

Supplementary Methods

PubMed Search Strategy

The PubMed search strategy included the following:

- esomeprazole[tiab] OR omeprazole[tiab] OR lansoprazole[tiab] OR dexlansoprazole[tiab] OR rabeprazole[tiab] OR pantoprazole[tiab] OR zegerid[tiab] OR proton pump inhibitor*[tiab]
- esomeprazole[mesh:noexp] OR omeprazole[mesh:noexp] OR lansoprazole[mesh:noexp] OR dexlansoprazole[mesh:noexp] OR rabeprazole[mesh:noexp] OR pantoprazole[mesh:noexp] OR zegerid[mesh:noexp] OR proton pump inhibitors[mesh:noexp]
- 1 OR 2
- “Clinical Trial” [PT:NoExp] OR “clinical trial, phase i”[pt] OR “clinical trial, phase ii”[pt] OR “clinical trial, phase iii”[pt] OR “clinical trial, phase iv”[pt] OR “controlled clinical trial”[pt] OR “multicenter study”[pt] OR “randomized controlled trial”[pt] OR “Clinical Trials as Topic”[mesh:noexp] OR “clinical trials, phase i as topic”[MeSH Terms:noexp] OR “clinical trials, phase ii as topic”[MeSH Terms:noexp] OR “clinical trials, phase iii as topic”[MeSH Terms:noexp] OR “clinical trials, phase iv as topic”[MeSH Terms:noexp] OR “controlled clinical trials as topic”[MeSH Terms:noexp] OR “randomized controlled trials as topic”[MeSH Terms:noexp] OR “early termination of clinical trials”[MeSH Terms:noexp] OR “multicenter studies as topic”[MeSH Terms:noexp] OR “Double-Blind Method”[Mesh] OR ([randomised(TIAB) OR randomized(TIAB)] AND [trial(TIAB) OR trials(tiab)]) OR ([single(TIAB) OR double(TIAB) OR double-d(TIAB) OR triple(TIAB) OR tripled(TIAB) OR treble(TIAB) OR treble(TIAB)] AND [blind*(TIAB) OR mask*(TIAB)]) OR (“4 arm”[tiab] OR “four arm”[tiab])
- 3 AND 5
- pH[tiab]
- 5 AND 7

Quality of Studies and Recommendations for Gastric pH Measurements

To determine whether intragastric pH data are both reliable and comparative requires a detailed description of how the pH measurements were obtained (eg, from pH electrodes placed in the stomach or pH measurements of intermittently aspirated gastric contents). Antimony electrodes provide slower response times, are more temperature-dependent, show more drift than glass electrodes, and many commercial buffer

solutions used to calibrate glass electrodes are incompatible with antimony electrodes (ie, provide erroneous calibration).^{1,2} Gastric electrodes should combine the reference electrode (ie, combination electrodes) because the use of a remote reference is markedly less reliable.²⁻⁴

Ideally, the methods should describe how and where the electrode was positioned,⁵ the sampling rate, the temperature, and the pH used for calibration, preferably 1 and 7 or 1, 4, and 7, whether periodic in vitro stability tests were performed during the recording, whether the electrodes were recalibrated after each test, and what level of drift was deemed acceptable (eg, 0.3 pH units). Meals generally are given during testing and their timing and description also should be given, whether the patients were fully ambulatory, whether smoking was allowed, what type of data collector was used, and which programs were used to analyze the data (see Savarino et al⁶). Errors in the analytical programs used also have been discovered that influenced the output.⁷ We only used studies that used combination electrodes and meals with data obtained over a 24-hour period.

References

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Supplementary Table 1. Studies Reporting pH4time

	OE, mg	Study arms, n	Total patients	Weighted mean pH4time	Weighted median pH4 time	References
Once daily						
Esomeprazole						
20 mg	32	8	280	53.4	55.8	8–13
40 mg	64	23	880	65.9	67.0	8,9,14,15–30
80 mg	128	2	72	65.8	65.8	8,9
Lansoprazole						
15 mg	13.5	6	216	57.0	43.0	8,11,31–34
30 mg	27	20	616	54.9	51.1	8,15,16,18,19,23,25,29,30,33,35–43
60 mg	54	3	65	51.5	51.6	8,35,42
Omeprazole						
10 mg	10	1	27	19.1	19.1	44
20 mg	20	11	245	46.9	47.6	6,10,15,16,33,36,39,45–48
20.6 mg	20.6	2	70	53.2	45.7	32,49
40 mg	40	5	179	61.7	62.0	26,45,48,50
Pantoprazole						
10 mg	2.25	1	36	34.8	34.8	31
20 mg	4.5	3	113	37.0	39.5	9,11,31
40 mg	9	16	541	50.8	52.3	6,9,15,16,25,27–31,40,41,43,51–53
80 mg	18	2	51	39.9	44.9	9,51
120 mg	27	1	15	37.6	37.6	51
Rabeprazole						
10 mg	18	3	92	48.2	48.0	11,12,44
20 mg	36	9	215	52.2	58.5	12,13,15,16,19,22,25,47,54
Twice daily						
Esomeprazole						
20 mg	32	2	51	72.9	72.9	24,55
40 mg	64	5	185	83.8	83.1	18,23,55,56,57
Lansoprazole						
15 mg	13.5	2	28	60.0	63.0	37,42
30 mg	27	5	130	66.7	65.5	18,23,37,39,42
60 mg	54	1	16	83.0	83.0	42
Omeprazole						
20 mg	20	6	85	71.4	76.3	39,50,58,60
40 mg	40	1	12	93.6	93.6	60
Pantoprazole						
40 mg	9	3	85	67.7	70.0	6,57,61
3 times/d						
Esomeprazole						
20 mg	32	1	31	80.4	80.4	56
40 mg	64	1	31	88.4	88.4	56
Lansoprazole						
15 mg	13.5	1	12	58.0	58.0	37
30 mg	27	1	16	87.0	87.0	42
60 mg	54	1	16	77.0	77.0	42

Supplementary Table 2. Studies Excluded Owing to Use of Esophageal Probes, External Electrodes, or in Which Intra-gastric pH Was Obtained by Aspiration

Types of electrodes used	Excluded studies
External electrodes	62–68
Aspirated studies	69–72
Esophageal probes (not intra-gastric)	73–79

Supplemental Table 3. Studies Reporting pH4time for Dexlansoprazole and Vonoprazan

	Study arms, n	Total patients	Weighted median pH4time, %	References
Dexlansoprazole				
30 mg	1	83	59	80
60 mg	2	232	70	81,82
90 mg	1	83	67	80
Vonoprazan				
10 mg	1	9	60	83
20 mg	1	9	85	83
30 mg	1	9	90	83
40 mg	1	9	93	83

NOTE. All regimens are once daily and were reported as median pH4time.

Supplemental Table 4. Individual Studies Reporting Median and Mean pH6time

	Total patients	Median pH6time, %	References
Once daily			
Lansoprazole			
15 mg	12	3	37
30 mg	12	4	37
Omeprazole			
20 mg	21	11.5	46
Twice daily			
Lansoprazole			
15 mg	12	6	37
30 mg	12	8	37
3 times/d			
Lansoprazole			
15 mg	12	6	37
Mean pH6time, %			
Once daily			
Esomeprazole			
40 mg	30	20	17
40 mg	83	36.5	30
Lansoprazole			
15 mg	29	18	33
30 mg	12	5	36
30 mg	16	17	42
30 mg	16	20	42
30 mg	29	22	33
30 mg	83	28.5	30
60 mg	16	19	42
Omeprazole			
20 mg	12	5	36
20 mg	29	19	33
20 mg	21	25.4	6
Pantoprazole			
40 mg	83	25	30
40 mg	20	42	6
Twice daily			
Lansoprazole			
15 mg	16	23	42
30 mg	16	28	42
60 mg	16	29	42
Omeprazole			
20 mg	12	40.7	60
40 mg	12	43.4	60
Pantoprazole			
40 mg	23	54.5	6
3 times/d			
Lansoprazole			
30 mg	16	45	42
60 mg	16	33	42