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Question: Should Bromesine hydrochloride compared to Standard treatment be used for COVID-19 patients?

Setting: Inpatient

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bromesine hydrochloride	Standard treatment	Relative (95% CI)	Absolute (95% CI)	
All-cause mortality											
2 ^{1,2}	randomised trials	serious ^a	serious ^b	not serious	serious ^c	none	2/87 (2.3%)	7/91 (7.7%)	RR 0.39 (0.03 to 4.79)	47 fewer per 1.000 (from 75 fewer to 292 more)	⊕○○○ VERY LOW
SARS-CoV-2 clearance											
1 ³	randomised trials	serious ^d	not serious	not serious	very serious ^e	none	11/12 (91.7%)	6/6 (100.0%)	RR 0.95 (0.72 to 1.27)	50 fewer per 1.000 (from 280 fewer to 270 more)	⊕○○○ VERY LOW
Improvement of lung disease on CT											
1 ³	randomised trials	serious ^d	not serious	not serious	very serious ^e	none	8/12 (66.7%)	2/6 (33.3%)	RR 2.00 (0.60 to 6.64)	333 more per 1.000 (from 133 fewer to 1.000 more)	⊕○○○ VERY LOW
Number of patients with adverse events											
1 ¹	randomised trials	serious ^d	not serious	not serious	serious ^f	none	No adverse events during the study for either group			⊕⊕○○ LOW	
Number of patients discharged											

1 ³	randomised trials	serious ^d	not serious	not serious	very serious ^e	none	10/12 (83.3%)	2/6 (33.3%)	RR 2.50 (0.78 to 7.97)	500 more per 1.000 (from 73 fewer to 1.000 more)	⊕○○○ VERY LOW
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Number of patients with serious adverse events

1 ²	randomised trials	serious ^g	not serious	not serious	serious ^f	none	No serious adverse event reported			⊕⊕○○ LOW
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Progression / exacerbation of lung disease on CT

1 ²	randomised trials	serious ^g	not serious	not serious	very serious ^h	none	5/48 (10.4%)	5/52 (9.6%)	RR 1.08 (0.33 to 3.51)	8 more per 1.000 (from 64 fewer to 241 more)	⊕○○○ VERY LOW
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Explanations

- Downgraded of one level for high risk of performance bias in 2 studies, unclear risk of selection bias in one study and unclear risk of attrition and reporting bias in the other study
- Downgraded of one level for heterogeneity $I^2=54\%$
- Downgraded of one level for wide CI
- Downgraded of one level for high risk of performance bias and unclear risk of selection bias
- Downgraded of two levels for very small sample size
- Downgraded of one level for small sample size
- Downgraded of one level for high risk of performance bias and unclear risk of selection bias
- Downgraded of two levels for small sample size and wide CI

References

- Ansarin K, Tolouian R, Ardalan M, Taghizadieh A, Varshochi M, Teimouri S, et al. Effect of bromhexine on clinical outcomes and mortality in COVID-19 patients: A randomized clinical trial. *Bioimpacts*. 2020;10(4):209-215. doi: 10.34172/bi.2020.27. Epub 2020 Jul 19.
- Tolouian R, Mulla ZD, Jamaati H, Babamahmoodi A, Marjani M, Eskandari R, et al. Effect of bromhexine in hospitalized patients with COVID-19. *Journal of Investigative Medicine*. 2021. Epub ahead of print: doi:10.1136/jim-2020-001747
- Li T, Sun L, Zhang W, Zheng C, Jiang C, Chen M, et al. Bromhexine Hydrochloride Tablets for the Treatment of Moderate COVID-19: An Open-Label Randomized Controlled Pilot Study. *Clin Transl Sci*. 2020 Sep 3. doi: 10.1111/cts.12881. Epub ahead of print.