Author(s):
Date:
Question: Long term Macrolide antibiotics compared to Usual care in patients with COPD to improve Quality of Life
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Long term Macrolide antibiotics	Usual care	Relative (95% CI)	Absolute (95% CI)		
SGRQ total score[1]												
3 [2,3,4]	randomised trials	not serious	serious [a]	not serious	not serious	none	506	513	-	MD **2.12 total score lower** (3.44 lower to 0.79 lower)	⨁⨁⨁◯ MODERATE	IMPORTANT
SGRQ total score												
3 [3,4]	randomised trials	serious [b]	not serious	not serious	not serious	none	491	498	-	MD **2.18 total score lower** (1.53 lower to 2.82 lower)	⨁⨁⨁◯ MODERATE	IMPORTANT
SGRQ total score												
1 [5]	randomised trials	not serious	not serious	not serious	not serious	none	37	37	-	MD **7.4 total score lower** (12.5 lower to 2.5 lower)	⨁⨁⨁⨁ HIGH	IMPORTANT [c]

CI: Confidence interval; **MD:** Mean difference

Explanations

a. high heterogeneity I2 = 97.10%
b. Low assessment rate for Quality of life introducing significant risk of selection bias.

References

1. Went Ni, Xiaodi Shao,et. al.. Prophylactic Use of Macrolide Antibiotics for the prevention of COPD Exacerbation: A Meta-Analysis. PLOS ONE; 2015.
2. JL Simpson, H Powell,et.al.. The Effect of Azithromycin in Adults with Stable Neutrophilic COPD: A Double Blind Randomised, Placebo Controlled Trial. PLoS ONE; 2014.
3. S Uzun, RS Djamin,et al.. Azithromycin maintenance treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial.. Lancet Respiratory Medicine; 2014.
4. Richard Albert, John Connett,et al. Azithromycin for Prevention of Exacerbations of COPD. The New England Journal of Medicine; 2011.
5. Farida Berkhof, Nynke E Doornewaard-ten Hertog,et. al.. Azithromycin and cough-specific health status in patients with chronic obstructive pulmonary disease and chronic cough: a randomised controlled trial. Respiratory Research; 2013.

Author(s):
Date:
Question: Long term Macrolide antibiotics compared to Usual care in patients with COPD to preserve lung function and limit disease progression
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Long term Macrolide antibiotics	Usual care	Relative (95% CI)	Absolute (95% CI)		
FEV1 decline (follow up: mean 12 months)												
1 [1]	randomised trials	serious [a]	not serious	not serious	not serious	none	44	45	-	MD **0.12 L higher** (0 to 0)	⨁⨁⨁◯ MODERATE	IMPORTANT [b]
FEV1 (follow up: mean 12 months)												
1 [2]	randomised trials	serious [a]	not serious	not serious	not serious	none	47	45	-	MD **0.03 L higher** (0.04 lower to 0.11 higher)	⨁⨁⨁◯ MODERATE	IMPORTANT
6min walk tests (follow up: mean 12 months)												
1 [2]	randomised trials	serious [a]	not serious	not serious	not serious	none	47	45	-	MD **19.3 meter higher** (17.8 lower to 56.5 higher)	⨁⨁⨁◯ MODERATE	IMPORTANT
FEV1 (follow up: mean 12 weeks)												
1 [3]	randomised trials	serious [a]	not serious	not serious	not serious	none	15	15	-	MD **5.62 % predicted lower** (16.17 lower to 4.93 higher)	⨁⨁⨁◯ MODERATE	IMPORTANT

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Small sample size - underpowered

References

1. Terence Seemungal, Tom Wilkinson,et al.. Long term Erythromycin Therapy is associated with decreased COPD excaerbations. Am J Resp Crit Care Med; 2008.
2. S Uzun, RS Djamin,et al.. Azithromycin maintenance treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial.. Lancet Respiratory Medicine; 2014.
3. JL Simpson, H Powell,et.al.. The Effect of Azithromycin in Adults with Stable Neutrophilic COPD: A Double Blind Randomised, Placebo Controlled Trial. PLoS ONE; 2014.

Author(s):
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Question: Long term Macrolide antibiotics compared to Usual care in patients with COPD to reduce acute exacerbations
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Long term Macrolide antibiotics	Usual care	Relative (95% CI)	Absolute (95% CI)		
Exacerbations Cochrane review 2013 (follow up: mean 12 months)												
3 [1,2,3]	randomised trials	not serious	serious [a]	not serious	not serious	none	354/629	436/633	**Rate ratio 0.73** (0.58 to 0.91)	**-- per 1000 patient(s) per years** (from -- to --)	⨁⨁⨁◯ MODERATE	CRITICAL
Exacerbations [4]												
8 [1,2,3,5,6,7,8,9]	randomised trials	not serious	serious [a]	not serious	not serious [b]	none			**Rate ratio 0.58** (0.43 to 0.78)	**-- per 1000 patient(s) per years** (from -- to --)	⨁⨁⨁◯ MODERATE	CRITICAL
Exacerbations Meta-analysis Yao and same data published Donath[1011]												
6 [1,2,3,6,7,8]	randomised trials	not serious	serious [a,c]	not serious	not serious	none	369/726 (50.8%)	478/734 (65.1%)	**RR 0.62** (0.43 to 0.89)	**247 fewer per 1,000** (from 371 fewer to 72 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Exacerbations (follow up: mean 12 months)												
1 [3]	randomised trials	not serious	not serious	not serious	not serious	none	741/558	900/559	**Rate ratio 0.83** (0.72 to 0.95)	**-- per 1000 patient(s) per years** (from -- to --)	⨁⨁⨁⨁ HIGH	CRITICAL
Exacerbations (follow up: mean 12 months)												
1 [2]	randomised trials	not serious	not serious	not serious	not serious	none	81/53	125/56	**Rate ratio 0.648** (0.489 to 0.859)	**-- per 1000 patient(s) per years** (from -- to --)	⨁⨁⨁⨁ HIGH	CRITICAL
Exacerbations (follow up: mean 12 months)												

1 [9]	randomised trials	not serious	not serious	not serious	not serious	none	84/47 (178.7%)	129/45 (286.7%)	**RR 0.58** (0.47 to 0.79)	**1,000 fewer per 1,000** (from 1,000 fewer to 602 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL

Exacerbations (follow up: mean 12 months)

1 [8]	randomised trials	not serious	not serious	not serious	not serious	none	6/11 (54.5%)	22/11 (200.0%)	**RR 0.72** (0.61 to 0.81) [d]	**560 fewer per 1,000** (from 780 fewer to 380 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL

Exacerbations (follow up: mean 12 months)

1 [7]	randomised trials	serious [e]	not serious	not serious	not serious	none	14/55 (25.5%)	64/54 (118.5%)	**RR 0.21** (0.13 to 0.33) [f]	**936 fewer per 1,000** (from 1,000 fewer to 794 fewer)	⨁⨁⨁◯ MODERATE	IMPORTANT

Exacerbations (follow up: mean 6 months)

1 [1]	randomised trials	not serious	not serious	not serious	not serious	none	11/18	20/18	**Rate ratio 0.55** (0.31 to 0.98)	**-- per 1000 patient(s) per years** (from -- to --)	⨁⨁⨁⨁ HIGH	CRITICAL

Exacerbations (follow up: mean 3 months)

1 [6]	randomised trials	serious [g]	not serious	not serious	very serious [h]	none	5/31 (16.1%)	2/36 (5.6%)	**RR -1.50** (-11.00 to 0.48)	**139 fewer per 1,000** (from 667 fewer to 29 fewer)	⨁◯◯◯ VERY LOW	NOT IMPORTANT

Exacerbations (follow up: mean 12 weeks)

1 [12]	randomised trials	not serious	not serious	not serious	serious [i]	none	51/97	67/94	**Rate ratio 0.26** (0.07 to 0.41)	**-- per 1000 patient(s) per years** (from -- to --)	⨁⨁⨁◯ MODERATE	IMPORTANT

Exacerbations (follow up: mean 12 months)

1 [13,j]	randomised trials	not serious	not serious	not serious	not serious	none			**Rate ratio 0.76** (0.63 to 0.91)	**-- per 1000 patient(s) per years** (from -- to --)	⨁⨁⨁⨁ HIGH	CRITICAL

Exacerbations (follow up: mean 12 weeks)

1 [5]	randomised trials	not serious	not serious	not serious	not serious	none	4/15	9/15	**Rate ratio 0.37** (0.11 to 1.21)	**-- per 1000 patient(s) per years** (from -- to --)	⨁⨁⨁⨁ HIGH	CRITICAL

Exacerbations (follow up: mean 12 months)

1 [14]	observational studies	serious [k]	serious [l]	not serious	serious [m]		10/45	19/78	**Rate ratio 0.49** (0.17 to 1.38)	**-- per 1000 patient(s) per years** (from -- to --)	-	NOT IMPORTANT

Exacerbations (follow up: mean 12 months)

1 [15]	observational studies	serious [n]	not serious	not serious	not serious		57/20	136/20	**Rate ratio 0.58** (0.49 to 0.65) [o]	**-- per 1000 patient(s) per years** (from -- to --)	-	NOT IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Significant heterogeneity in studies in terms of intervention, concomitant medication to treat COPD and definition of exacerbation.
b. Wide confidence interval in Banerjee study, but other studies narrower CI with consistent results
c. Banerjee paper demonstrated higher exacerbations in intervention arm.
d. Please note IDR calculated from first medical stats principles and double checked with stats programme. Not reported in study due to small number of patients (11 in each arm) calculated for the six months on the Azithromycin.
e. Prospective open label study - risk of selection and reporting bias significant
f. IDR calculated
g. Small study, short treatment and follow up duration, high drop out and some differences in the treatment and placebo group - selection bias
h. Only published study with more exacerbations in the intervention group. The intervention group was statistically less mobile with poorer QofLife and less able to function physically - could account for exacerbation rate - also very short follow up period.
i. Short intervention period, included patients with 3 exacerbation over 2 years and intervention therefore too short to measure exacerbation rate for three months on treatment.
j. please note this is sub-group analysis of Albert paper - reported here for exacerbations requiring both steroids and antibiotics
k. retrospective multicentre co-hort - high risk of selection bias
l. Intervention Erythromycin/Clarithromycin different dose used in different patients - not defined intervention
m. Patients with COPD and Asthma included will impact on exacerbation rate measured
n. Observational study observed exacerbations before and measured exacerbations after azithromycin high risk bias!
o. IDR calculated not in paper reported - small number

References

1. ZY He, LM Ou,et al.. Effect of 6 months of erythromycin treatment on inflammatory cells in induced sputum and exacerbations in chronic obstructive pulmonary disease.. Respiration; 2010.
2. Terence Seemungal, Tom Wilkinson,et al.. Long term Erythromycin Therapy is associated with decreased COPD excaerbations. Am J Resp Crit Care Med; 2008.
3. Richard Albert, John Connett,et al. Azithromycin for Prevention of Exacerbations of COPD. The New England Journal of Medicine; 2011.
4. Went Ni, Xiaodi Shao,et. al.. Prophylactic Use of Macrolide Antibiotics for the prevention of COPD Exacerbation: A Meta-Analysis. PLOS ONE; 2015.
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8. Francesco Blasi, Daniela Bonardi,et al.. Long term azithromycin use in patient with COPD and Tracheostomy. Pulm Pharmacol Ther; 2010.
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10. Elie Donath, Abubakr Chaudhry,et al.. A Meta-Analysis on the prophylactic use of macrolide antibiotics for the prevention of disease exacerbations in patients with COPD. Respiratory Medicine; 2013.
11. Guo-Yan Yao, Yan-Liang Ma,et al. Macrolide Therapy Decrease Chronic Obstructive Pulmonary Disease Exacerbation: A Meta-Analysis. Respiration; 2013.
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14. M Yamaya, A Azuma,et al.. Inhibitory effects of macrolide antibiotics on exacerbations and hospitalization in chronic obstructive pulmonary disease in Japan: a retrospective multicenter analysis. J Am Geriatr Soc; 2008.
15. X Pomares, C Montón,et al.. Long-term azithromycin therapy in patients with severe COPD and repeated exacerbations. Int J Cron Obstruct Pulmon Dis; 2011.

Author(s):
Date:
Question: Long term Macrolide antibiotics compared to Usual care for reducing hospitalisation in patients with COPD
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Long term Macrolide antibiotics	Usual care	Relative (95% CI)	Absolute (95% CI)		
Hospitalisation [1]												
5 [2,3,4,5,6]	randomised trials	not serious	not serious	not serious	not serious	none			**RR 0.89** (0.64 to 1.24)	**1 fewer per 1,000** (from 1 fewer to 1 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL
Hospitalisation (follow up: mean 12 months)												
1 [6]	randomised trials	not serious	not serious	not serious	not serious	none	156/558 (28.0%)	200/559 (35.8%)	**RR 0.98** (0.89 to 1.09)	**7 fewer per 1,000** (from 39 fewer to 32 more)	⨁⨁⨁⨁ HIGH	CRITICAL
Hospitalisation (follow up: mean 12 months)												
1 [4]	randomised trials	not serious	not serious	not serious	not serious	none			**RR 1.20** (0.72 to 2.00)	**1 fewer per 1,000** (from 2 fewer to 1 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL
Hospitalisation (follow up: mean 6 months)												
1 [3]	randomised trials	serious [a]	serious [b]	not serious	not serious	none	1/11 (9.1%)	6/11 (54.5%)	**RR 0.20** (0.03 to 1.45)	**436 fewer per 1,000** (from 529 fewer to 245 more)	⨁⨁◯◯ LOW	IMPORTANT [a]
Hospitalisation (follow up: mean 12 months)												
1 [5]	randomised trials	not serious	not serious	not serious	not serious	none			**RR 0.45** (0.19 to 1.09)	**0 fewer per 1,000** (from 1 fewer to 0 fewer)	⨁⨁⨁⨁ HIGH	
Hospitalisation (follow up: mean 12 weeks)												

1 [2]	randomised trials	not serious	not serious	not serious	not serious	none	4/42 (9.5%)	5/42 (11.9%)	**RR 0.80** (0.23 to 2.77)	**24 fewer per 1,000** (from 92 fewer to 211 more)	⨁⨁⨁⨁ HIGH	IMPORTANT

Hospitalisation (follow up: mean 12 months)

1 [7]	observational studies	serious [c]	serious [c]	not serious	serious [c]		28/20 (140.0%)	72/20 (360.0%)	**RR 0.61** (-- to --)	**1,000 fewer per 1,000** (from -- to --)	-	NOT IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Open label study therefore risk of bias and very small number. Note wide CI - uncertainty of evidence
b. study demonstrating this reduction in hospitalisation, it was open label study and small number - therefore likely not significant
c. Retrospective co-hort study with significant risk of bias

References

1. Went Ni, Xiaodi Shao,et. al.. Prophylactic Use of Macrolide Antibiotics for the prevention of COPD Exacerbation: A Meta-Analysis. PLOS ONE; 2015.
2. Farida Berkhof, Nynke E Doornewaard-ten Hertog,et. al.. Azithromycin and cough-specific health status in patients with chronic obstructive pulmonary disease and chronic cough: a randomised controlled trial. Respiratory Research; 2013.
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7. X Pomares, C Montón,et al.. Long-term azithromycin therapy in patients with severe COPD and repeated exacerbations. Int J Cron Obstruct Pulmon Dis; 2011.

Author(s):
Date:
Question: Long term Macrolide antibiotics compared to usual care in patients with COPD or is risk of microbial resistance too high?
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	long term Macrolide antibiotics	usual care	Relative (95% CI)	Absolute (95% CI)		
Bacterial resistance (follow up: mean 12 months)												
1 [1]	randomised trials	not serious	not serious	not serious	not serious		38/47 (80.9%)	44/108 (40.7%)	**RR 3.76** (1.95 to 7.23)	**1,000 more per 1,000** (from 387 more to 1,000 more)	-	CRITICAL
Colonisation (follow up: mean 12 months)												
1 [1]	randomised trials	not serious	not serious	not serious	not serious		66/550 (12.0%)	172/550 (31.3%)	**RR 0.45** (0.35 to 0.58)	**172 fewer per 1,000** (from 203 fewer to 131 fewer)	-	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

References

1. Richard Albert, John Connett,et al. Azithromycin for Prevention of Exacerbations of COPD. The New England Journal of Medicine; 2011.

Author(s):
Date:
Question: Long term Macrolide antibiotics compared to usual care in patients with COPD or is side effect profile unacceptable?
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Long term Macrolide antibiotics	usual care	Relative (95% CI)	Absolute (95% CI)		
Adverse events in all studies reported[1]												
9 [2,3,4,5,6,7,8,9,10]	randomised trials	serious [a]	serious [b]	not serious	not serious	none			**OR 1.55** (1.00 to 2.39)	**2 fewer per 1,000** (from 2 fewer to 1 fewer)	⨁⨁◯◯ LOW	CRITICAL
Adverse events in Erythromycin group[1]												
3 [5,6,9]	randomised trials	not serious	serious [c]	not serious	not serious	none			**OR 1.22** (0.56 to 2.66)	**1 fewer per 1,000** (from 3 fewer to 1 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Adverse events with Azithromycin[1]												
5 [2,3,7,8,10]	randomised trials	not serious	serious [d]	not serious	not serious	none			**OR 2.08** (0.80 to 5.37)	**2 fewer per 1,000** (from 5 fewer to 1 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Adverse events with Clarithromycin												
1 [4]	randomised trials	not serious	not serious	serious	not serious	none			**OR 3.27** (0.59 to 18.21)	**3 fewer per 1,000** (from 18 fewer to 1 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Serious adverse events ATS/ERS reported												
3 [6,8,10]	randomised trials	not serious	not serious	not serious	serious [e]	none	187/660 (28.3%)	217/658 (33.0%)	**RR 0.86** (0.74 to 1.01)	**46 fewer per 1,000** (from 86 fewer to 3 more)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio; **RR:** Risk ratio

Explanations

a. Heterogeneity and self reported side effect profile in some studies, risk of selection bias - only reporting more severe side effects, Suzuki not blinded - risk of detection bias, not all studies reported on all side effects introducing attrition bias.
b. He and Uzun reported less side-effects in intervention group, note different macrolide antibiotics with different doses used and dose effect might contribute to side effect profile
c. One study used variable dose of Erythromycin that will affect the GI side effect profile
d. Different dose regimes used

e. Inconsistency: I2 = 85%

References

1. Went Ni, Xiaodi Shao,et. al.. Prophylactic Use of Macrolide Antibiotics for the prevention of COPD Exacerbation: A Meta-Analysis. PLOS ONE; 2015.
2. Farida Berkhof, Nynke E Doornewaard-ten Hertog,et.al.. Azithromycin and cough-specific health status in patients with chronic obstructive pulmonary disease and chronic cough: a randomised controlled trial. Respiratory Research; 2013.
3. JL Simpson, H Powell,et.al.. The Effect of Azithromycin in Adults with Stable Neutrophilic COPD: A Double Blind Randomised, Placebo Controlled Trial. PLoS ONE; 2014.
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Author(s):
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Question: Long term Macrolide antibiotics compared to Usual care in patients with COPD to delay onset of acute exacerbations
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Long term Macrolide antibiotics	Usual care	Relative (95% CI)	Absolute (95% CI)		
Time to first exacerbation												
3 [1,2,3]	randomised trials	not serious	not serious	not serious	not serious	none	658	660	-	MD **82 days more** (53 more to 110 more)	⨁⨁⨁⨁ HIGH	CRITICAL
Time to onset for first acute exacerbation (follow up: mean 12 months)												
1 [3]	randomised trials	not serious	not serious	not serious	not serious	none	558	559	-	MD **92 days more** (0 to 0)	⨁⨁⨁⨁ HIGH	CRITICAL
Time to onset of first acute exacerbation (follow up: mean 12 months)												
1 [2]	randomised trials	not serious	not serious	not serious	not serious	none	53	56	-	MD **182 days more** (0 to 0)	⨁⨁⨁⨁ HIGH	CRITICAL
Time to onset of first acute exacerbation (follow up: mean 12 months)												
1 [1]	randomised trials	not serious	not serious	not serious	not serious	none	47	45	-	MD **71 days more** (0 to 0)	⨁⨁⨁⨁ HIGH	CRITICAL
Time to onset of first acute exacerbation (follow up: mean 6 months)												
1 [4]	randomised trials	not serious	not serious	not serious	not serious	none	18	18	-	MD **69 days more** (0 to 0)	⨁⨁⨁⨁ HIGH	CRITICAL
Time to onset of first acute exacerbation (follow up: mean 12 weeks)												
1 [5]	randomised trials	not serious	not serious	not serious	not serious	none	97	94	-	MD **7 days more** (27.21 fewer to 41.24 more)	⨁⨁⨁⨁ HIGH	IMPORTANT [b]
Time to onset of first acute exacerbation (follow up: mean 26 weeks)												
1 [6]	randomised trials	not serious	not serious	not serious	not serious	none	15	15	-	**0** (0 to 0)	⨁⨁⨁⨁ HIGH	IMPORTANT [c]
Time to onset of first acute exacerbation (follow up: mean 6 months)												

1 [7]	randomised trials	not serious	not serious	not serious	not serious	none	11	11	-	**0** (0 to 0)	⨁⨁⨁⨁ HIGH	IMPORTANT [a]

CI: Confidence interval; **MD:** Mean difference

References

1. S Uzun, RS Djamin,et al.. Azithromycin maintenance treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial.. Lancet Respiratory Medicine; 2014.
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7. Francesco Blasi, Daniela Bonardi,et al.. Long term azithromycin use in patient with COPD and Tracheostomy. Pulm Pharmacol Ther; 2010.

Author(s):
Date:
Question: Long term Macrolide antibiotics compared to Usual care in patients with COPD to reduce airway inflammation, sputum volume, colour and viscosity
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Long term Macrolide antibiotics	Usual care	Relative (95% CI)	Absolute (95% CI)		
Serum CRP (follow up: mean 12 months)												
1 [1]	randomised trials	not serious	not serious	not serious	not serious	none	41	42	-	MD **2.54 mg/l lower** (0 to 0)	⨁⨁⨁⨁ HIGH	IMPORTANT
Serum CRP (follow up: mean 12 months)												
1 [2]	randomised trials	not serious	not serious	not serious	not serious	none	47	45	-	MD **27.1 mg/l lower** (42.3 lower to 8 lower)	⨁⨁⨁⨁ HIGH	IMPORTANT

CI: Confidence interval; **MD:** Mean difference

References

1. Terence Seemungal, Tom Wilkinson,et al.. Long term Erythromycin Therapy is associated with decreased COPD excaerbations. Am J Resp Crit Care Med; 2008.
2. S Uzun, RS Djamin,et al.. Azithromycin maintenance treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial.. Lancet Respiratory Medicine; 2014.

Author(s):
Date:
Question: Long term Macrolide antibiotics compared to Usual care in patients with COPD to reduce mortality
Setting:
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Long term Macrolide antibiotics	Usual care	Relative (95% CI)	Absolute (95% CI)		
Mortality[1]												
3 [2,3,4]	randomised trials	not serious	serious [a]	not serious	not serious	none	18/660 (2.7%)	20/657 (3.0%)	**RR 0.90** (0.48 to 1.69)	**3 fewer per 1,000** (from 16 fewer to 21 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Mortality (follow up: mean 12 months)												
1 [4]	randomised trials	not serious	not serious	not serious	not serious	none	18/558 (3.2%)	20/558 (3.6%)	**OR 0.90** (0.47 to 1.72)	**3 fewer per 1,000** (from 19 fewer to 24 more)	⨁⨁⨁⨁ HIGH	CRITICAL
Mortality (follow up: mean 6 months)												
1 [5]	randomised trials	not serious	not serious	not serious	not serious	none	3/11 (27.3%)	5/11 (45.5%)	**RR 0.60** (0.19 to 1.92)	**182 fewer per 1,000** (from 368 fewer to 418 more)	⨁⨁⨁⨁ HIGH	CRITICAL
Mortality[6]												
3 [2,4,5]	randomised trials	not serious	not serious	not serious	not serious	none			**RR 0.85** (0.49 to 1.46)	**1 fewer per 1,000** (from 1 fewer to 0 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio

Explanations

a. Some inconsistency I2 = 85%

References

1. Went Ni, Xiaodi Shao,et. al.. Prophylactic Use of Macrolide Antibiotics for the prevention of COPD Exacerbation: A Meta-Analysis. PLOS ONE; 2015.
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5. Francesco Blasi, Daniela Bonardi,et al.. Long term azithromycin use in patient with COPD and Tracheostomy. Pulm Pharmacol Ther; 2010.
6. Elie Donath, Abubakr Chaudhry,et al.. A Meta-Analysis on the prophylactic use of macrolide antibiotics for the prevention of disease exacerbations in patients with COPD. Respiratory Medicine; 2013.