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Combination Dornase and Alteplase for Intra-abdominal Drain, Abscess, and Hematoma Clearance: A Retrospective Case Series

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Abstract

Background: Since the advent of the MIST2 trial, the combined instillation of dornase and alteplase has become an effective nonsurgical treatment option for empyema and pleural fluid collection. Percutaneous drainage of abdominal abscesses and fluid collections, rather than open surgical treatment, also has become commonplace. The are several case reports and studies on the use of fibrinolytics to drain abdominal fluid collections but no literature reporting use of both alteplase and dornase for abdominal administration. **Objective:** We present a case series from an academic medical center where dornase therapy was added to fibrinolytic therapy to treat intra-abdominal fluid collections, hematoma, and abdominal drainage catheters with low output. **Methods:** This is an institutional review board-approved retrospective case series of 13 patients who underwent combination use of alteplase and dornase via intra-abdominal route. The primary objective was to assess for increased drain output, reduction in size of the fluid collection, and adverse events. **Results:** Many patients had improved drain output after dornase-alteplase therapy. One patient had significant bleeding complications. **Conclusions:** All patients were discharged alive from the hospital. Clinical success was difficult to define due to variable goals of therapy. Further data are needed to establish the safety and efficacy of this practice, especially compared with intra-abdominal alteplase alone. Patients in our series generally received larger doses of alteplase than in prior studies due to use of dosing modeled on the MIST2 trial. Based on the limited experience of our study, we recommend holding therapeutic anticoagulation during the administration of intra-abdominal dornase-alteplase.

Keywords

surgery, clinical pharmacy, bleeding, thrombolytics, clinical practice

Introduction

In the past decade since the MIST2 trial, use of combination alteplase-dornase in the clearance of empyema and pleural drains has become commonplace in thoracic surgery. The coupling of dornase to alteplase therapy adds an additional mechanism of liquefaction for fluid collection clearance because the dornase breaks down extracellular DNA and reduces fluid viscosity. Since the MIST2 trial, additional studies, mostly retrospective, have examined various modes of administration and dose adjustments for dornase-alteplase use in the pleural cavity. These modifications of therapy include variations such as concomitant instead of sequential administration and reductions in the amount of alteplase give per dose.[1-5]

Although there are volume and physiologic differences between the pleural and peritoneal spaces, both cavities are lined by serous membranes, and the idea that tissue plasminogen activator might assist abscess drainage has existed since at least the early 1990s, with Lahorra et al[6] and Park et al[7] examining urokinase. Since then, and the subsequent market dominance of alteplase in many institutions, there have been a few small studies evaluating alteplase monotherapy for intra-abdominal drain clearance. A retrospective single-center study done in 2008 by Beland et al[8] used 4 to 6 mg of alteplase instilled twice

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daily for drainage of abdominal and pelvic collections that were refractory to simple catheter drainage. Complete drainage was achieved in 89.1% of patients and partial drainage in 6.5% of patients.[8] A prospective single-center study done by Cheng et al[9] used 2 to 4 mg of alteplase instilled twice daily in patients with loculated abdominopelvic abscesses requiring percutaneous catheter drainage. These authors found a higher abscess resolution rate, a decrease in abscess volume, decreased catheter time, and decreased length of hospital stay in the treatment group versus the placebo group.[9] In 2018, Falsarella et al[10] reported a retrospective series of 53 drainage procedures with recombinant tissue plasminogen activator (tPA) injections. The mean dose of tPA was 5.7 mg, and drainage was successful in 96% of patients. In addition to these larger studies, other papers have reported the use of alteplase for clearance of various abdominal pathologies, including hepatic abscess, abdominal fluid collections, and necrotizing pancreatitis. Like the work of Beland et al and Cheng et al, these practitioners generally use doses of ~4 mg of tPA per procedure. [11-15]

Following the commonplace yet off-label use of pleural alteplase and dornase at our institution, a new school of thought has been to use the combination of alteplase and dornase for intra-abdominal fluid collections as well. It is currently unknown whether patients who receive combination alteplase and dornase in this manner have better overall outcomes or drain clearance than those who receive alteplase alone. We report a case series of this therapeutic variant from a tertiary care academic medical center.

Methods

Design

This is a case series reviewing the use of combination alteplase-dornase via the intra-abdominal route. This study was approved by the institutional review board. Data were collected through manual chart review of electronic medical records. All tests ordered, imaging performed, and therapies were done at the discretion of the treating physicians.

Participants and Setting

This is a case series from a tertiary academic medical center. We included adult patients who received combination alteplase-dornase therapy via the intra-abdominal route between April 2018 and July 2022. Thirteen patients who were 18 years of age or older (including 2 patients older than 65 years of age) were identified using medication order identity information and medication route information. All patients included are listed in Table 1.

Interventions

The intervention we examined was any dose of intra-abdominal alteplase and/or dornase charted in the medication administration record. Route of administration was via abdominal drain without exception. Duration and number of administrations were determined by the treating medical or surgical team.

Outcome

The primary outcome examined in our review was any report of increased abdominal drain output, reduction in size of fluid collection per chart notes, or other identifiable outcome related to therapy for the patient. Secondary outcomes included chart note report of major bleeding and concurrent use of prophylactic or therapeutic doses of anticoagulants.

Discussion

To our knowledge, this is the first paper presenting the use of both alteplase and dornase to treat abdominal fluid collections, abdominal hematomas, and low-output abdominal drains. Although many of our patients were subjectively noted to have increased drain output after therapy and went on to eventual resolution of their abdominal fluid collections, determination of "successful" outcomes was hampered by unclear chart documentation of drainage volumes and lack of comparator patients who received alteplase alone. Additionally, almost all patients were highly medically and surgically complicated with multiple surgical procedures and infection-related interventions prior to dornase-alteplase use. More data are needed to establish determinants of efficacy for this therapy, especially as compared with abdominal alteplase. Several of our patients received treatment in preparation for video-assisted retroperitoneal debridement procedures or because further surgical intervention or alteration of drains was difficult or too risky for the patient. These factors leave the potential place in therapy and precise indication for abdominal dornase-alteplase to be determined.

Regarding safety, no anaphylactic, cardiac, or respiratory reactions were seen. Bleeding was our main safety concern during this case series. We had 2 patients receive dornase-alteplase therapy while on active therapeutic anticoagulation. For 1 of these patients, no harm occurred; for the other, life-threatening bleeding resulted. The patient with major bleeding was being treated for complications of necrotizing pancreatitis, a condition that may warrant extra caution for this therapy if fluid collections are not well walled off and the state of the patient's abdominal anatomy is uncertain. Although Gilbert at al[16]

Table 1. Patients receiving alteplase-dornase via the intra-abdominal route.

Drain indication	Indication for therapy	Drain size	Dose administered	Number of doses	Administered concurrently or sequentially	Anticoagulants and/or antiplatelets held (yes/no)	Complications (yes/no)	Results (discharge, death, surgical procedure, etc.)
Pancreatic and psoas walled-off pancreatic necrosis/abscess, VARD preparation	Low-output abdominal drain	14 Fr	10 mg alteplase 5 mg dornase	7 doses	Sequential	No (prophylaxis)	No	Mild decrease in fluid collection, eventual VARD and discharge on antibiotics
Pancreatic abscess after necrotizing pancreatitis and cholecystectomy	Low-output abdominal drain	2 drains of unknown size placed	10 mg alteplase and 5 mg dornase, both in 30-mL volume	7 doses	Sequential	No—patient on therapeutic heparin infusion for DVT	Yes—dark, bloody output from drains Blood pressure dropped to 87/49 Patient received PRBCs, heparin held, active bleed from splenic artery embolized by IR	Increase in drain output, 2 weeks later patient required large-volume abdominal hematoma evacuation
Hepatic abscess	Low-output abdominal drain	14 Fr or 10 Fr, unclear which	10 mg alteplase and 5 mg dornase, in only 10-mL volume for both	2 doses	Concurrent	Yes (prophylaxis)	No, but received blood products/ vitamin K concurrently due to liver synthetic dysfunction	Increase in drain output, discharged on antibiotics
Abdominal fluid collection	Possibly clotted abdominal drain	14 Fr	10 mg alteplase and 5 mg dornase, only 10-mL volume for both	1 dose	Concurrent	Yes	No	Discharged
Right lower quadrant abscess	Low-output abdominal drain	12 Fr	10 mg alteplase and 5 mg dornase	2 doses	Concurrent	No	No	Increase in drain output, discharged on antibiotics
Peritonitis caused by sigmoid perforation	Inability to flush left distal drain	3 drains of unknown size	10 mg alteplase and 5 mg dornase	First course 8 doses, second course 6 doses, third course 5 doses, 3 courses of 6 doses of dornase	Concurrent	No	No	Decrease in fluid collection volume, discharged to rehab on antibiotics

(continued)

Table 1. (continued)

Drain indication	Indication for therapy	Drain size	Dose administered	Number of doses	Administered concurrently or sequentially	Anticoagulants and/or antiplatelets held (yes/no)	Complications (yes/no)	Results (discharge, death, surgical procedure, etc.)
Nondraining abdominal drain	Left hemiabdomenal collection	14 Fr	10 mg alteplase and 5 mg dornase	3 doses each	Concurrent	Yes—due to prior bleed and previous therapeutic anticoagulation	Yes. Bleeding from abdomen-requiring PRBCs	Discharged to SAR
Surgical-site infection	Reduced JP drain output	14 Fr	10 mg alteplase and 5 mg dornase	2 doses each	Concurrent	No	No	Therapy stopped due to drain migration into pleural space
Infected pancreatic pseudocyst	Reduced JP drain output that became thick with debris	14 Fr	10 mg alteplase and 5 mg dornase	6 doses each	Concurrent	Yes	No	Stable fluid collection, drain with output, discharged on antibiotics
Necrotizing pancreatitis	New Blake drain placed—prophylaxis	Unknown	10 mg alteplase and 5 mg dos	2 doses each	Concurrent	No	No	VARD for necrotizing pancreatitis, discharged
For biliary leak and to possibly reduce amount of external drainage	Nondraining abdominal drains	14 Fr (×2)	1 mg alteplase, 10 mg alteplase, and 5 mg dornase	1 dose of alteplase, 1 mg in each drain; 12 doses of alteplase, 10 mg (total between 2 drains); 10 mg dornase, 9 doses of dornase (total between 2 drains)	Sequential	No	No (just complained of abdominal pain)	Drain exchange 4 days after last doses given, back to OR 3 days after drain exchange for abdominal wound debridement, drainage of abscess, and drain placement
Rectus sheath hematoma	To help with hematoma evacuation	14 Fr	10 mg alteplase and 5 mg dornase	5 doses of alteplase, 6 doses of dornase	Sequential	No—continued heparin infusion and warfarin	No	Good drainage, discharged
Infected loculated hemoperitoneum	Nondraining abdominal drain	14 Fr	10 mg alteplase and 5 mg dornase	5 doses	Concurrent	N/A, not on AC	No	Blood draining in JP appropriately, discharged

Fr, French; VARD, video-assisted retroperitoneal debridement; DVT, deep vein thrombosis; PRBCs, packed red blood cells; IR, interventional radiology; SAR, subacute rehabilitation; JP, Jackson-Pratt; OR, operating room; N/A, not applicable; AC, anticoagulation

found no increased bleeding risk with dornase-alteplase administered in patients on anticoagulation with tunneled indwelling pleural catheters and Marston et al[17] found minimal systemic absorption of pleural drug administration, our experience mirrored that of the Akulian et al.[18] Based on our data, our safety preference would be to temporarily stop therapeutic anticoagulation if abdominal dornase-alteplase is required, especially when the existence of damaged or pathologic vasculature in the abdominal cavity cannot be excluded.

Almost all patients in our case series received the same dose of alteplase-dornase, likely because most orders were entered via our institution's pleural order panel reflecting MIST2 dosing. This resulted in our patients receiving double the alteplase dose of most prior abdominal alteplase studies. It is reasonable that successful drainage is possible with a lower dose, and this should be considered in any future studies of this therapy. Reduced alteplase dose may lower bleeding risk for this treatment and result in reduced cost per dose to the institution. Dose finding also would be useful for variations in indications of abdominal dornase-alteplase; some of our patients required simple drain declotting or declogging, while for other patients the medications were used as an abscess or full abdominal lavage. Some patients, particularly those with hepatic abscesses, received a more highly concentrated dose of dornase-alteplase due to condensed volume (10 mL vs standard volume of 30 mL) of the same milligram dose due to abscess cavity space limitations. Our patients received a mix of sequential and concurrent dosing patterns of the 2 drugs. Additionally, there are no existing stability data for dornase dilutions beyond a single preclinical study by McGuire et al.[19] Our institution requires immediate use of diluted dornase due to its lack of stability and requires provider administration due to institutional nursing policy. Lack of stability data causes logistical complications for both this treatment and intrapleural use of the same medications at our institution and would be a valuable area of future research.

Our case series demonstrates a new and unique use of combined dornase-alteplase therapy for drainage of abdominal fluid collections and is meant to contribute guidance for an unusual medication use. Intra-abdominal dornase-alteplase use was rare at our institution (13 patients in 4 years at a medical center that performs about fifty thousand procedures annually). Our patient population was mostly surgical but otherwise heterogeneous, and likewise, precise indication of use was heterogeneous. Place in therapy, methods to improve the safety of this medication combination, most appropriate dose, and stability data for pharmacy logistics are all items that remain to be determined in future studies.

Declaration of Conflicting Interests

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References

1. Rahman NM, Maskell NA, West A, et al. Intrapleural use of tissue plasminogen activator and DNase in pleural infection. *N Engl J Med*. 2011;365:518-526. doi:10.1056/NEJMoa1012740.
2. Majid A, Kheir F, Folch A, et al. Concurrent intra-pleural instillation of tissue plasminogen activator and DNase for pleural infection:. a single-center experience. *Ann Am Thorac Soc*. 2016;13(9):1512-1518. doi:10.1513/AnnalsATS.201602-127OC.
3. Kheir F, Cheng G, Rivera E, et al. Concurrent versus sequential intrapleural instillation of tissue plasminogen activator and deoxyribonuclease for pleural infection. *J Bronchology Interv Pulmonol*. 2018;25(2):125-131. doi:10.1097/LBR.0000000000000461.
4. Popowicz N, Ip H, Lau E, et al. Alteplase Dose Assessment for Pleural infection Therapy (ADAPT) Study-2: use of 2.5 mg alteplase as a starting intrapleural dose. *Respirology*. 2022;27(7):510-516. doi:10.1111/resp.14261.
5. Popowicz N, Bintcliffe O, De Fonseka D, et al. Dose de-escalation of intrapleural tissue plasminogen activator therapy for pleural infection. The Alteplase Dose Assessment for Pleural Infection Therapy Project. *Ann Am Thorac Soc*. 2017;14(6):929-936. doi:10.1513/AnnalsATS.201609-673OC.
6. Lahorra JM, Haaga JR, Stellato T, Flanigan T, Graham R. Safety of intracavitary urokinase with percutaneous abscess drainage. *AJR Am J Roentgenol*. 1993;160(1):171-174. doi:10.2214/ajr.160.1.8416619.
7. Park JK, Kraus FC, Haaga JR. Fluid flow during percutaneous drainage procedures: an in vitro study of the effects of fluid viscosity, catheter size, and adjunctive urokinase. *AJR Am J Roentgenol*. 1993;160(1):165-169. doi:10.2214/ajr.160.1.8416618.
8. Beland MD, Gervais DA, Levis DA, Hahn PF, Arellano RS, Mueller PR. Complex abdominal and pelvic abscesses: efficacy of adjunctive tissue-type plasminogen activator for drainage. *Radiology*. 2008;247(2):567-573. doi:10.1148/radiol.2472070761.
9. Cheng D, Nagata KT, Yoon HC. Randomized prospective comparison of alteplase versus saline solution for percutaneous treatment of loculated abdominopelvic abscess. *J Vasc Interv Radiol*. 2008;19(6):906-911.

10. Falsarella PM, Rocha RD, Rahal A Jr, Mendes GF, Garcia RG. Minimally invasive treatment of complex collections: safety and efficacy of recombinant tissue plasminogen activator as an adjuvant to percutaneous drainage. *Radiol Bras*. 2018;51(4):231-235. doi:10.1590/0100-3984.2017.0086.
11. Zee-Cheng J, Fox T, Patel S, Abu-Sultaneh S. Successful use of tissue plasminogen activator in an adolescent male with pyogenic liver abscess. *Case Rep Crit Care*. 2019;2019:5735312. doi:10.1155/2019/5735312.
12. Bhargava V, Gupta R, Vaswani P, et al. Streptokinase irrigation through a percutaneous catheter helps decrease the need for necrosectomy and reduces mortality in necrotizing pancreatitis as part of a step-up approach. *Surgery*. 2021; 170(5):1532-1537. doi:10.1016/j.surg.2021.05.028.
13. Bansal A, Gupta P, Singh AK, et al. Drainage of pancreatic fluid collections in acute pancreatitis: a comprehensive overview. *World J Clin Cases*. 2022;10(20):6769-6783. doi:10.12998/wjcc.v10.i20.6769.
14. Mirrakhimov AE, Boivin M. Use of the recombinant tissue plasminogen activator in the management of complex infected intraperitoneal fluid collection. *Case Rep Infect Dis*. 2019;2019:8943837. doi:10.1155/2019/8943837.
15. Shenoy-Bhangle AS, Gervais DA. Use of fibrinolytics in abdominal and pleural collections. *Semin Intervent Radiol*. 2012;29(4):264-269. doi:10.1055/s-0032-1330060.
16. Gilbert CR, Wilshire CL, Chang SC, Gorden JA. The use of intrapleural thrombolytic or fibrinolytic therapy, or both, via indwelling tunneled pleural catheters with or without concurrent anticoagulation use. *Chest*. 2021;160(2):776-783. doi:10.1016/j.chest.2021.03.023.
17. Marston TW, Rajdev K, Samson KK, Hershberger DM. Understanding the systemic effects of intrapleural tPA and DNase by evaluating effects on coagulation. *J Thorac Dis*. 2024;16(1):91-98. doi:10.21037/jtd-23-847.
18. Akulian J, Bedawi EO, Abbas H, et al; Interventional Pulmonary Outcomes Group. Bleeding risk with combination intrapleural fibrinolytic and enzyme therapy in pleural infection: an international, multicenter, retrospective cohort study. *Chest*. 2022;162(6):1384-1392. doi:10.1016/j.chest.2022.06.008.
19. McGuire AL, Bennett SC, Lansley SM, et al. Preclinical assessment of adjunctive tPA and DNase for peritoneal dialysis associated peritonitis. *PLoS One*. 2015;10(3):e0119238. doi:10.1371/journal.pone.0119238.