: Is the aerosol drug deposited into MS efficient ? i.e Is a local effect induced ?

Proposition: Comparison with an effective lung treatment

IN VITRO DRUG DEPOSITION

In terms of the tissue surface deposition

45 mg/ml

3.31 µg

Both MS gentamicine deposition

Both MS tissue surface = 61.8 cm²

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IN VIVO DRUG DEPOSITION

In terms of the tissue surface

+0.036 µg/cm²

+0.052 µg/cm²

MILLIIAR SINUS DRUG DEPOSITION EQUIVALENT TO LUNG DEPOSITION, in terms of the tissue surface

Conclusions

IN VIVO study demonstrated that

The 100Hz sound used by the NL11SN improves the maxillary sinuses ventilation ;

The NL11NS sonic nebuliser optimized NASAL AEROSOL DEPOSITION

IN VITRO, the 100Hz sound used by the NL11SN increases ANTIINOCIC AEROSOL DEPOSITION into maxillary sinuses.

Expressed per unit of tissue surface, the SINUS aminocide deposition was equivalent to a LUNG aminocide deposition recognized as effective lung treatment in CF patients, & can be considered sufficient to induce a therapeutic local effect.