Antiviral Polymers - A Novel Concept for Prophylactic and Therapeutic Interventions

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Summary:
While science and societies are struggling to find ways to protect humankind from recurring epidemics and pandemics of influenza, cheap and readily available prophylactic and therapeutic options are still needed. Here we introduce the concept of creating a protective physical barrier in the nasal cavity with an antiviral polymer (Carrageenan)1-3 that works as inhibitor against virus entry for prophylaxis and therapy of influenza.

Independent clinical trials in adults and children revealed that the intranasal administration of iota-Carrageenan significantly reduced the time to disease clearance of patients with common cold and decreased the virus load in nasal lavages. This was also true for a subgroup of patients infected with influenza A virus.

In addition, a combination of Carrageenan with the NA inhibitors Oseltamivir2 or Zanamivir showed superior results in lethal influenza infection mouse models when compared with each compound alone. Thus, we suggest the combination of Carrageenan and Zanamivir in a nasal spray as novel concept for prophylactic and therapeutic intervention against influenza virus infection.

Carrageenan

Figure 1. Iota-Carrageenan is marketed in Austria as the active component of the nasal spray Coldamaris Prophylactic®. Carrageenan is a sulfated polymer derived from red seaweed that has been extensively used in the food, cosmetic and pharmaceutical industry and has been generally recognized as safe by the FDA (GRAS). The intranasal application of Carrageenan creates a protective physical barrier in the nasal cavity and works as inhibitor against virus entry.

Pooled analysis of two clinical trials conducted with similar design: randomized, parallel group, double blind and placebo-controlled studies in therapeutic natural setting with common cold infected patients experiencing symptoms ≤48 hours

Therapy: 3x / day application of the Carrageenan containing nasal spray

1. Children’s trial in St. Anna hospital, Vienna: 213 patients enrolled, >1 year, average age 4 years
2. Adult’s trial in Vienna: 220 patients enrolled, >18 years, average age 33.5 years

Conclusion

Data from clinical studies demonstrate that Carrageenan containing nasal spray is effective against respiratory viruses. Patients experienced reduced duration of common cold symptoms and faster elimination of viruses from nasal cavities. Based on the superior efficacy results of the combination of Carrageenan and Zanamivir in animals, we suggest a clinical trial for prevention or treatment of influenza A in humans. Because alternatives to Oseltamivir are desperately needed, we propose the nasal spray containing Carrageenan and Zanamivir as an option for treatment of influenza.

Combination of Carrageenan and Zanamivir - Advantages

- Combination of 2 clinically proven marketed products
- Clinical effectiveness of intranasal application
  - Carrageenan: 468 patients
  - Zanamivir: 297 patients
- Safety evaluation of intranasal application
  - ≥ 400,000 units sold
  - 1496 patients
- Nasal application of the combination product
- Suitable for children <5 years
- Two different mechanisms of action
  - Reduced risk of escape mutants
- Both products reduce viral load in the nasal cavity
- Both products shorten the duration of viral disease
- Broad antiviral effectiveness of Carrageenan
- Additional treatment of concomitant viruses

Clinical Study Design

Broad Anti-Viral Effectiveness of Carrageenan

Figure 2. Significantly shorter duration of disease compared to placebo (1.9 days in ITT, p=0.002)

Figure 3. Significant reduction of viral load in nasal secretions (ITT, p=0.015)

Anti-Influenza A Effectiveness of Carrageenan

Figure 4. Significantly shorter duration of disease compared to placebo (3.3 days in ITT, p=0.002)

Figure 5. Significant reduction of influenza virus load in nasal secretions (ITT, p=0.002)

Combination = Proof of Concept

Figure 6. In-vivo experiment set-up
The infectious dose of A/PR/8/34 (H1N1) 6.3×10^7 PFU and the treatment started (48 hours post infection) was determined to get a set up that shows minimum activity of both components tested alone. This same set-up was used to test the single components in combination.

Figure 7. In-vivo efficacy of the Combination
Ten mice per group were intranasally infected with 6.3×10^7 PFU A/PR/8/34 (H1N1) viral particles at day 0.

Intranasal therapy started 48 hours post infection twice daily with 240 µg Carrageenan in 0.5% NaCl plus 0.5 mg/kg/day Zanamivir (blue) or 0.5% NaCl as Placebo (red).

* Wilcoxon test p=0.0221

References: