Efficacy of N-acetylcysteine Plus Simethicone in Improving Mucosal Visibility During Upper Gastrointestinal Endoscopy: A Systematic Review and Meta-Analysis

Mudasar Nisar; Rabia Javed; Mohammed Dheyaa Marsool Marsool; Haris Bin Khalid; Yousef M. Husseiny; Sameen Tahira; Shree Rath; Azeem Khalid; Hamza Ashraf; Haider Ashfaq

Department of Gastroenterology, Services Institute of Medical Sciences, Lahore, Pakistan, Department of Medicine, Allama Iqbal Medical College, Lahore, Pakistan, Department of Medicine, Central Park Medical College, Lahore, Pakistan, Medical Student, New Giza University, Giza, Egypt, Department of Medicine, Mayo Clinic Arizona, Phoenix, Arizona, USA, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India, Department of Gastroenterology, Services Institute of Medica, Sciences, Lahore, Pakistan, Allama Iqbal Medical College, Lahore, Department of Internal Medicine, Aiken Regional Medical Centers, SC, USA

BACKGROUND

Upper Gastrointestinal Endoscopy (UGE) is a common diagnostic and therapeutic method used for detection of several disease lesions. However, mucosal visibility is often limited by bubbles and foam. Several premedications have been used to achieve sufficient visualization. This study evaluates the efficacy of different doses of N-acetylcysteine (NAC) plus simethicone in enhancing mucosal visibility compared to water/placebo.

METHODS

We systematically searched PubMed, COCHRANE library, clinicaltrials.gov, and EMBASE databases to collect relevant articles. A total of 1351 articles, excluding duplicates, were screened using Rayyan AI. Article selection was based on well-defined inclusion and exclusion criteria. Baseline characteristics and outcomes were extracted thoroughly in the form of quantitative data. Primary outcome was total mucosal visibility (TMV) score, and secondary outcome was procedure time. Analysis was performed on Revman 5.4 to evaluate the pooled effect with forest and funnel plots generated. Subgroup analysis was done based on doses of NAC as 500mg or less, 600mg, and 1000mg. Heterogeneity was assessed by sensitivity analysis. ROB scale was used to assess the quality of included studies.

RESULTS

Ten studies with a combined total of 1615 patients were included in this meta-analysis. The pooled effect of the overall TMV score depicted improved mucosal visibility in the NAC plus simethicone group (SMD = -1.89, 95% CI: -2.59 to -1.14, p<0.00001, I^2 = 97%) compared to water or placebo. 600mg dose of NAC showed significantly improved TMV score (SMD= -2.64, 95% CI: -3.59 to -1.69, p<0.00001), while no significant improvement was observed with NAC doses of 500mg or less (SMD=-0.85, 95% CI: -2.18 to 0.48, p=0.21, I^2=97%) and 1000mg (SMD= -1.60, 95% CI: -3.95 to 0.79, p=0.18, I^2 = 97%). Intervention did not significantly reduce the procedure time, as the overall mean difference across all studies was -0.63 (95% CI: -1.88 to 0.62, I^2 = 95%), which is not statistically significant (p = 0.32).

RESULTS CON'T

TABLE 1

	Intervention			Water/Placebo				Std. Mean Difference		
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**	**Std. Mean Difference IV, Random, 95% CI**
1.1.1 500mg or less NAC										
Monrroy(L) 2017	7.06	3.83	46	8.06	5.36	46	8.5%	-0.21 [-0.62, 0.20]	2017	
Stepan 2017	15.35	2.447	44	16.55	2.61	44	8.5%	-0.47 [-0.89, -0.05]	2021	
Valenzuela 2022	5.86	0.655	101	7.91	0.818	104	8.5%	-2.75 [-3.14, -2.37]	2022	
Stepan (B) 2023	16.78	2.945	30	16.61	3.068	30	8.4%	0.06 [-0.45, 0.56]	2023	
Subtotal (95% CI)			**221**			**224**	**33.8%**	**-0.85 [-2.18, 0.48]**		
Heterogeneity: Tau^2 = 1.80; Chi^2 = 116.91, df = 3 (P < 0.00001); I^2 = 97%										
Test for overall effects: Z = 1.25 (P = 0.21)										
1.1.2 600mg NAC										
Elvas 2016	3.94	0.733	98	5.44	0.98	98	8.6%	-1.73 [-2.06, -1.40]	2016	
Mahawongkajit 2020	7.15	0.98	32	13.4	1.86	32	7.7%	-4.15 [-5.04, -3.26]	2020	
Anikhindi 2021	6.89	0.377	104	8.72	0.61	106	8.4%	-3.59 [-4.03, -3.15]	2021	
Krishnamurthy 2022	8.31	1.73	192	12.06	2.3	192	8.6%	-1.84 [-2.08, -1.60]	2022	
Stepan (A) 2023	15.29	2.49	30	16.61	3.068	30	8.3%	-0.47 [-0.98, 0.05]	2023	
Cossio 2024	6.49	0.156	40	7.68	0.342	43	7.9%	-4.38 [-5.19, -3.58]	2024	
Subtotal (95% CI)			**496**			**501**	**49.5%**	**-2.64 [-3.59, -1.69]**		
Heterogeneity: Tau^2 = 1.33; Chi^2 = 143.60, df = 5 (P < 0.00001); I^2 = 97%										
Test for overall effects: Z = 5.44 (P < 0.00001)										
1.1.3 1000mg NAC										
Basford 2016	5.4	1.31	41	8.44	0.75	40	8.2%	-2.81 [-3.43, -2.19]	2016	
Monrroy (H) 2017	6.77	5.36	46	9.13	6.12	46	8.5%	-0.41 [-0.82, 0.01]	2017	
Subtotal (95% CI)			**87**			**86**	**16.7%**	**-1.60 [-3.95, 0.76]**		
Heterogeneity: Tau^2 = 2.82; Chi^2 = 39.86, df = 1 (P < 0.00001); I^2 = 97%										
Test for overall effect: Z = 1.33 (P = 0.18)										
Total (95% CI)			**804**			**811**	**100.0%**	**-1.86 [-2.59, -1.14]**		
Heterogeneity: Tau^2 = 1.56; Chi^2 = 372.46, df = 11 (P < 0.00001); I^2 = 97%										
Test for overall effect: Z = 5.06 (P < 0.00001)										
Test for subgroup differences: Chi^2 = 4.73, df = 2 (P = 0.09), I^2 = 57.7%										

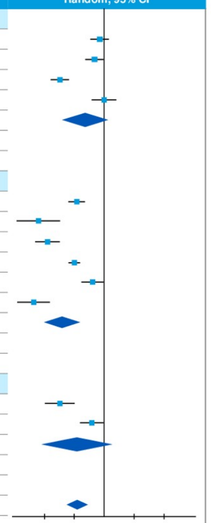
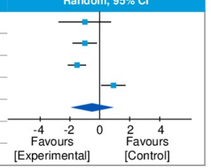


TABLE 2

	Intervention			Water/Placebo				Mean Difference		
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**	**Mean Difference IV, Random, 95% CI**
Basford 2016	5.15	2.15	41	5.87	3.6	40	21.2%	-0.72 [-2.02, 0.58]	2016	
Mahawongkajit 2020	8.81	1.2	32	9.56	1.43	32	25.6%	-0.75 [-1.40, -0.10]	2020	
Krishnamurthy 2022	5.27	1.28	192	6.95	1.8	192	27.0%	-1.68 [-1.99, -1.37]	2022	
Valenzuela 2022	6	1.5	101	5.35	2.255	104	26.2%	0.65 [0.13, 1.17]	2022	
Total (95% CI)			**366**			**368**	**100.0%**	**-0.63 [-1.88, 0.62]**		
Heterogeneity: Tau^2 = 1.48; Chi^2 = 57.20, df = 3 (P < 0.00001); I^2 = 95%										
Test for overall effect: Z = 0.98 (P = 0.32)										



CONCLUSION

This meta-analysis indicates that NAC plus simethicone, particularly the dose of 600mg, is effective in improving the mucosal visibility and reducing procedure time during endoscopy. These findings have important implications, as enhanced mucosal visibility during endoscopy can significantly increase procedural efficacy, leading to better patient outcomes and increased endoscopist's satisfaction.

REFERENCES

1. Morrissey JF, Reichelderfer M. Gastrointestinal Endoscopy. New England Journal of Medicine. 1991 Oct 17;325(16):1142–9.
2. Waddingham W, Kamran U, Kumar B, Trudgill NJ, Tsiamoulos ZP, Banks M. Complications of diagnostic upper Gastrointestinal endoscopy: Common and rare – recognition, assessment and management. BMJ Open Gastroenterol. 2022 Dec 26;9(1):e000688.
3. Offman J, Fitzgerald RC. Alternatives to Traditional Per-Oral Endoscopy for Screening. Gastrointest Endosc Clin N Am. 2017 Jul;27(3):379–96.
4. Nguyen V, Nguyen CC, Nguyen. Appropriate use of endoscopy in the diagnosis and treatment of gastrointestinal diseases: Up-to-date indications for primary care providers. Int J Gen Med. 2010 Nov;345.
5. Lee JM, Park Y, Park JM, Park HJ, Bae JY, Seo SY, et al. New sedatives and analgesic drugs for gastrointestinal endoscopic procedures. Clin Endosc. 2022 Sep 30;55(5):581–7.