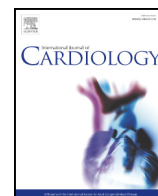




Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Short communication

A systematic review of the efficacy and safety of intrapericardial fibrinolysis in patients with pericardial effusion

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ARTICLE INFO

Article history:

Received 19 September 2017

Accepted 13 October 2017

Available online xxxx

Keywords:

Intrapericardial fibrinolysis

Pericardial effusion

Pericarditis

ABSTRACT

Pericardial effusion is the abnormal accumulation of fluid in the pericardial space. The complications of pericardial effusion can either be acute (e.g., cardiac tamponade) or chronic (e.g., constrictive pericarditis). We have conducted a systematic review of the scientific literature to evaluate the efficacy and safety of intrapericardial fibrinolysis in preventing complications of pericardial effusion.

We searched for both published and unpublished studies. 29 studies, with a total of 109 patients were included in this review; 17 case reports, 11 case series, and one randomised controlled trial (RCT). All included studies had a high risk of bias. The most common causes of pericardial effusion were *Staphylococcus aureus* (12 studies with 23 cases) and *Mycobacterium tuberculosis* (2 studies with 19 cases). The most common fibrinolytic agents used were streptokinase (15 studies) and urokinase (5 studies). Intrapericardial fibrinolysis prevented complications in 94 (86.2%) patients. Non-fatal procedure-related complications were reported 21 (19.2%) patients. No patient died following intrapericardial fibrinolysis.

There is very low certainty of the efficiency and safety of intrapericardial fibrinolysis in preventing the complications of pericardial effusion. High quality RCTs are required to address this question.

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1. Introduction

Pericardial effusion is the abnormal accumulation of fluid in the pericardial space due to either a known or an unknown (idiopathic) cause [1]. Causes of pericardial effusion include infection, cancer, connective tissue disease, pericardial injury, metabolic derangement, myopericardial disease, and aortic disease [2]. The complications of pericardial effusion are persistent effusion, cardiac tamponade, recurrence of effusion, constrictive pericarditis, and death [3,4]. Studies reporting the management of pericardial effusion using non-steroidal anti-inflammatory drugs (NSAIDs) in association with colchicine, corticosteroids [5], azathioprine, cyclophosphamide and anakinra have produced variable results [4]. Re-accumulation rates tend to be high following pericardiocentesis which is currently the treatment of

choice [6]. Over the past 20 years, intrapericardial fibrinolysis has been increasingly used in patients with effusive pericarditis, with promising results [3]. Our objective was to determine the efficacy and safety of this intervention when used to prevent or treat complications in patients with pericardial effusion.

This systematic review was registered in PROSPERO (CRD42014015238) and the protocol published [7]. We searched for all primary studies that met our eligibility criteria, irrespective of the language of publication. Studies carried out on people of all ages and both sexes, with pericardial effusion due to any cause, were included. Fibrinolytic agents administered intrapericardially alone or in combination with any other intervention were compared to placebo, no intervention or any other intervention to prevent complications of pericardial effusion.

The primary outcomes were cardiac tamponade, persistent or recurrent pericardial effusion, and constrictive pericarditis. Other outcomes included procedure related complications (incidence of haemorrhage, procedure-related cardiac tamponade, allergic reactions, and adverse events), long-term complications, and death.

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Table 1
Table of general study characteristics.

Study ID	Country	Study design	Number of patents	Population		Preceding/associated Pathologies	Aetiology	Modality of diagnosis	Complications of pericardial effusion present prior to intervention
				Age	Sex				
Dybowska 2015	Poland	CR	1	63 yrs	M	Purulent inflammation of the right knee	Unknown. Cultures and <i>Mycobacterium tuberculosis</i> tests were negative	Echocardiography	None before streptokinase and Pericardial Constriction prior to tPA
Ideh 2014	The Gambia	CR	1	9 yrs	M	Treated for pneumonia, malaria	<i>Staphylococcus aureus</i>	Echocardiography	Recurrence
Lee 2014	Taiwan	CR	1	60 yrs	M	Abscesses over the right chest wall and prostate, hyperglycemia	<i>Staphylococcus aureus</i>	Echocardiography	None reported
Abamukov 2010	Russia	CS	100 (Only 7 got the intervention)	15–82 yrs	92 M & 8F	Trauma (79 stab thoracic and 29 blunt thoracic trauma)	Unclear	Echocardiography	None reported
Bigham 2008	USA	CR	1	4 m	F	Glycogen storage disease type IB	<i>Staphylococcus aureus</i>	Echocardiography	Recurrence
Johnson 2007	USA	CR	1	79 yrs	F	Mesothelioma	mesothelioma	Echocardiography	Recurrence
Cui 2005	China	RCT	94 (47 got the intervention)	9 yr to 66 yrs	23 M & 24 F	Not stated	18 due to <i>Mycobacterium tuberculosis</i> and 29 purulent pericarditis	Echocardiography	Tamponade (11) & pericardial calcifications [8]
Ekim 2004	Turkey	CS	9	3 yrs to 13 yrs	5 M & 4 F	Bronchopulmonary infections in 8 and septic arthritis in 1 patient	<i>Staphylococcus aureus</i> in 2 patients and negative bacteriologic cultures in 7 patients	Echocardiography	Tamponade in 4 patients
Tomkowski 2004	Poland	CS	3	40 yrs to 64 yrs	1 M & 2 F	Peri-tonsillar abscess in patient 1, prolonged use of corticosteroids in patient 2, Pneumonia in patient 3.	Patient 1: <i>Streptococcus species</i> . Culture was negative for patient 2. <i>Streptococcus intermedius</i> , <i>Enterococcus faecalis</i> for patient 3	Echocardiography	None
Reznikoff 2003	USA	CR	1	61 yrs	M	Periorbital abscess	<i>Staphylococcus aureus</i>	Echocardiography	None
Tomkowski 2003	Poland	CR	1	50 yrs	M	Purulent tonsillitis	<i>Streptococcus species</i>	Echocardiography	None
Zimmerman 2003	Germany	CR	1	23 yrs	M	Hodgin's disease and C-protein deficiency	Unknown	Echocardiography	None
Kamimura 2002	Japan	CR	1	41 yrs	male	Unsterilized deep skin fistula	<i>Mycobacterium tuberculosis</i> . Secondary bacterial pericarditis with α - <i>Streptococcus</i>	Chest computed tomography	None
Keersmakers 2002	Belgium	CR	1	36 yrs	M	Unknown	<i>Streptococcus viridans</i>	Transthoracic and Transoesophageal Echocardiography	None
Ustonsoy 2002	Turkey	CS	9	5 yr to 50 yrs	5 M & 4 F	7 had extra cardiac infections, 1 had heart surgery for ASD, & one had DM	<i>Staphylococcus aureus</i> in 8 patients and 1 unknown	Echocardiography	1 patient had Tamponade
Omer 2002	Turkey	CS	3	10 m, 18 m & 4 yrs	1 M & 2 F	Respiratory infections in 2 out of 3	<i>Staphylococcus aureus</i> in 1 patient and unknown in rest.	Echocardiography	None
Schafer 2002	Switzerland	CR	1	39 yrs	M	Acute bronchitis	Unknown (sterile cultures)	Echocardiography	Recurrence
Bridgman 2001	New Zealand	CR	1	61 yrs	F	Unclear	<i>Staphylococcus aureus</i>	Echocardiography	Recurrence
Svendsen 2001	Norway	CS ^a	1	67 yrs	F	Osteomyelitis	<i>Streptococcus pneumoniae</i>	Echocardiography	None
Juneja 1999	India	CS	6	8 m to 12 yrs	Unknown	extra cardiac infections in 2 (arthritis, osteomyelitis and parietal abscesses)	4 patients had <i>Staphylococcus aureus</i> infection	Echocardiogram	None
Defouillois 1997	France	CS	2	16 yrs and 38 yrs	M	Oesophageal squamous carcinoma for patient 1 and flulike symptoms for patient 2	Unknown	Echocardiography	Constrictive pericarditis for patient 1 and cardiac tamponade for patient 2
Maynar 1997	Spain	CR	1	78 yrs	F	Not stated	<i>Streptococcus pneumoniae</i>	Transthoracic Echocardiography	Cardiac tamponade
Mann-Segal 1996	Australia	CR	1	76 yrs	M	lingular harmatoma	<i>Staphylococcus aureus</i>	Echocardiography	Cardiac tamponade
Winkler 1994	Austria	CS	3	21, 38 & 54 yrs	M	Patient 1: Mediastinitis and septic shock, patient 2: cirrhosis,	Patient 1: <i>Bacteroides species</i>) and Patient 2: <i>Staphylococcus</i>	Echocardiography	None

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