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Meta-Analysis

Efficacy of hemostatic powders in upper gastrointestinal bleeding: A systematic review and meta-analysis

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ABSTRACT

Background: There is limited evidence on the efficacy of hemostatic powders in the management of upper gastrointestinal bleeding.
Aims: Provide a pooled estimate of the efficacy and safety profile of hemostatic powders in digestive endoscopy.
Methods: A computerized bibliographic search on the main databases was performed through December 2018. Pooled effects were calculated using a random-effects model. The primary outcome was immediate hemostasis rate. Secondary outcomes were rebleeding rate (either at 7 and 30 days), bleeding-related mortality, and all-cause mortality rate.
Results: A total of 24 studies, of which three were randomized-controlled trials, with 1063 patients were included in the meta-analysis. Immediate hemostasis was achieved in 95.3% (93.3%–97.3%) of patients, with no difference based on treatment strategy, hemostatic agent used, bleeding etiology. Success rate was slightly lower in spurting bleeding (91.9%). Hemostatic powders showed similar efficacy as compared to conventional endoscopic therapy (odds ratio: 0.84, 0.06–11.47; p = 0.9). Thirty-day rebleeding rate was 16.9% (9.8%–24%) with no difference in comparison to other endoscopic treatments (odds ratio 1.59, 0.35–7.21; p = 0.55). All-cause and bleeding-related mortality rates were 7.6% (4%–10.8%) and 1.4% (0.5%–2.4%), respectively.
Conclusion: Novel hemostatic powders represent a user-friendly and effective tool in the management of upper gastrointestinal bleeding.

1. Introduction

Gastrointestinal bleeding remains a major cause of morbidity and mortality worldwide. Therapeutic management of gastrointestinal bleeding could represent a real challenge even for an experienced endoscopist although several effective hemostatic techniques have been developed and successfully practiced over the years. In particular, management of profound venous or arterial bleeding and malignant lesions with large surface area are not frequently amenable to traditional endoscopic hemostatic techniques, hence the unmet need to take advantage of novel therapeutic strategies.

In this regard topical hemostatic agents, such as hemostatic powders, represent a valuable option relatively easy to use and able to show promising results in preliminary studies [1].

Among hemostatic topical powders, TC-325 with the brand name Hemospray® (Cook Medical, Bloomington, USA) represents the most investigated agent which was proven to be effective in determining immediate hemostasis when sprayed onto active bleeding [1,2]. Other topical agents, such as the starch-derived polysaccharide hemostatic system (EndoClot®, EndoClot Plus, Suzhou Industrial Park, China) are emerging and have been recently used either as a primary hemostasis agent or as a second-line salvage therapy [3].

Based on the limited published experience, current guidelines suggest the use of hemostatic topical agents preferentially in high risk cases as a temporizing measure or a bridge toward more defini-

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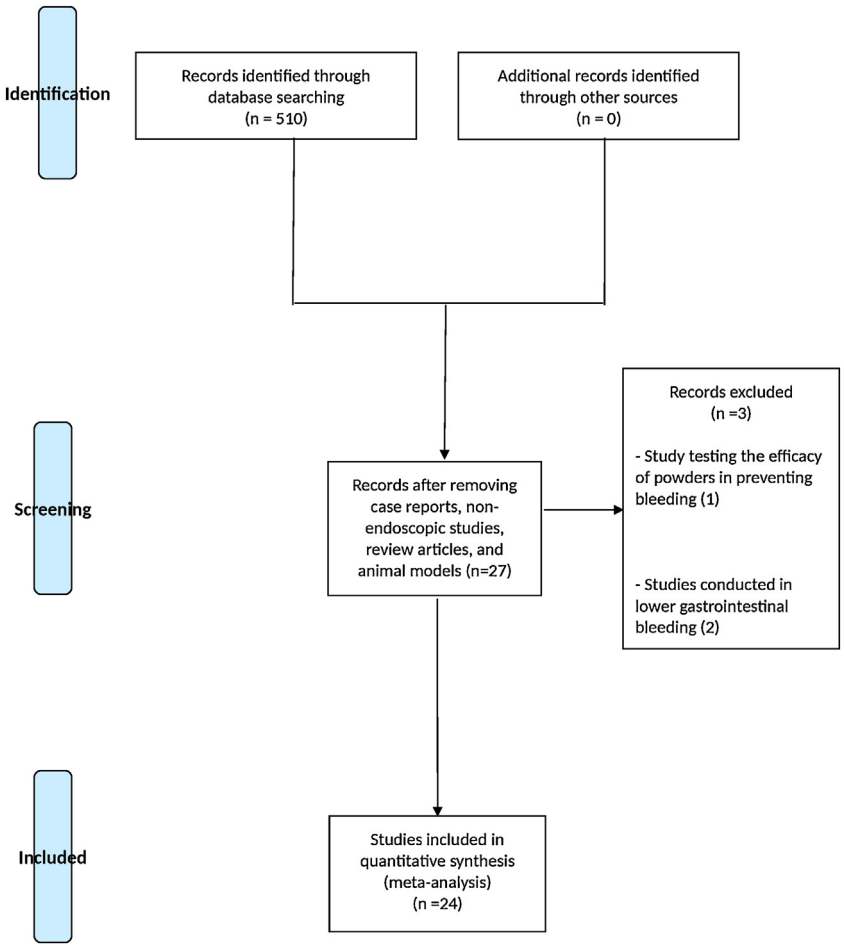

Fig. 1. Flow chart of included studies.

tive treatment [4]; however, there is limited comparative evidence on the efficacy of these agents in clinical practice, hence the pressing need to systematically assess the increasing body of evidence in the field.

The aim of this meta-analysis is to provide a pooled estimate of the efficacy and safety profile of hemostatic powders in upper gastrointestinal bleeding thus attempting to determine their potential utility in digestive endoscopy.

2. Materials and methods

2.1. Inclusion and exclusion criteria

Only studies meeting the following criteria were included: (1) full-text articles recruiting patients with upper gastrointestinal bleeding treated with hemostatic powders; (2) studies published in English; (3) articles reporting at least one of the following data: hemostatic success or rebleeding rate. Case reports, non-endoscopic studies, review articles, and animal models were excluded.

2.2. Search strategy

Fig. 1 reports the search strategy followed in the meta-analysis.

Bibliographic research was conducted on PubMed, EMBASE, Cochrane Library and Google Scholar, including all studies fulfilling inclusion criteria published until December 2018. The following search strategy was adopted: (((TC-325[MeSH Terms]) OR Hemospray[MeSH Terms]) OR hemostatic powder[MeSH Terms]) OR microporous polysaccharides[MeSH Terms].

Relevant reviews on the use of hemostatic powders in endoscopy were examined for potential suitable studies. Authors of included studies were contacted to obtain full text or further information when needed.

Data extraction was conducted by two authors (AF and MST) using a standardized approach (PRISMA Statement) [5]. The quality of included studies was assessed by two authors independently (AF, CEP) according to the Cochrane Collaboration's tool for assessing the risk of bias [6] for RCTs and the Newcastle–Ottawa scale [7] for non-randomized studies.

2.3. Statistical analysis

Primary outcome was treatment success defined as immediate hemostasis rate. Secondary outcomes were rebleeding rate (either at 7 and 30 days), bleeding-related mortality, and all-cause mortality rate. Safety data were inconsistently reported, hence they were analyzed descriptively.

As recommended by recent Cochrane guidelines [8], efficacy outcomes were pooled from included studies through a random-effects model based on DerSimonian and Laird test and summary estimates were expressed in terms of rate and 95% Confidence Interval (CI).

Chi-square and I^2 tests were used for across studies comparison of the percentage of variability attributable to heterogeneity beyond chance. $P < 0.10$ for chi-square test and $I^2 < 20\%$ were interpreted as low-level heterogeneity..

Table 1
Characteristics of included studies.

Study	Arm	Sample size	Study period/ design	Country	Age	Gender male	Antithrombotic agents	Etiology (Ulcer/Tumor)	Forrest Ia/Ib	Location Stomach	Monotherapy
Hemospray®											
Arena 2017 [12]	Hemospray	15	2014–2015/ Retrospective	Italy	74 ± 7.7	8 (53.3%)	8 (53.3%)	Tumor: 100%	NR	7 (47%)	15 (100%)
Cahyadi 2017 [13]	Hemospray	52	2013–2017/ Retrospective	Germany	69 (32–92)	31 (59.6%)	26 (50%)	Ulcer: 34.6% Tumor: 19.2%	0/13.4%	16 (30.7%)	23 (44.2%)
Chen 2015 [14]	Hemospray	50	2011–2013/ Retrospective	Canada	NR	22 (44%)	16 (32%)	Ulcer: 30% Tumor: 38%	6%/20%	NR	NR
Giles 2016 [15]	Hemospray	36	2013–2016/ Retrospective	New Zealand	68.5	25 (69%)	23 (63.8%)	Ulcer: 66.6% Tumor: 2.7%	13.8%/38.8%	17 (47.2%)	9 (25%)
Haddara 2016 [16]	Hemospray	202	2013–2015/ Prospective	France	68.9 ± 14	140 (69.3%)	88 (43.6%)	Ulcer: 37.1% Tumor: 30.1%	7.4%/21.2%	NR	94 (46.5%)
Hagel 2017 [17]	Hemospray	35	2013–2014/ Retrospective	Germany	72 (40–88)	19 (76%)	6 (17%)	Ulcer: 51.4% Tumor: 11.4%	NR	NR	14 (40%)
Holster 2013 [18]	Hemospray	16	2011–2012/ Retrospective	Holland	69.5 (47–88)	12 (75%)	16 (100%)	Ulcer: 56.2% Tumor: 12.5%	18.7%/25%	4 (25%)	16 (100%)
Ibrahim 2013 [19]	Hemospray	9	2013/ Prospective	Belgium/Egypt	NR	7 (77.7%)	0 (0%)	Varices: 100%	–	0 (0%)	9 (100%)
Ibrahim 2015 [20]	Hemospray	38	NR/ Prospective	Belgium/Egypt	59.5 (32–73)	21 (70%)	0 (0%)	Varices: 100%	–	4 (10%)	100% but ligation after 24 h
Leblanc 2013 [21]	Hemospray	12	2011–2012/ Retrospective	France	65.5	9 (75%)	NR	100% after EMR	0/91.6%	1 (8.3%)	8 (75%)
Masci 2014 [22]	Hemospray	13	NR/ Retrospective	Italy	70.3 (42–88)	9 (69.2%)	3 (23.1%)	Ulcer: 100%	30.7%/64.3%	3 (23.1%)	7 (53.8%)
Pittayanon 2018 [23]	Hemospray	88	2011–2016/ Retrospective	Thailand/Canada	65.1 ± 14	62 (70.5%)	22 (25%)	Tumor: 100%	0/94.3%	0 (0%)	77 (87.5%)
Sinha 2016 [24]	Hemospray	20	2013–2015/ Retrospective	UK	75	10 (50%)	10 (50%)	Ulcer: 100%	60%/40%	1 (5%)	0 (0%)
Smith 2014 [25]	Hemospray	63	2011/ Prospective	Multicenter Europe	68	44 (69.8%)	0 (0%)	Ulcer: 52.3% Tumor: 7.9%	NR	33 (52.3%)	55 (87.3%)
Sulz 2014 [26]	Hemospray	16	2013/ Retrospective	Switzerland	67 (40–87)	13 (81.2%)	4 (25%)	Ulcer: 25% Tumor: 12.5%	0/25%	5 (31.2%)	2 (12.5%)

Table 1 (*Continued*)

Study	Arm	Sample size	Study period/ design	Country	Age	Gender male	Antithrombotic agents	Etiology (Ulcer/Tumor)	Forrest Ia/Ib	Location Stomach	Monotherapy
Sung 2011 [27]	Hemospray	20	2009–2010 /Prospective	Hong Kong	60.2 ± 13.8	18 (90%)	NR	Ulcer: 100%	5%/95%	6 (30%)	20 (100%)
Yau 2014 [28]	Hemospray	19	2012–2013/ Retrospective	Canada	67.6 (29–94)	14 (73.7%)	4 (21%)	Ulcer: 63.2%)	0/57.8%	5 (26.3%)	3 (15.7%)
Hemospray® versus Pharmacological Therapy											
Ibrahim 2018 [29]	Hemospray Drug therapy followed by endoscopy on day 2	43 43	2014–2016/ RCT	Belgium/Egypt	58.5 (31–76) 59.3 (50–77)	25 (58%) 27 (63%)	0 (0%) 0 (0%)	Varices: 100% Varices: 100%	–	0 (0%) 0 (0%)	100% but ligation after 24 h
Hemospray® versus Conventional endoscopic therapy											
Kwek 2017 [30]	Hemospray Epinephrine + clips	10 10	2013–2015/ RCT	Singapore	67.9 ± 18.4 72.1 ± 11.4	9 (90%) 7 (70%)	0 (0%) 0 (0%)	Ulcer: 100% Ulcer: 100%	40% 30%	4 (40%) 6 (60%)	10 (100%) 10 (100%)
EndoClot®											
Beg 2015 [31]	EndoClot	21	2012–2014/ Retrospective	UK	72.7	12 (57.1%)	–	Ulcer: 76.1%	23.9%/76.1%	2 (9.5%)	0 (0%)
Kim 2018 [32]	EndoClot	12	2016–2017/ Retrospective	Korea	72.5 (57–89)	8 (66.6%)	3 (25%)	Tumor:100%	0/100%	12 (100%)	7 (58.3%)
Prei 2016 [33]	EndoClot	58	2012–2014/ Prospective	Germany	67 ± 13	51 (73%)	NR	Ulcer: 46.5% Tumor: 17.2%	0/66%	17 (28%)	47 (81%)
EndoClot® versus Conventional Endoscopic Therapy											
Park 2018 [34]	EndoClot Epinephrine + clips	30 60	2016–2017/ Retrospective	Korea	65.8 ± 11.1 65.1 ± 13.7	21 (70%) 42 (70%)	11 (36.6%) 17 (28.3%)	Ulcer: 50% Tumor: 33.3% Ulcer: 66.7% Tumor: 28.3%	70% 73.3%	24 (80%) 40 (66.7%)	10 (33.3%)
CEGP-003 versus Conventional Endoscopic Therapy											
Bang 2018 [35]	CEGP-003 Epinephrine	35 37	2014–2015/ RCT	Korea	60.9 ± 10 62.1 ± 12.1	25 (71.4%) 21 (56.7%)	20 (56.7%) 21 (56.7%)	Ulcer: 17.1% ESD: 82.0% Ulcer: 25.6% ESD: 74.4%	85.7% 81.1%	31 (88–6%) 35 (94.6%)	35 (100%)

Abbreviations: EMR, Endoscopic Mucosal Resection; ESD, Endoscopic Submucosal Dissection; NR, Not Reported; RCT, Randomized Controlled Trial.

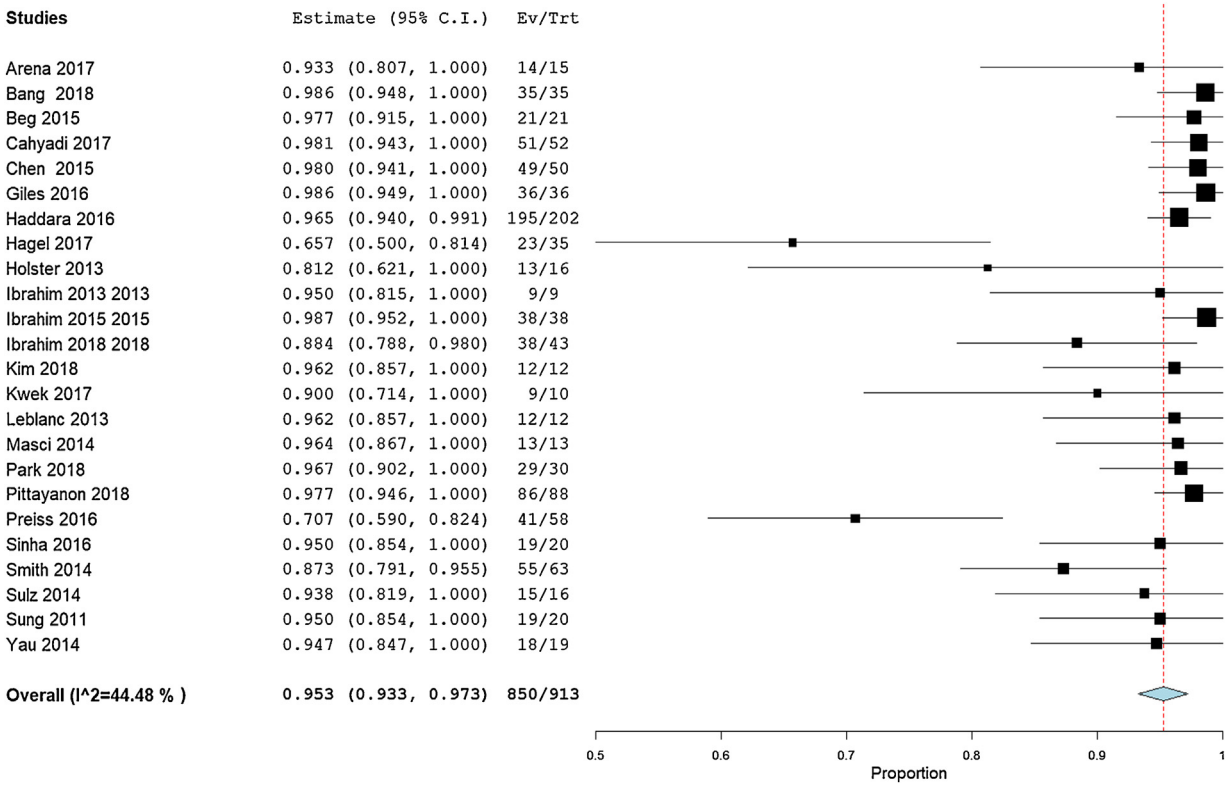

Fig. 2. Pooled analysis of immediate hemostasis rate achieved with hemostatic powders.
Immediate hemostasis was achieved in 95.3% (93.3%–97.3%) patients, with moderate evidence of heterogeneity (I^2 = 44.4%).

Table 2
Sensitivity Analyses. Pooled estimates of the primary outcome, namely immediate hemostasis, obtained according to (a) treatment strategy (monotherapy vs combined), (b) hemostatic agent (Hemospray® vs EndoClot®), (c) bleeding etiology (peptic ulcer disease vs tumor vs varices); (d) bleeding source (spurting vs oozing). Numbers in parentheses indicate 95% confidence intervals.

Subgroup		No. of studies	No. of patients	Immediate hemostasis rate (95% CI)	Within-group heterogeneity (I^2)
Treatment strategy	Monotherapy	22	592	94.4% (91.8%–97%)	44%
	Combined	15	321	96% (93.9%–98.1%)	0%
Hemostatic agent	Hemospray®	19	757	95.8% (93.9%–97.8%)	41%
	EndoClot®	4	121	91.2% (81.3%–100%)	82.7%
Etiology	Peptic ulcer disease	12	244	96.1% (93.7%–98.5%)	0%
	Tumor	9	208	96.8% (94.5%–99.2%)	0%
	Varices	3	90	95.2% (88.4%–100%)	50.8%
Bleeding source	Spurting	6	44	91.9% (84.2%–99.6%)	0%
	Oozing	17	306	96.8% (94.9%–98.7%)	0%

Abbreviation: CI, Confidence Interval.

Probability of publication bias was assessed using funnel plots and with Egger's test. Several sensitivity and subgroup analyses were conducted according to the quality and design of included studies (moderate vs high, and retrospective vs prospective), treatment strategy (monotherapy vs combined), hemostatic agent used (Hemospray® vs Endoclot®), type of bleeding (spurting vs oozing), and etiology (peptic ulcer vs tumor vs variceal bleeding).

All statistical analyses were conducted using RevMan version 5 from the Cochrane collaboration and OpenMeta[Analyst] software. For all calculations a two-tailed p value of less than 0.05 was considered statistically significant.

3. Results

3.1. Characteristics of included studies

As shown in Fig. 1, out of 510 studies initially identified, and after preliminary exclusion of papers not fulfilling inclusion criteria, 27 potentially relevant studies were examined. Among these studies, three were excluded because they tested the efficacy of hemostatic powders in the setting of primary prevention of gastrointestinal bleeding [9] or in lower gastrointestinal bleeding [10,11].

Finally, 24 studies [12–35] with 1063 patients (913 subjects treated with hemostatic powders and 150 with other treatments) were included in the meta-analysis.

Main characteristics of the included studies are reported in Table 1 The recruitment period ranged from 2009 to 2017. Three studies were RCTs [29,30,35], one retrospective study was a propensity-score based comparative analysis [34], all the other studies were single cohort series, of which 17 tested Hemospray® [12–28] and three EndoClot [31–33]. In comparative studies, control arm treatment was conventional endoscopic therapy in three studies [30,34,35], and pharmacological therapy in a single trial [29]. Six studies were conducted in Asia [23,27,30,32,34,35] and the most common sources of bleeding were peptic ulcer disease and tumors. Of note, three studies were conducted in cirrhotic patients

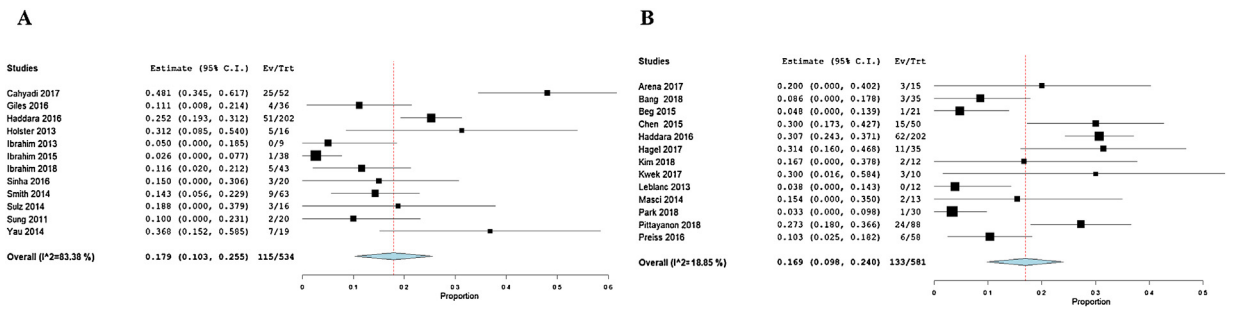

Fig. 3. Pooled analysis of 7-day (A) and 30-day (B) rebleeding rate after use of hemostatic powders.
Rate of bleeding recurrence within 7 days from the index procedure was 17.9% (10.3%–25.5%), with high evidence of heterogeneity (I^2 = 83.4%) (Fig. 3A). Thirty-day rebleeding rate was 16.9% (9.8%–24%) with low evidence of heterogeneity (I^2 = 18.85%) (Fig. 3B).

with active variceal bleeding[19,20,29]. As reported in Table 1, most of the bleeding events were classified as oozing bleeding (Forrest Ib).

Quality was deemed high in eight studies [12,14,18–20, 25,27,34], and moderate or low in the other cases.

Details on the methodological characteristics and quality of included articles are shown in Supplementary Table 1.

3.2. Immediate hemostasis

As depicted in Fig. 2, immediate hemostasis was achieved in 95.3% (93.3%–97.3%) of patients, with moderate evidence of heterogeneity (I^2 = 44.4%). There was no evidence of publication bias (Supplementary Fig. 1; p = 0.38).

The findings of main analysis were confirmed in sensitivity analyses performed according to treatment strategy (monotherapy vs combined), hemostatic agent (Hemospray® vs EndoClot®), bleeding etiology (peptic ulcer disease vs tumor vs varices),and bleeding source (spurting vs oozing) (Table 2). Success rate of hemostatic powders was slightly lower in Forrest Ia ulcers (spurting ulcers) as compared to oozing bleeding sources (Forrest Ib) (91.9% vs 96.8%; Table 2).

Findings regarding EndoClot® should be interpreted with caution due to the limited number of available studies and the strikingly negative results of a single outlier study [33] (Supplementary Fig. 2).

Direct comparison between hemostatic powders and conventional endoscopic therapy was available in three studies [30,34,35] and results are reported in Supplementary Fig. 3. The odds ratio for immediate hemostasis was 0.84 (0.06–11.47; p = 0.9), thus showing no difference between the two treatment regimens.

3.3. Rebleeding rate

The seven-day rebleeding rate was reported in 12 studies [13,15,16,18–20,24–29], (534 patients) as depicted in Fig. 3A. Rate of bleeding recurrence within seven days from the index procedure was 17.9% (10.3%–25.5%). The high heterogeneity observed (I^2 = 83.4%) prevents to draw conclusions about this outcome. Subgroup analysis according to treatment strategy (monotherapy vs combined/rescue) showed 13.5% (7%–20.1%) and 24.8% (15%–34.7%) rebleeding rate, respectively (Supplementary Figs. 4 A and 4B). In particular, high rebleeding rates were observed in three outlier studies [13,18,28] where hemostatic powders were used mainly as salvage therapy for patients after unsuccessful hemostasis with conventional methods (e. g. peptic ulcers with large diameter and/or difficult anatomy). High heterogeneity was confirmed in subgroup analysis according to treatment strategy (monotherapy vs combined/rescue), study design (retrospective vs prospective), and sample size (excluding studies with ≤20 patients; Supplementary Figs. 4A to 4E).

The thirty-day rebleeding rate was reported in 13 studies [12,14,16,17,21–23,30–35],(581 patients) as described in Fig. 3B. Pooled analysis of 30-day rebleeding rate after use of hemostatic powders showed 16.9% (9.8%–24%) rebleeding in the first month from the treatment. Heterogeneity was found to be low (I^2 = 18.85%) and no evidence of publication bias was found (Supplementary Fig. 5, p = 0.41). This finding was confirmed in the subgroup analysis based on treatment strategy with 17.3% (10.1%–24.5%) and 14.2% (0%–30.6%) rebleeding rate after monotherapy and combined/rescue therapy, respectively (Supplementary Figs. 6A and 6B).

Supplementary Figure 7 reports the results of direct comparison between hemostatic powders and conventional endoscopic therapy, with no evidence of superiority of any of the tested treatments in preventing 30-day rebleeding (odds ratio 1.59, 0.35–7.21; p = 0.55), with moderate evidence of heterogeneity (I^2 = 22%).

3.4. Mortality and adverse events

As reported in Fig. 4, all-cause mortality rate (mainly within one month from the treatment) was 7.6% (4%–10.8%) while bleeding-related mortality was 1.4% (0.5%–2.4%) (Figs. 4A and B, respectively). Heterogeneity was high in the former analysis (I^2 = 70.7%) due to the different potential causes of death considered, whereas no heterogeneity was registered in bleeding-related mortality analysis (I [2] = 0%). No evidence of publication bias was observed (Supplementary Figs. 8A and 8B; p values: 0.39 and 0.47, respectively).

Details on safety profile of the two devices are reported in Supplementary Table 2. Two adverse events were reported, of which a case of mild abdominal pain and a gastric perforation in a single German study [17].

4. Discussion

Although conventional endoscopic hemostatic therapies constitute the landmark in the management of gastrointestinal bleeding, these treatments have their limitations, such as the risk for perforation and worsening of bleeding. Furthermore, conventional treatments may represent a technical challenge in presence of large, friable bleeding surfaces such as hemorrhage arising from tumors or large ulcers.

Novel hemostatic products, such as Hemospray® and EndoClot®, have been recently adapted to digestive endoscopy, showing promising results in preliminary uncontrolled data and animal models [1–3].

The growing body of evidence currently published concerning novel hemostatic powders determines a pressing need to system-

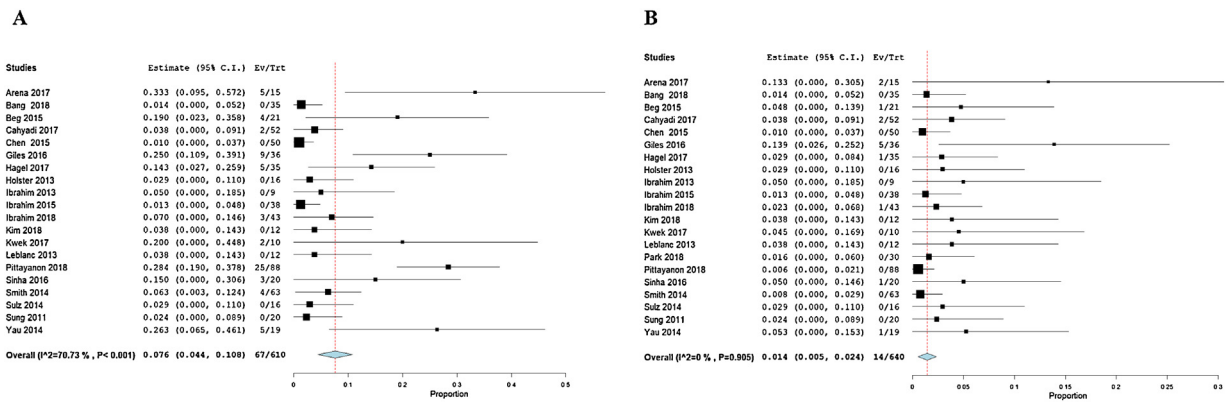

Fig. 4. Pooled analysis of all-cause (A) and bleeding-related (B) mortality rate after use of hemostatic powders.
All-cause mortality rate (mainly within 1 month from the treatment) was 7.6% (4%–10.8%; $I^2 = 70.7\%$) while bleeding-related mortality was 1.4% (0.5%–2.4%; $I^2 = 0\%$).

atically assess the efficacy and safety profile of these agents in order to inform the guidelines.

To the best of our knowledge, the current manuscript represents the first meta-analysis in the field and the first attempt to systematically compare hemostatic powders with conventional endoscopic treatments.

Through a meta-analysis of 24 studies, several key observations were made. First, hemostatic powders are effective in achieving immediate hemostasis with 95.3% pooled success rate. Considering that the majority of the treated lesions were bleeding sources usually not amenable to effective conventional treatments, the pooled efficacy of these agents represents a striking result enabling to consider hemostatic powders as a valuable tool in the management of upper gastrointestinal bleeding. Second, no difference between the available devices was found and hemostatic powders were proved to be effective both in monotherapy and in combination with conventional endoscopic treatments. As expected, success rate was slightly lower in Forrest Ia ulcers (spurting bleeding) where immediate hemostasis rate was assessed as 91.9%, a value in keeping with other conventional modalities. Third, direct comparison between hemostatic powders and conventional endoscopic therapy based on three head-to-head studies [30,34,35] confirmed the competitive role of these agents in the management of upper gastrointestinal bleeding with an OR for immediate hemostasis of 0.84 (0.06–11.47; p = 0.9). Fourth, 7- and 30-day rebleeding rates were 17.9% and 16.9%, respectively. It is important to note that 7-day rebleeding results were weakened by high heterogeneity, thus preventing to draw conclusions about this outcome. Moreover, many of the included studies did not report data on timing of rebleeding, therefore explaining the apparent paradox of higher rebleeding rate at seven days in comparison to one month. The relatively high rebleeding rate (24.8%) observed when hemostatic powders were used in combined regimens or as a rescue therapy is mainly due to the difficult-to-treat nature of these bleeding sources (e. g. peptic ulcers with large diameter and/or difficult anatomy) requiring multiple treatments. It is likely that in these high-risk lesions hemostatic powders may play a role as a temporizing agent, which could allow for more definitive therapy such as conventional therapy and non-emergency surgery to occur. Again, direct comparison between hemostatic powders and conventional endoscopic therapy did not show evidence of superiority of any of the tested treatments in preventing 30-day rebleeding (OR 1.59, p = 0.55). Finally, the safety profile of hemostatic powders was excellent and the mortality rate, in particular the bleeding-related mortality rate, was extremely low.

Although being supported by a limited number of studies, hemostatic powders resulted effective even in difficult-to-manage events such as variceal bleeding in cirrhotic patients. In fact, two cohort studies and an RCT (all authored by the same group) proved the effectiveness and safety of TC-325 in this setting, in particular as bridge therapy to definitive hemostatic treatments feasible during second-look endoscopy. This finding is of particular interest since variceal bleeding constitutes a major cause of mortality in cirrhotic patients and availability of a novel easy-to-use device which does not require the usual endoscopic expertise (like conventional endoscopic ligation/sclerotherapy) represents an encouraging novelty in the field. As conventional hemostatic procedures require adequate training and experience, hemostatic powders with their noncontact and non-traumatic application and their ability to cover a large irregular surface of bleeding may represent an ideal rescue treatment as a bridge to a second look endoscopy by more expert endoscopists.

There are some limitations to our study. First of all, the limited number of case-control or randomized studies does not allow a strong comparison between hemostatic powders and conventional endoscopic treatments. However, the positive outcomes registered in our analysis both in terms of immediate hemostasis and rebleeding rate are in line or even better than those reported in the current literature with conventional endoscopic treatments [22,36]. Second, early rebleeding analysis was impaired by high heterogeneity, thus requiring particular caution in interpreting these findings. Third, a number of variables, such as use of antithrombotic therapy or location of bleeding source, could not be explored in separate subgroup analyses due to the lack of individual patient data.

In conclusion, despite these weaknesses, the meta-analysis favors the use of novel hemostatic powders as user-friendly and effective tool in the management of upper gastrointestinal bleeding. In particular, they may represent a valuable option in those lesions, such as tumors or large ulcers in difficult locations, not easy to manage through conventional endoscopic treatments.

Further RCTs directly comparing hemostatic powders and conventional treatments are required in order to better define the role of these agents in the management algorithm of upper gastrointestinal bleeding.

Specific author contributions

Antonio Facciorusso designed the study and performed the statistical analysis; Marcelo Straus Takahashi and Ceren Eyileten Postula collected the data; Vincenzo Rosario Buccino and Nicola Muscatiello revised the manuscript. All the authors approved the final draft submitted.

Conflict of interest

None declared.

Disclosures

None of the authors have any relevant financial disclosures.

CRediT authorship contribution statement

Antonio Facciorusso: Conceptualization, Formal analysis. **Marcelo Straus Takahashi:** Data curation. **Ceren Eyileten Postula:** Data curation. **Vincenzo Rosario Buccino:** Supervision. **Nicola Muscatiello:** Supervision.

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