EPOS2020 from bench to bedside
Management of patients, what is new

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EPOS 2020: Management of patients, what is new

- Integrated care pathways in ARS
- New classification of CRS, primary versus secondary CRS: consequences for treatment
- Evidence based treatment
- New integrated care pathways in CRS

web: www.epos2020.com, rhinologyjournal.com
Definition of Acute Rhinosinusitis

Increase in symptoms after 5 days, or persistent symptoms after 10 days with less than 12 weeks duration

Common Cold

Post-Viral Acute Rhinosinusitis

Increase in symptoms after 5 days

Persistent symptoms after 10 days

Signs of potential acute bacterial rhinosinusitis

At least 3 of:

- Fever above 38°C
- Double sickening
- Unilateral disease
- Severe pain
- Raised ESR/CRP

Graph showing symptoms over days:

- Nasal discharge
- Cough
- Headache
- Fever
- Nasal obstruction

Days of illness
Antibiotics in patients with ABRS

Figure 4.6.1. Forest plot of the effect of antibiotic versus placebo for cure at completion of intervention (day 6-10) in adult patients with acute bacterial rhinosinusitis.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antibiotics Events</th>
<th>Placebo Events</th>
<th>M-H, Fixed, 95% CI</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hadley 2010</td>
<td>57</td>
<td>73</td>
<td>45</td>
<td>1.17 [0.92, 1.49]</td>
</tr>
<tr>
<td>Lindbaek 1996 (Amoxi)</td>
<td>39</td>
<td>44</td>
<td>44</td>
<td>1.56 [1.18, 2.06]</td>
</tr>
<tr>
<td>Lindbaek 1996 (Penicillin)</td>
<td>32</td>
<td>39</td>
<td>44</td>
<td>1.44 [1.07, 1.94]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>156</td>
<td>133</td>
<td>100.0%</td>
<td>1.36 [1.16, 1.59]</td>
</tr>
<tr>
<td>Total events</td>
<td>128</td>
<td>80</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 2.58, df = 2 (P = 0.27); I² = 23%
Test for overall effect: Z = 3.89 (P < 0.0001)

Figure 4.6.2. Forest plot of the effect of antibiotic versus placebo to assess improvement at day 3 of treatment of adult patients with acute bacterial rhinosinusitis.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antibiotics Events</th>
<th>Placebo Events</th>
<th>M-H, Random, 95% CI</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hadley 2010</td>
<td>62</td>
<td>73</td>
<td>45</td>
<td>1.16 [0.95, 1.42]</td>
</tr>
<tr>
<td>Lindbaek 1996 (Amoxi)</td>
<td>35</td>
<td>44</td>
<td>44</td>
<td>2.06 [1.38, 3.08]</td>
</tr>
<tr>
<td>Lindbaek 1996 (Penicillin)</td>
<td>32</td>
<td>39</td>
<td>44</td>
<td>2.12 [1.42, 3.17]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>156</td>
<td>133</td>
<td>100.0%</td>
<td>1.68 [1.04, 2.71]</td>
</tr>
<tr>
<td>Total events</td>
<td>129</td>
<td>67</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.15; Chi² = 12.84, df = 2 (P = 0.002); I² = 84%
Test for overall effect: Z = 2.10 (P = 0.04)

CI, confidence interval; M-H, Mantel Haenszel.
Antibiotics in patients with postviral ARS

Figure 4.6.7. Forest plot of the effect of antibiotic versus placebo for cure at completion of the intervention (days 10-14) in adult patients with acute post-viral acute rhinosinusitis.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antibiotics</th>
<th>Placebo</th>
<th>Std. Mean Difference IV, Random, 95% CI</th>
<th>Total</th>
<th>Heterogeneity: Tau^2 = 2.75, df = 6 (P = 0.84); I^2 = 0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garbutt 2012</td>
<td>63</td>
<td>81</td>
<td>-0.78 [-1.33, -0.24]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Haye 2000</td>
<td>80</td>
<td>86</td>
<td>1.06 [0.96, 1.17]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Lindbaek 1998 (Amox)</td>
<td>17</td>
<td>22</td>
<td>1.16 [0.79, 1.69]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Lindbaek 1998 (pen V)</td>
<td>15</td>
<td>20</td>
<td>1.13 [0.76, 1.67]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Merenstein 2005</td>
<td>32</td>
<td>67</td>
<td>1.30 [0.87, 1.94]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Stalman 1997</td>
<td>56</td>
<td>94</td>
<td>1.00 [0.79, 1.26]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Van Buchem 1997</td>
<td>87</td>
<td>105</td>
<td>1.07 [0.94, 1.23]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>475</td>
<td>456</td>
<td>100.0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events 350

NNT: 17

Figure 4.6.8. Forest plot of the effect of antibiotic versus placebo to assess the difference (mean difference) in the number of days to achieve cure after treatment in adult patients with acute post-viral acute rhinosinusitis.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antibiotics</th>
<th>Placebo</th>
<th>Std. Mean Difference IV, Random, 95% CI</th>
<th>Total</th>
<th>Heterogeneity: Tau^2 = 0.14, df = 1 (P = 0.05); I^2 = 73%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merenstein 2005</td>
<td>8.1</td>
<td>3.6</td>
<td>-0.17 [-0.47, 0.12]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Stalman 1997</td>
<td>4</td>
<td>5.7</td>
<td>0.43 [-1.02, 0.16]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>116</td>
<td>116</td>
<td>100.0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events 350

Figure 4.6.9. Forest plot of the effect of antibiotic versus placebo to assess improvement at day 3 of treatment of adult patients with acute post-viral acute rhinosinusitis.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antibiotics</th>
<th>Placebo</th>
<th>Std. Mean Difference IV, Random, 95% CI</th>
<th>Total</th>
<th>Heterogeneity: Tau^2 = 1.95, df = 4 (P = 0.74); I^2 = 0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garbutt 2012</td>
<td>30</td>
<td>81</td>
<td>1.10 [0.72, 1.68]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Haye 2000</td>
<td>79</td>
<td>84</td>
<td>1.07 [0.97, 1.18]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Lindbaek 1998 (Amox)</td>
<td>2</td>
<td>22</td>
<td>0.95 [0.15, 6.17]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Lindbaek 1998 (pen V)</td>
<td>5</td>
<td>20</td>
<td>2.63 [0.57, 12.02]</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>458</td>
<td>449</td>
<td>100.0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events 349

NNT: 17

CI, confidence interval; M-H, Mantel Haenszel.
Intranasal corticosteroids in postviral ARS

Figure 4.6.16. Forest plot of the effect of intranasal corticosteroids versus placebo on change from baseline of total symptom score in acute post-viral rhinosinusitis.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intranasal corticosteroid Mean</th>
<th>SD</th>
<th>Total</th>
<th>Placebo Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Std. Mean Difference IV, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.1 Single treatment</td>
<td>Keith 2012 220</td>
<td>3.33</td>
<td>0.82</td>
<td>252</td>
<td>2.97</td>
<td>1.87</td>
<td>245</td>
<td>14.3%</td>
<td>0.25 [0.07, 0.43]</td>
</tr>
<tr>
<td></td>
<td>Keith 2012 110</td>
<td>3.36</td>
<td>2.03</td>
<td>240</td>
<td>2.97</td>
<td>1.87</td>
<td>245</td>
<td>14.1%</td>
<td>0.20 [0.02, 0.38]</td>
</tr>
<tr>
<td></td>
<td>Meltzer 2005 400</td>
<td>4.48</td>
<td>1.21</td>
<td>220</td>
<td>3.75</td>
<td>1.21</td>
<td>219</td>
<td>13.3%</td>
<td>0.60 [0.41, 0.79]</td>
</tr>
<tr>
<td></td>
<td>Meltzer 2005 200</td>
<td>4.01</td>
<td>0.82</td>
<td>220</td>
<td>3.75</td>
<td>1.21</td>
<td>219</td>
<td>13.5%</td>
<td>0.25 [0.06, 0.44]</td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td>932</td>
<td></td>
<td>928</td>
<td></td>
<td></td>
<td>55.3%</td>
<td>0.32 [0.15, 0.50]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heterogeneity: Tau² = 0.02; Chi² = 11.22, df = 3 (P = 0.01); I² = 73%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: Z = 3.58 (P = 0.0003)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1.2 Addition to antibiotics</td>
<td>Nayak 2002 400</td>
<td>5.89</td>
<td>3.45</td>
<td>318</td>
<td>5.22</td>
<td>3.45</td>
<td>325</td>
<td>15.8%</td>
<td>0.19 [0.04, 0.35]</td>
</tr>
<tr>
<td></td>
<td>Nayak 2002 800</td>
<td>5.86</td>
<td>3.39</td>
<td>324</td>
<td>5.22</td>
<td>3.39</td>
<td>325</td>
<td>15.9%</td>
<td>0.19 [0.03, 0.34]</td>
</tr>
<tr>
<td></td>
<td>Meltzer 2000</td>
<td>5.87</td>
<td>3.2</td>
<td>200</td>
<td>5.05</td>
<td>3.2</td>
<td>207</td>
<td>13.1%</td>
<td>0.26 [0.06, 0.45]</td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td>842</td>
<td></td>
<td>857</td>
<td></td>
<td></td>
<td>44.7%</td>
<td>0.21 [0.11, 0.30]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heterogeneity: Tau² = 0.00; Chi² = 0.32; df = 2 (P = 0.85); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: Z = 4.25 (P &lt; 0.0001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total (95% CI)</td>
<td>1774</td>
<td></td>
<td>1785</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>0.27 [0.17, 0.37]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heterogeneity: Tau² = 0.01; Chi² = 14.26; df = 6 (P = 0.03); I² = 58%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: Z = 5.21 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for subgroup differences: Chi² = 1.30, df = 1 (P = 0.26); I² = 22.8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cl, confidence interval; M-H, Mantel Haenszel.
Antibiotics prescription and resistance

Figure 4.6.13. Consumption of antibiotics for systemic use in the community by antibiotic group in 30 EU/EEA countries, 2013 (expressed in DDD per 1 000 inhabitants and per day).

Figure 4.6.14. Proportion of macrolide Resistant (R) Streptococcus pneumonia isolates in participating countries in 2013.
EPOS 2020: Care pathways for acute rhinosinusitis (ARS)

Self-Care Pharmacy
Two ARS symptoms
One of which should be nasal obstruction and/or discoloured discharge
± facial pain/pressure
± reduction or loss of smell
<10 days

Check for likely ABRS
≥ 3 of the following:
• Fever above 38°C
• Double sickness
• Unilateral disease
• Severe pain
• Raised ESR/CRP

Self-Care
• Self-education / e-Health
• Decongestants <10 days
• NSAIDs / paracetamol
• Herbal medicine
• Zinc
• Vitamin C
• Consider saline spray / rinses
• Avoid antibiotics

Refer to / Treatment by Primary Care

Primary Care
Check for likely ABRS
≥ 3 of the following:
• Fever above 38°C
• Double sickness
• Unilateral disease
• Severe pain
• Raised ESR/CRP

Symptoms >10 days or increased after 5 days?

≥3 episodes of ABRS last year?

Consider antibiotics
No other investigations

Appropriate therapy
• INCS
• Decongestants <10 days
• Herbal medicine
• Saline spray / rinses
• Avoid antibiotics

Improvement after 10 days of antibiotics?

Secondary/Tertiary Care
Consider and test for differential diagnosis and treat accordingly
(e.g., odontogenic, fungal ball, bacterial resistance, immunodeficiency)

or non-sinus diagnoses
(e.g., migraine)

Refer to Secondary / Tertiary Care

Immediate Referral

Presence of alarm symptoms
- Periorbital oedema/erythema
- Severe headache
- Displaced globe
- Frontal swelling
- Signs of sepsis
- Signs of meningitis
- Ophthalmoplegia
- Reduced visual acuity
- Neurological signs

IMMEDIATE REFERRAL
EPOS 2020:
Management of patients, what is new

• Integrated care pathways in ARS
• New classification of CRS, primary versus secondary CRS: consequences for treatment
• Evidence based treatment
• New integrated care pathways in CRS

New Classification of CRS

Primary CRS

Anatomic distribution
- Localized (unilateral)
  - Type 2
  - Non-type 2
- Diffuse (bilateral)
  - Type 2
  - Non-type 2

Endotype dominance
- Type 2
- Non-type 2

Examples of phenotypes
- AFRS
- Isolated sinusitis
- CRSwNP/eCRS
  - AFRS
  - CRSP eCRS
- CCAD
- Non-eCRS

web: www.epos2020.com, rhinologyjournal.com
New Classification of CRS

web: www.epos2020.com, rhinologyjournal.com
Montelukast in diffuse bilateral CRS

Table 6.1.9.1. Montelukast for the treatment of patients with CRS.

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Participants</th>
<th>Interventions</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schaper, 2011</td>
<td>SRCT</td>
<td>24 CRSwNP patients and asthma (12 with N-EOS)</td>
<td>Montelukast 10 mg tid for 6 weeks (n=24)</td>
<td>Nasal symptoms (B-12)</td>
<td>Total symptom score improved by 5.9 to 1.75 in montelukast group and not in placebo. No direct comparison. No data for piriton. Significant reduction in nasal reflux; antihistamines, lubrication compared to placebo at nasal endoscopy. Significant improvement in nasal airflow in montelukast group. Significant improvement in nasal function.</td>
</tr>
<tr>
<td>Paul, 2017</td>
<td>CRCT</td>
<td>30 CRSwNP patients</td>
<td>Montelukast 10 mg tid for 4 weeks (n=25)</td>
<td>HQOL</td>
<td>Significant reduction in most domains of HQOL. No significant difference in nasal endoscopy score or IGC in nasal secretion.</td>
</tr>
</tbody>
</table>

CRSwNP, chronic rhinosinusitis with nasal polyposis; SRCT, double-blind placebo-controlled trial; ECI, eosinophilic cationic protein; HQQOL, health-related quality of life; N-EOS, NS-RAID-exacerbated respiratory disease; SRCT, single-blind placebo-controlled trial.

Table 6.1.9.2. Montelukast added to intranasal corticosteroids for the treatment of patients with CRS.

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Participants</th>
<th>Interventions</th>
<th>Interventions (mean)</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Cerven, 2018</td>
<td>RCT</td>
<td>72 CRSwNP postoperative</td>
<td>Montelukast 10 mg tid together with mometasone furoate 200 μg 2 times a day for 1 year (n=36)</td>
<td>TSS (TS50) 4.7 and 12 months</td>
<td>No significant difference between the treatments for any outcome measured.</td>
<td></td>
</tr>
<tr>
<td>Suri, 2017</td>
<td>RCT</td>
<td>40 CRSwNP</td>
<td>Montelukast 10 mg for 8 weeks + prednisolone 35 mg reducing by 5 mg every second day over 14 days + budesonide nasal spray 2 metered doses at each nostril for 8 weeks (n=20)</td>
<td>Total symptoms and nasal blockage, headache, facial pain, sense of smell, nasal discharge and sneezing (0-10) at 8 weeks</td>
<td>Significant better effect of montelukast group for total symptoms (8 and 2 weeks), headache (1 and 2 weeks), sense of smell (1 and 2 weeks) and sneezing (8 weeks).</td>
<td></td>
</tr>
<tr>
<td>Stewart, 2016</td>
<td>RCT</td>
<td>38 CRSwNP (33 analyzed)</td>
<td>Montelukast 10 mg for 8 weeks + prednisolone 35 mg reducing by 5 mg every second day over 14 days + budesonide nasal spray 2 metered doses at each nostril for 8 weeks (n=21)</td>
<td>Total symptoms, nasal blockage, headache, facial pain, sense of smell, nasal discharge and sneezing (0-10) at 8 weeks</td>
<td>Significant better effect of montelukast group for facial pain (8 weeks) and sneezing (8 weeks).</td>
<td></td>
</tr>
</tbody>
</table>

TSS, Total Symptom Score; BAST-24, Barcelona Smell Test 24; CRSwNP, chronic rhinosinusitis with nasal polyposis; LMS, Lund-McKay score; RCT, randomized clinical trial; SF-36, short form 36; TSS, Total Symptom Score.
Regular or high dose of INCS in diffuse bilateral CRS

web: www.epos2020.com, rhinologyjournal.com
### Difference in effect of INCS in CRS patients without or with surgery

#### Figure 6.1.5.15. Forest plot of the effect of nasal corticosteroid versus placebo on the proportion of patients with nasal polyp score reduction in subgroups of CRS patients with and without sinus surgery.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>placebo</th>
<th>steroid</th>
<th>Risk Ratio</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td><strong>Patients with sinus surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vickova 2009</td>
<td>5</td>
<td>55</td>
<td>31</td>
<td>54</td>
</tr>
<tr>
<td>Penttila 2000</td>
<td>7</td>
<td>47</td>
<td>19</td>
<td>47</td>
</tr>
<tr>
<td>Keith 2000</td>
<td>8</td>
<td>52</td>
<td>14</td>
<td>52</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>154</td>
<td>153</td>
<td>37.5%</td>
<td>0.31 [0.20, 0.49]</td>
</tr>
<tr>
<td>Total events</td>
<td>20</td>
<td>64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Chi² = 4.87, df = 2 (P = 0.09); η² = 59%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 5.07 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>placebo</th>
<th>steroid</th>
<th>Risk Ratio</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td><strong>Patients without sinus surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leopold 2019</td>
<td>7</td>
<td>79</td>
<td>23</td>
<td>82</td>
</tr>
<tr>
<td>Kobayashi 2018</td>
<td>2</td>
<td>12</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Stjärne 2006b</td>
<td>39</td>
<td>145</td>
<td>63</td>
<td>153</td>
</tr>
<tr>
<td>Holmstrom 1999</td>
<td>8</td>
<td>49</td>
<td>15</td>
<td>51</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>285</td>
<td>297</td>
<td>62.5%</td>
<td>0.54 [0.41, 0.70]</td>
</tr>
<tr>
<td>Total events</td>
<td>56</td>
<td>109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Chi² = 4.74, df = 3 (P = 0.19); η² = 37%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 4.46 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total (95% CI)</th>
<th>439</th>
<th>450</th>
<th>100.0%</th>
<th>0.45 [0.36, 0.57]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total events</td>
<td>76</td>
<td>173</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Chi² = 13.20, df = 6 (P = 0.04); η² = 55%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 6.67 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi² = 4.07, df = 1 (P = 0.04), η² = 75.5%</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Aspirin treatment after desensitisation (ATAD)
No effect of short term antibiotics after (F)ESS

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Participants</th>
<th>Interventions</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albu</td>
<td>DBPCT</td>
<td>75 CRS</td>
<td>Amoxicillin + clavulanate 625 mg twice daily for 14 days (n=40)</td>
<td>Symptom questionnaire day 5, 12, 21 and 30</td>
<td>Amoxicillin + clavulanate versus placebo resulted in:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>patients (40)</td>
<td>Placebo twice daily for 14 days (n=35)</td>
<td>Perioperative sinus endoscopy (POSE) score at day 5, 12, 21, and 30</td>
<td>Significant lower scores for nasal obstruction and nasal discharge on postoperative day 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CRSwNP</td>
<td></td>
<td>Endoscopic examination at day 5 until all blood crusts resolved</td>
<td>Significant lower POSE scores on day 5 and 12</td>
</tr>
<tr>
<td>Schalk</td>
<td>DBPCT</td>
<td>23 CRS</td>
<td>Amoxicillin + clavulanato, guinolone or co-trimoxazole for 3 weeks (n=13)</td>
<td>SNOT-22 (Czech translation) at 3 and 6 months</td>
<td>No statistically significant difference in overall symptom scores or POSE scores at 21 or 30 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>patients</td>
<td>Placebo for 3 weeks (n=10)</td>
<td>Clinical symptom-specific scores at 3 and 6 months</td>
<td>Patients displaying blood crusts within 12 days post-surgery were lower in the antibiotic treated group as compared to the placebo group (p=0.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Endoscopic score at 3 and 6 months</td>
<td>Mean endoscopic scores after 3 months approached significance (p=0.036)</td>
</tr>
<tr>
<td>Jiang</td>
<td>RCT</td>
<td>71 CRS</td>
<td>Amoxicillin + clavulanate 375 mg three times daily for 3 weeks (n=31)</td>
<td>Rhinosinusitis symptom scores at week 3</td>
<td>There was no statistical difference with regard to which particular antibiotic was used</td>
</tr>
<tr>
<td></td>
<td></td>
<td>patients</td>
<td>No treatment (n=40)</td>
<td>Antibiotic sensitivity rate at week 3</td>
<td>No significant difference in the short-term subjective or objective outcomes of CRS 3 weeks after endoscopic sinus surgery</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Culture rate at week 3</td>
<td>Bacterial culture rates increased in the study group after FESS (38.7% vs. 61.3%, p=0.014) but no significant difference in antibiotic sensitivity to amoxicillin/ clavulanato</td>
</tr>
<tr>
<td>Armyns</td>
<td>DBPCT</td>
<td>202 CRS</td>
<td>Cefuroxime axetil 250 mg twice daily (n=101)</td>
<td>Symptoms</td>
<td>No significant differences between the groups</td>
</tr>
<tr>
<td></td>
<td></td>
<td>patients</td>
<td>Placebo twice daily, all patients received nasal saline and nasal corticosteroids (n=101)</td>
<td>Nasal endoscopy</td>
<td></td>
</tr>
</tbody>
</table>

DBPCT, Double Blind Placebo Controlled Trial; CRS, Chronic Rhinosinusitis; CRSwNP, Chronic Rhinosinusitis with nasal polyps; RCT, Randomised Controlled Trial; SNOT-22, Sino-Nasal Outcome Test-22; POSE, Perioperative Sinus Endoscopy score;
Reverse Trendelenburg position reduces blood loss during (F)ESS

Figure 6.2.4.1. Forest plot of the effect of reverse Trendelenburg position compared to the horizontal position on surgical field quality.

Figure 6.2.4.2. Forest plot of the effect of reverse Trendelenburg position compared to the horizontal position on blood loss.

Figure 6.2.4.3. Forest plot of the effect of reverse Trendelenburg position compared to the horizontal position on operation time.
EPOS 2020: Care pathways for CRS

Self-Care Pharmacy
- Two CRS symptoms
  - One of which should be nasal obstruction and/or discoloured discharge
  - ± facial pain/pressure
  - ± reduction or loss of smell
  - > 12 weeks
- Self-Care
  - Self-education / e-Health
  - Saline sprays / rinses
  - INCS (if not OTC)
  - Avoid antibiotics
  - Avoid exacerbating factors
- 6-12 weeks: improvement?
  - Refer to Primary Care

Primary Care
- Primary care follow-up
  - Saline rinses
  - INCS (if not OTC)
  - Educate compliance/technique
  - Check treatable traits and comorbidities
- 6-12 weeks: improvement?
  - Refer to Secondary/Tertiary Care

Secondary/Tertiary Care
- Check treatable traits / comorbidities
  - History and full ENT exam
  - Nasal endoscopy
- Diffuse / bilateral CRS
  - Follow EPOS 2020 management scheme on diffuse / bilateral CRS
- Localized / unilateral CRS
  - CT scan (urgent if suspicion of tumour)
  - Diagnosis rejected
    - Reconsider differential diagnosis
  - Diagnosis confirmed
    - Surgery likely
    - Refer if necessary / suspected malignancy
- No (apparent) CRS
  - Consider CT scan
  - Reconsider differential diagnosis

PRESENCE OF ALARM SYMPTOMS
- Periorbital oedema/erythema
- Displaced globe
- Double vision
- Ophthalmoplegia
- Reduced visual acuity
- Severe headache
- Frontal swelling
- Signs of sepsis
- Signs of meningitis
- Neurological signs
- Unilateral symptoms
- Bleeding
- Crusting
- Cacosmia
IMMEDIATE REFERRAL

web: www.epos2020.com, rhinologyjournal.com
Diffuse bilateral CRS management scheme

AMT, appropriate medical treatment; INCS, intranasal corticosteroids;
Treatment of Type 2 Inflammation in Chronic Rhinosinusitis

anti- IL-5
- mepolizumab
- reslizumab.
anti-IL-4/anti-IL-13
- dupilumab
anti-IgE
- omalizumab

Type 2 inflammation and biologics. B B cell; baso basophil; DC dendritic cell; ECP eosinophilic cationic protein; eos eosinophils; ILC2 type 2 innate lymphoid cell; Th T helper cell

Dupilumab in CRSwNP
Responder Analysis: Percent of Patients With NPS Improvement from Baseline

- Improvement by at least 1 point in NPS from baseline
- Improvement by at least 2 points in NPS from baseline

Placebo
- Improvement by at least 1 point: 12%
- Improvement by at least 2 points: 5%

Dupilumab 300 mg Q2W
- Improvement by at least 1 point: 66%
- Improvement by at least 2 points: 54%

SINUS-52
Week 52

All P-values <0.0001
NPS, nasal polyp score; Q2W, every 2 weeks.
Data on file.

Bachert, Fokkens et al. Lancet 2019
Dupilumab in CRSwNP:
Secondary Efficacy: LS Mean Change from Baseline in SNOT-22 Total Score

Week 24
- Placebo
- Dupilumab 300 mg Q2W

Week 24
- Placebo
- Dupilumab 300 mg Q2W

P<0.0001 LS mean difference for all points from Week 4–EOT vs placebo.

Bachert, Fokkens et al. Lancet 2019
Dupilumab in CRSwNP:
Secondary Efficacy: LS Mean Change from Baseline in Daily Assessed Loss of Smell

**Graphs:**
- **SINUS-24:**
  - Baseline: 2.73 (0.51)
  - Week 24: -0.23
  - LS Mean Change from Baseline (± SE)

- **SINUS-52:**
  - Baseline: 2.70 (0.57)
  - Week 24: -1.21
  - LS Mean Change from Baseline (± SE)

**Legend:**
- Placebo
- Dupilumab 300 mg Q2W

**Statistical Note:**
P<0.0001 LS mean difference for all points from Week 4–EOT vs placebo.
### Indications for biological treatment in CRSwNP

**Presence of bilateral polyps in a patient who had ESS***

**THREE criteria are required**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Cut-off points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence of type 2 inflammation</td>
<td>Tissue eos ≥10/hpf, OR blood eos ≥250, OR total IgE ≥100</td>
</tr>
<tr>
<td>Need for systemic corticosteroids or contraindication to systemic steroids</td>
<td>≥ 2 courses per yr, OR long term (&gt;3 months) low dose steroids</td>
</tr>
<tr>
<td>Significantly impaired quality of life</td>
<td>SNOT-22 ≥ 40</td>
</tr>
<tr>
<td>Significant loss of smell</td>
<td>Anosmic on smell test (score depending on test)</td>
</tr>
<tr>
<td>Diagnosis of comorbid asthma</td>
<td>Asthma needing regular inhaled corticosteroids</td>
</tr>
</tbody>
</table>

*exceptional circumstances excluded (e.g., not fit for surgery)

---

EUFORIA consensus on biologics for CRSwNP with or without asthma. Allergy. 2019
web: www.epos2020.com, rhinologyjournal.com
AMT, appropriate medical treatment; INCS, intranasal corticosteroids;
Thank you for listening

www. rhinology.com
www.epos2020.com