Nasal nebulisation of tobramycin: Preclinical and clinical study on post-operative suppurations in nasal polyposis patient.

The choice of nasal treatment for patients is mainly conducted by EPOS guidelines. Treatments concern saline irrigation, spray of corticosteroid, oral antibiotic. Nasal nebulisation or topical antibiotic are not recommended due to the lack of published data regarding its efficacy. However, nasal nebulisation seems particularly suited to patients undergoing bilateral ethmoidal resection for nasal polyposis (NP), in view of the wide opening of the sinuses.

This poster presents the preclinical and clinical results of the evaluation of tobramycin administered by nasal nebulisation in nasal polyposis patients.

The 4 PRECLINICAL STEPS

**The CLINICAL context.**
An operated NP patient.

NP patients often present recurring suppurations even after ethmoidal surgery. Episodes are associated with heightened sinus secretion and abundant purulent secretion in the nasal cavity1,2.

**METHOD:** Bacteriological analysis of exudate specimens from 60 NP patients, obtained after ethmoidal surgery.

**RESULTS:** 80% of patients with pathogenic bacteria. S. aureus was predominantly identified (60%). S. pneumoniae (5%), H. influenzae (0.7%) various Enterobacteriaceae (13.3%). P. aeruginosa (0.7%) (Day et al., 2009).

**Development of the NASAL NEBULIZER.**

**OBJECTIVE:** Develop a nasal device adapted for -tobramycin administration; -delivering drug into nasal cavity only; -delivering drug into target infected site of operated NP patients.

**METHOD-1:** A specific nasal nebulizer (Easy nose) has been developed to administer small particle sizes into nasal cavities without lung penetration.

**METHOD-2: IN VITRO EVALUATION:** Nasal cast was built from a sinus CT scan of a operated NP patient (3D analysis/3D printing in ABS). Nebulisations of tobramycin (150mg/3ml+15mg/ml) with Easy nose were performed in the nasal replica (8 min).

**RESULTS:**
1. The aerosol is nasally administered during mouth breathing.
2. In vitro scintigraphy study: 12mg of tobramycin was deposited in the target area (2+3), equivalent to 8% of nebulizer charge.

**TOBRAMYCIN HAS BEEN SELECTED FOR NASAL DRUG DELIVERY SYSTEM DEVELOPMENT.**

**IN VIVO Deposition.**

**THE PRECLINICAL VALIDATION.**

**OBJECTIVE:** Measure and validate in vivo the deposition into the respiratory tract of aerosols administered with the Easy nose nasal nebulizer.

**METHOD:** Easy nose nebulisations were performed with 10/15mg/3ml+15mg/3ml in 7 healthy volunteers. Aerosol deposition was quantified into total nasal cavities, ethmoid, maxillary sinuses, and lungs, by gamma camera.

**RESULTS:** Preclinical study has validated the feasibility to target specifically nasal cavity with Easy nose nebulizer (99% of deposited aerosol). No penetration of aerosol in the lungs (<1%). (Le Guellec et al., 2009; Vecellio et al., 2017).

**EASYNOSE HAS BEEN SELECTED FOR TOBRAMYCIN NASAL TREATMENT.**

**The CLINICAL STUDY**

**OBJECTIVES:** To compare the efficacy of tobramycin aerosols (150mg/3ml) to isotonic saline aerosols (3ml), on eradication of bacteria involved in post-operative suppurations in NP.

**PATIENTS:** 55 NP patients (20-70 years) operated, with total ethmoidectomy (>3months) included for episodes of infection with aggravation of symptoms (>3months). Bonfils et al., 2015.

**RESULTS:**
Tobramycin susceptibility of isolates at D0.

<table>
<thead>
<tr>
<th>Percentage of isolates at D0</th>
<th>Saline Isotonic</th>
<th>Tobramycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>20.4%</td>
<td>0%</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>13.9%</td>
<td>0%</td>
</tr>
<tr>
<td>Streptococcus group A</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>17.39%</td>
<td>7%</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>17.39%</td>
<td>7%</td>
</tr>
<tr>
<td>Total</td>
<td>77.4%</td>
<td>73.3%</td>
</tr>
</tbody>
</table>

**Comparison of post-treatment bacteriological data per group, in terms of the positive cultures at D10. Differences were significant (p=0.02).**

**A drug & device nebulizer has been developed for nasal treatment. Tobramycin administered by nasal nebulisation is more efficient than isotonic saline for nasal bacteria eradication.**