VIRAL INHIBITION BY SODIUM CHLORIDE

HARNESSING A NOVEL INNATE IMMUNE MECHANISM

LABORATORY AND CLINICAL EVIDENCE

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CONSULTANT VIROLOGIST
ROYAL INFIRMARY OF EDINBURGH
The need for a generic antiviral

- The problem:
  - Viral Infections: Generic diagnosis
  - Antiviral treatment: Specific (e.g. Influenza, HSV, Adenovirus...)

- So why not test for viruses?
  - Time & Money
  - What’s the point? There are no antivirals for most anyway!

- We need a **generic antiviral** that can work against:
  - DNA / RNA viruses
  - Enveloped / non-enveloped viruses
The story

- Sore throat
  - Salt water gargles

- ENT surgery:
  - Nasal irrigation with Sodium Bicarbonate
  - Swapped NaCl

- Common cold
Supporting Literature

- Nasal Irrigation for a year in wood workers ¹
  - Reduction in sore throat (p=0.009) & colds (p=0.03)

- Nebulised HTS in Cystic Fibrosis patients (bd) ²
  - Exacerbations reduced by 56% (P = 0.02)

- Bronchiolitis: Being debated

Effect of salts on Mengo virus

<table>
<thead>
<tr>
<th>Diff. Sodium Salts</th>
<th>Diluent (150mM)</th>
<th>Virus LD$<em>{50}$ -log$</em>{10}$ 0’</th>
<th>120’</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NaCl</td>
<td>7.7</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>NaClO$_4$</td>
<td>8.4</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>NaNO$_3$</td>
<td>8.7</td>
<td>7.8</td>
</tr>
<tr>
<td></td>
<td>NaH$_2$PO$_4$</td>
<td>7.5</td>
<td>6.5</td>
</tr>
<tr>
<td></td>
<td>Na$_2$HPO$_4$</td>
<td>7.8</td>
<td>7.1</td>
</tr>
<tr>
<td></td>
<td>Na$_2$SO$_4$</td>
<td>7.8</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td>Na formate</td>
<td>8.2</td>
<td>6.8</td>
</tr>
<tr>
<td></td>
<td>Na acetate</td>
<td>7.8</td>
<td>6.5</td>
</tr>
<tr>
<td></td>
<td>DW</td>
<td>8.3</td>
<td>7.5</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Diff. Chloride Salts</th>
<th>Diluent</th>
<th>Virus LD$<em>{50}$ -log$</em>{10}$ 0’</th>
<th>120’</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl (150mM)</td>
<td></td>
<td>7.7</td>
<td>3.4</td>
</tr>
<tr>
<td>KCl (150mM)</td>
<td></td>
<td>8.0</td>
<td>3.5</td>
</tr>
<tr>
<td>MgCl$_2$ (75mM)</td>
<td></td>
<td>7.8</td>
<td>3.5</td>
</tr>
<tr>
<td>CaCl$_2$ (75mM)</td>
<td></td>
<td>7.1</td>
<td>3.5</td>
</tr>
<tr>
<td>DW</td>
<td></td>
<td>8.3</td>
<td>7.8</td>
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</table>

<table>
<thead>
<tr>
<th>Diff. Halide Salts</th>
<th>Diluent (150mM)</th>
<th>Virus LD$<em>{50}$ -log$</em>{10}$ 0’</th>
<th>120’</th>
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</thead>
<tbody>
<tr>
<td>NaF</td>
<td>8.3</td>
<td>7.4</td>
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<tr>
<td>NaCl</td>
<td>7.8</td>
<td>3.5</td>
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<tr>
<td>NaBr</td>
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<td>3.6</td>
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<tr>
<td>NaI</td>
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<td>4.5</td>
<td></td>
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<tr>
<td>NaSCN</td>
<td>7.0</td>
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</tr>
<tr>
<td>DW</td>
<td>8.2</td>
<td>7.6</td>
<td></td>
</tr>
</tbody>
</table>

Fruit fly: Gut epithelial cells produce HOCl

- They took some bacteria and ground it up and added sugar to it.
- Fruit fly were fed the sweet solution containing the bacterial lysate.
- An hour later they cut open the fruit fly and stained the gut epithelium for HOCl.
- Bottom Right – Gut epithelial cells are fluorescing (i.e. producing HOCl).
- HOCl is the active ingredient in bleach!

Hypothesis

- Chloride salts (e.g. NaCl) can help suppress viral infection
- The suppression is mediated through increased HOCl production
- This antiviral mechanism can be used by the cell against different viruses
Methods

- **HeLa**, A549, Mewo (epithelial cells) and 293T, Vero (kidney cells) were infected at different MOIs.
- Cells were treated with different concentrations of NaCl before, during or after virus infection (**HSV-1**).
- All experiments were done in triplicates.
- HSV-1 replication was quantified by
  - eGFP expression (virus mutants)
- Cell Viability measured by CellTitre Glo (Promega)
Effect of NaCl on eGFP HSV-1 in HeLa Cells

NaCl inhibits HSV-1 in a dose dependent manner
Viability of HeLa cells

![Viability of HeLa cells in NaCl](chart)

- 24 hours
- 48 hours
NaCl works after the virus enters the cell.

Hulo C et al. Nucleic Acid Res 2011; V39, D576-582

**Pre-Incubating HSV-1 with NaCl before adsorption has no effect**

<table>
<thead>
<tr>
<th>NaCl (mM)</th>
<th>0hr</th>
<th>1hr</th>
<th>2hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>10</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>20</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>30</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>40</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>50</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>100</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**NaCl inhibits virus replication after virus adsorption**

- **Virus Adsorption Alone**
- **Virus Replication Alone**
- **Both Adsorption & Replication**

<table>
<thead>
<tr>
<th>NaCl (mM)</th>
<th>Normalised Replication Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>10</td>
<td>0.6</td>
</tr>
<tr>
<td>20</td>
<td>0.4</td>
</tr>
<tr>
<td>30</td>
<td>0.2</td>
</tr>
<tr>
<td>40</td>
<td>0.0</td>
</tr>
<tr>
<td>50</td>
<td>0.0</td>
</tr>
<tr>
<td>100</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Cl⁻ channel blocker: inhibition reversed

Chloride channels blocked - viral Inhibition is reversed

![Graph showing the effect of NPPB on replication slope with or without 0mM or 50mM NaCl.](image-url)
Na⁺ channel blockers: inhibition not reversed
HOCl is produced within a few hours:
Block Cl⁻ to HOCl pathway: Inhibition reversed
Dose dependent inhibition: HSV, VZV, RSV & Influenza

**HSV**

- Normalized virus replication slope vs. Sodium chloride concentration (mM)

**VZV**

- Normalized virus replication slope vs. Sodium chloride concentration (mM)

**RSV**

- Normalized virus replication slope vs. Sodium chloride concentration (mM)

**Influenza A**

- Normalized relative quantity of HP expression vs. Sodium chloride concentration (mM)
Dose dependent inhibition: CV-B3, HCoV 229E
Summary

• NaCl has a dose-dependent antiviral effect

• Antiviral effect is
  • Intracellular
  • Needs Chloride ion
  • Cl\(^-\) is converted to HOCl
  • If you block conversion of Cl\(^-\) to HOCl, viral inhibition is reversed

• Chloride salts can be a therapeutic antiviral agent
Antiviral innate immune response in non-myeloid cells is augmented by chloride ions via an increase in intracellular hypochlorous acid levels

Sandeep Ramalingam, Baiyi Cai, Junsheng Wong, Matthew Twomey, Rui Chen, Rebecca M. Fu, Toby Boote, Hugh McCaughan, Samantha J. Griffiths & Jürgen G. Haas

Scientific Reports 8, Article number: 13630 (2018)
Hypertonic Saline Nasal Irrigation and Gargling for the Common Cold: Results of a pilot RCT

ELVIS: The Edinburgh and Lothians Viral Intervention Study

Sandeep Ramalingam, Catriona Graham, Jenny Dove, Lynn Morrice, Aziz Sheikh
Aim & Outcome Measures

**Aim:** To assess the feasibility of undertaking a RCT of Hypertonic Saline Nasal Irrigation and Gargling (HSNIG) in adults with URTI

**Primary outcome measure:** What is the recruitment rate?

**Secondary outcome measures:**
- Rate of sample return; Rate of diary completion
- Compliance with the intervention regime; Participant views on acceptability
- Difference between arms in: quality-of-life, duration of symptoms / or viral shedding
Sample Size

- Maximum of 80 participants
- Aimed to get feedback from ~30 participants / arm

- 27 per group: Can express proportion of those who return the symptom score diary & samples to within ±19%
  - Based on a two-sided 95% CI around an expected proportion of 0.5
- Two groups combined (n= 54): Able to express proportion to within ±13%
- Allow for 10% dropouts: Sample size was increased to 30/arm
Inclusion

- >16 years
- URTI <48 hours of onset
- Yes to:
  - Do you have a cold? Or
  - Do you think you are coming down with a cold?
- AND Jackson Score of ≥2
  1. Nasal discharge
  2. Nasal obstruction
  3. Sneezing
  4. Sore throat
  5. Headache
  6. Malaise
  7. Chilliness
  8. Cough

At least one of the first four symptoms

Exclusion

- URTI >48 hours
- On antibiotics
- Pregnant
- Chronic conditions
- Immunosuppressed
- Allergic rhinitis
  - H/o allergy + eye/nose itching or sneezing
- Unable to perform HSNIG
- Taking part in another medical trial

31/01/2019
Daily Forms (2x “not unwell” OR 14 days max)
Intervention Arm

- **Taught:**  [WWW.ELVISSTUDY.COM](WWW.ELVISSTUDY.COM)
  - To prepare hypertonic saline solution
  - To perform Nasal Irrigation and Gargling
  - Number of times: Depending on symptoms

---

### Amount of Salt in grams to be added to make different volumes of solution

<table>
<thead>
<tr>
<th>Bowl Size</th>
<th>Concentration of Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>100ml – Bowl</td>
<td>3.0%</td>
</tr>
<tr>
<td>200ml – Bowl</td>
<td>6g</td>
</tr>
<tr>
<td>500ml – Flask</td>
<td>15g</td>
</tr>
</tbody>
</table>
Both Groups

- Consented & Randomisation (online):
  - Minimisation by Sex and Smoking Status

- Taught:
  - To fill daily form (paper / online):
    - Wisconsin Upper Respiratory Symptom Survey – 21 (WURSS-21)
    - EQ-5D-5L Quality of Life
  - Mid-Turbinate Swabs in eNAT medium (Copan, Italia):
    - Shown a video
    - Baseline + 4 subsequent days
    - Specimen posted with Royal Mail Safeboxes

- Allowed over the counter medication
CONSORT 2010 FLOW DIAGRAM

ENROLLMENT
Assessed for eligibility (n=171)
- Excluded (n=103)
  - Not meeting inclusion criteria (n=80)
  - Declined to participate (n=15)
  - Other reasons (i.e. unable to attend within 48 hours (n=8)

Randomized (n=68)

Allocated to Intervention (n=33)
  - Received allocated intervention (n=32)
  - Did not receive allocated intervention (Declined to perform HSNIG) (n=1)

Allocated to Control (n=35)
  - Removed (Was on antibiotics) (n=1)

ALLOCATION

FOLLOW-UP

Lost to follow-up (n=2)
  - Did not return daily form (n=2)
  - Did not return swabs (n=4)
  - Did not return end of study form (n=4)
  - Discontinued intervention (n=0)

Lost to follow-up (n=3)
  - Did not return daily form (n=3)
  - Did not return swabs (n=3)
  - Did not return end of study form (n=5)

ANALYSIS

Analysed (n=30)
Analysed (n=31)
## Baseline Characteristics Similar

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td><strong>%</strong></td>
<td><strong>n</strong></td>
</tr>
<tr>
<td>Randomised</td>
<td>32</td>
<td>100</td>
</tr>
<tr>
<td>Sex - F</td>
<td>24</td>
<td>75</td>
</tr>
<tr>
<td>Non/Ex-Smokers</td>
<td>31</td>
<td>97</td>
</tr>
<tr>
<td>&gt;1 adults at home</td>
<td>26</td>
<td>81</td>
</tr>
<tr>
<td>No kids at home</td>
<td>19</td>
<td>59</td>
</tr>
<tr>
<td>Nobody sick before them</td>
<td>19</td>
<td>59</td>
</tr>
<tr>
<td>Full time employment</td>
<td>20</td>
<td>63</td>
</tr>
<tr>
<td>Part time employment</td>
<td>7</td>
<td>22</td>
</tr>
<tr>
<td>Full time education</td>
<td>4</td>
<td>13</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td><strong>SD</strong></td>
<td><strong>Mean</strong></td>
</tr>
<tr>
<td>Age</td>
<td>34.6</td>
<td>9.3</td>
</tr>
<tr>
<td>WURSS-21 Scot Score</td>
<td>65.9</td>
<td>13.6</td>
</tr>
<tr>
<td>EQ-VAS (QoL score)</td>
<td>41.6</td>
<td>18.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preference</td>
<td></td>
</tr>
<tr>
<td>Feedback</td>
<td></td>
</tr>
<tr>
<td>Paper / Online</td>
<td><strong>75</strong> / <strong>25</strong></td>
</tr>
<tr>
<td>Hypertonic saline concentration</td>
<td><strong>81</strong> / <strong>9</strong> / <strong>9</strong></td>
</tr>
</tbody>
</table>
### Intervention arm: Well 2 days earlier:

- Diary from 61 participants
  - 5 – Did not reach end point on day 14
  - 11 – Stopped before scoring 0 for 2 days
    - 8 – Scored 0 on last day
    - 2 – Scored 1 on last day
    - 1 – Scored 6 on last day

<table>
<thead>
<tr>
<th></th>
<th>Intervention n=30</th>
<th>Control n=31</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>6.8</td>
<td>8.7</td>
<td>0.012</td>
</tr>
<tr>
<td>SD</td>
<td>2.2</td>
<td>3.3</td>
<td></td>
</tr>
</tbody>
</table>

PLIG 2019
Days to clear symptoms:

Mean days = 8.5
Mean days = 6.7
p = 0.01

Mean days = 8.7
p < 0.001

Mean days = 6.0
Mean days = 5.1
p = 0.09

Mean days = 6.4
Mean days = 5.1
p = 0.09

Mean days = 7.3
Mean days = 6.3
Cough

Mean days = 5.7
p = 0.02

Mean days = 5.1
p = 0.09

Mean days = 7.4
Mean days = 4.9
p = 0.003

31/01/2019
Days to clear symptoms:

- Mean days = 6.5
- Mean days = 7.3
- Mean days = 5.2
- Mean days = 4.4
- Mean days = 4.8
- Mean days = 6.5
- Mean days = 7.9

Median (IQR) days of HSNIG = 5 (3,6)
Median (IQR) n/day = 3 (2,3)
## Feedback from participants

### Time off work
- **Intervention**: 3 days off work
- **Control**: 7 days off work

### Medication for URTI
- **Intervention**: 14 days of medication
- **Control**: 25 days of medication

### Symptoms after participant
- **Intervention**: 8 days of symptoms
- **Control**: 19 days of symptoms

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th></th>
<th>Control</th>
<th></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n=28</strong></td>
<td>31%</td>
<td></td>
<td>n=29</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Time off work</td>
<td></td>
<td>11%</td>
<td></td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>3 days off work</td>
<td>0</td>
<td>0%</td>
<td>4</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Medication for URTI</td>
<td>14</td>
<td>50%</td>
<td>25</td>
<td>86%</td>
<td>0.004</td>
</tr>
<tr>
<td>Symptoms after participant</td>
<td>8</td>
<td>31%</td>
<td>19</td>
<td>66%</td>
<td>0.005</td>
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</table>
## HSNIG – Feedback:

### Preparation of solution

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<tr>
<th>Preparation of solution</th>
<th>n=28</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Flask</td>
<td>24</td>
<td>86</td>
</tr>
<tr>
<td>Easy</td>
<td>28</td>
<td>100</td>
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### Procedure

<table>
<thead>
<tr>
<th>Procedure</th>
<th>n=28</th>
<th>%</th>
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<tbody>
<tr>
<td>Small bowl</td>
<td>21</td>
<td>75</td>
</tr>
<tr>
<td>Comfortable</td>
<td>11</td>
<td>39</td>
</tr>
<tr>
<td>Moderately comfortable</td>
<td>14</td>
<td>50</td>
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</tbody>
</table>

### Cleaning

<table>
<thead>
<tr>
<th>Cleaning</th>
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<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy</td>
<td>27</td>
<td>96</td>
</tr>
</tbody>
</table>

### Outside home

<table>
<thead>
<tr>
<th>Outside home</th>
<th>n=28</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy</td>
<td>8</td>
<td>28</td>
</tr>
<tr>
<td>Moderately Easy</td>
<td>11</td>
<td>39</td>
</tr>
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</table>

### Carrying

<table>
<thead>
<tr>
<th>Carrying</th>
<th>n=28</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy</td>
<td>16</td>
<td>57</td>
</tr>
<tr>
<td>Moderately easy</td>
<td>7</td>
<td>25</td>
</tr>
</tbody>
</table>

### On the whole

<table>
<thead>
<tr>
<th>On the whole</th>
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<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convenient</td>
<td>11</td>
<td>40</td>
</tr>
<tr>
<td>Moderately convenient</td>
<td>14</td>
<td>50</td>
</tr>
</tbody>
</table>

### Did HSNIG make a difference

<table>
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<tr>
<th>Did HSNIG make a difference</th>
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<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>26</td>
<td>93</td>
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</table>

### Will you use procedure?

<table>
<thead>
<tr>
<th>Will you use procedure?</th>
<th>n=28</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely</td>
<td>17</td>
<td>61</td>
</tr>
<tr>
<td>Undecided</td>
<td>7</td>
<td>25</td>
</tr>
<tr>
<td>Unlikely</td>
<td>4</td>
<td>15</td>
</tr>
</tbody>
</table>

### If more convenient

<table>
<thead>
<tr>
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<th>n=28</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely</td>
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<td>86</td>
</tr>
<tr>
<td>Undecided</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Unlikely</td>
<td>2</td>
<td>7</td>
</tr>
</tbody>
</table>

### As a preventative measure

<table>
<thead>
<tr>
<th>As a preventative measure</th>
<th>n=28</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Undecided</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Unlikely</td>
<td>20</td>
<td>72</td>
</tr>
</tbody>
</table>
Virology

- 18 – No virus identified
- 44 – One virus
- 4 – Two viruses identified
  - 3 – Rhinovirus + enterovirus,
    - 1 – Confirmed
    - 1 – No followup
  - 1 – Rhinovirus + Coronavirus OC43

<table>
<thead>
<tr>
<th>Virus</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinovirus</td>
<td>15 (47%)</td>
<td>13 (38%)</td>
</tr>
<tr>
<td>All Coronaviruses</td>
<td>7 (22%)</td>
<td>8 (24%)</td>
</tr>
<tr>
<td>Coronavirus 229E</td>
<td>3 (9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Coronavirus OC43</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Coronavirus HKU1</td>
<td>3 (9%)</td>
<td>5 (15%)</td>
</tr>
<tr>
<td>Coronavirus NL63</td>
<td>1 (3%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Influenza A</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Parainfluenza virus -3</td>
<td>2 (6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Enterovirus</td>
<td>2 (6%)</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>
Symptoms, Irrigation Vs Viral shedding:
Symptoms, Irrigation Vs Viral shedding:

11: COV HKU1
12: Rhinovirus
13: Rhinovirus
14: Enterovirus
15: Rhinovirus
16: COV NL63
17: Rhinovirus
18: Influenza A
19: Rhinovirus
20: Rhinovirus

PLIG 2019
Symptoms, Irrigation Vs Viral shedding:
Reduction in Viral Shedding:

- The mean inter-assay variation for the Day 0 sample was 0.21 log$_{10}$ (SD = 1.17)
  - A reducing trend in viral shedding was seen on days HSNIG was done in 20 individuals.
  - Among these viral shedding increased after HSNIG was stopped in 8/20 (40%)
  - Two participants restarted HSNIG (1 with an increase in viral shedding)

- Fall in viral shedding by ≥0.5 log$_{10}$/day:
  - Intervention arm 73% [n=16/22]
  - Control arm 43% [n=9/21]
  - Difference -30%, 95% CI for difference in proportion (-58, -2) ($p=0.038$)
Conclusions:

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>Our findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are we able to recruit and retain participants?</td>
<td>Yes</td>
</tr>
<tr>
<td>Is procedure acceptable?</td>
<td>Yes</td>
</tr>
<tr>
<td>Is there a difference in the quality of life?</td>
<td>Less Medication</td>
</tr>
<tr>
<td>Is there a Reduction in Duration of symptoms?</td>
<td>By 2 days</td>
</tr>
<tr>
<td>Is there a Reduction in Viral Shedding?</td>
<td>Yes + Less transmission</td>
</tr>
</tbody>
</table>

Time for a larger study with efficacy end points
A pilot, open labelled, randomised controlled trial of hypertonic saline nasal irrigation and gargling for the common cold

Sandeep Ramalingam, Catriona Graham, Jenny Dove, Lynn Morrice & Aziz Sheikh

Scientific Reports 9, Article number: 1015 (2019)
ANTIBACTERIAL IMMUNITY

A pinch of salt

Kirsty Minton

Nature Reviews Immunology 15, 202 (2015) doi:10.1038/nri3835
Published online 13 March 2015

Short Article

Cutaneous Na⁺ Storage Strengthens the Antimicrobial Barrier Function of the Skin and Boosts Macrophage-Driven Host Defense

Jonathan Jantsch¹²,², Valentin Schatz⁵, Diane Friedrich⁵, Agnes Schroder, Christoph Kopp, Isabel Siegert, Andreas Maronna, David Wendelborn, Peter Linz, Katrina J. Binger, Matthias Gehardt, Matthias Henig, Patrick Neubert, Fabian Fischer, Stefan Teufel, Jean-Pierre David, Clemens Neufert, Alexander Cavallaro, Natalia Rakoza, Christoph Kueper, Franz-Xaver Beck, Wolfgang Neuhofer, Dominik N. Muller, Gerald Schuier, Michael Uder, Christian Bogdan, Friedrich C. Luft, Jens Titze
Possibilities:

Relatively Easy:
- Larger study in adults / children with URTI
- Recurrent cold sores / genital HSV – Local application
- Viral Diarrhoea – salty drink?
- Conjunctivitis – Hypertonic saline drops?
- Keratitis – Hypertonic saline drops?

Challenging:
- Pneumonia – nebulised hypertonic saline?
- Hepatitis E
ELVIS Kids Study:

- Healthy Children (Before 7th birthday)
- With or without a cold
- Salt water Nose Drops vs control arm

- 07973 657 457
- www.elviskids.co.uk
- Twitter: @elviskids
- Facebook: ELVIS Kids Study
Acknowledgements – HOCl work

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Junsheng Wong
Matthew Twomey
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University of Berne, Switzerland

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Ethics Committee

Lothian GP’s

Participants

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Copan Italia – Santina Castriciano

Butterfly Films - Ryan

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Department of Virology – Jenny Dove and Julie White
Finance Department – Glen Merritt
Communications - Clifford Burden

31/01/2019 PLIG 2019