Cardiovascular Revascularization Medicine 16 (2015) 484–490

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Intra-arterial vasodilators to prevent radial artery spasm: a systematic review and pooled analysis of clinical studies

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ARTICLE INFO

Article history:
Received 19 June 2015
Received in revised form 6 August 2015
Accepted 13 August 2015

Keywords:
Vasodilator
Radial artery catheterization
Radial artery spasm

ABSTRACT

Objectives: The aim of this study is to review the available literature on the efficacy and safety of agents used for prevention of RAS.
Background: Different vasodilator agents have been used to prevent radial artery spasm (RAS) in patients undergoing transradial cardiac catheterization.
Methods: We included studies that evaluated any intra-arterial drug administered in the setting cardiac catheterization that was undertaken through the transradial access site (TRA). We also compared studies for secondary outcomes of major bleeding, procedure time, and procedure failure rate in setting of RAS prevention, patent hemostasis and radial artery occlusion.
Results: 22 clinical studies met the inclusion criteria. For placebo, RAS rate was 12% (4 studies, 638 participants), which was similar to 2.5 mg of verapamil 12% (3 studies, 768 participants) but greater than 5 mg of verapamil (4%, 2 studies, 497 participants). For nicorandil, there was a much higher RAS rate compared to placebo (16%, 3 studies, 447 participants). The lowest rates of RAS was found for nitroglycerin at both 100 μg (4%) and 200 μg (2%) doses, isosorbide mononitrate (4%) and nicardipine (3%). We found no information regarding the procedure failure rates, patent hemostasis, and radial artery occlusion in these studies.
Conclusions: In this largest and up-to-date review on intra-arterial vasodilators use to reduce RAS, we have found that the verapamil at a dose of 5 mg or verapamil in combination with nitroglycerine are the best combinations to reduce RAS.

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1. Introduction

The radial artery is fast becoming the preferred access site for performing coronary angiography and percutaneous coronary intervention (PCI) [1]. In UK, adoption of the transradial access site (TRA) for PCI has increased from 10% in 2006 to over 60% in 2012 [2]. TRA is associated with reduced mortality and major adverse cardiac events (MACE) in selected cohorts at high risk of bleeding complications [2–4], thought to be related to a reduction in major access site related bleeding complications [1,5]. Transradial access is also associated with improved patient comfort and has also shown to be the preferred access site amongst patients undergoing PCI and be more cost effective than transfemoral access [6–8].

However, TRA approach is not without limitations, it is associated with a longer learning curve and complex procedures requiring large French size guide catheters may not always be possible particularly in patients with small diameter radial arteries. Furthermore operators may encounter radial artery spasm (RAS) [9] during TRA particularly at the beginning of the learning curve, or when encountering radial anomalies. A previous review of 19 papers with 7197 participants found that the incidence of RAS was 14.7% in patients in whom the radial artery was chosen as the access site for coronary angiography or PCI [10].

RAS leads to patient discomfort, increased risk of vascular complications and procedure failure rate. Various drugs such as nitroglycerin, verapamil, isosorbide mononitrate are used to reduced the risk of RAS. However, there is high variability in practice amongst operators for administration of these drugs. Furthermore, there are no guidelines or recommendations for using such drugs in day-to-day practice. Therefore, we conducted a systematic review of the available literature to evaluate the efficacy of agents used for prevention of RAS.

2. Methods

We searched MEDLINE and EMBASE on October 2014 using the broad search terms: “vasodilator” AND “radial artery occlusion” OR “radial

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http://dx.doi.org/10.1016/j.carrev.2015.08.008
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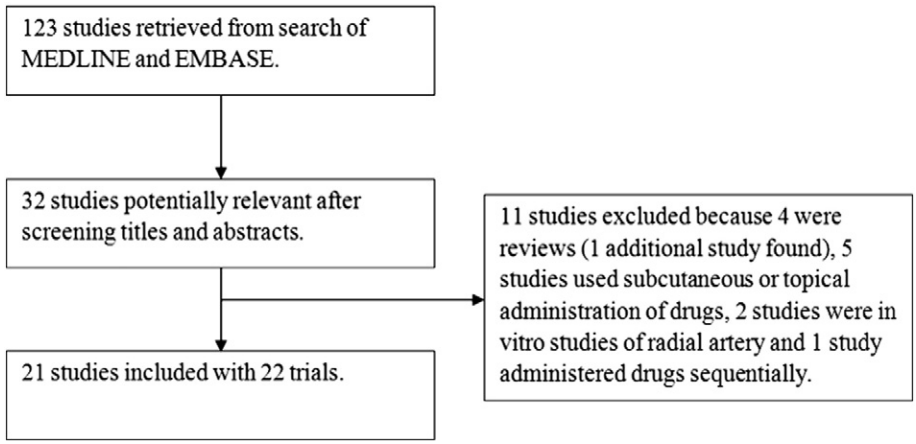

Fig. 1. Flow diagram of study selection.

artery spasm" OR "transradial." The search results were reviewed by two independent judicators (CSK, MR) for studies that met the inclusion criteria and relevant reviews. The bibliographies of included studies and relevant reviewers were screened for additional studies.

We included studies that evaluated any intra-arterial drug administered in the setting of TRA. The inclusion criteria were

1. Studies had to compare more than one agent or include a control group. There was no restriction based on sample size.
2. The studies had to evaluate some form of measure related to RAS such as incidence of RAS, change in diameter of radial artery and any adverse events associate with intra-arterial drug administration.

We excluded studies that administered drugs that were not intra-arterial and in-vitro studies.

Data was extracted from each study into preformatted spreadsheets. The data collected was on the year, country, number of participants, age of participants, % of male participants, participant inclusion criteria, and type of treatments, efficacy outcomes and safety outcomes. These results were narratively synthesized and trials with similar treatment arms were pooled using methods previous described [11].

We also compared studies for secondary outcomes of procedure time, and procedure failure rate in setting of RAS prevention and radial artery occlusion.

3. Results

Our search yielded 123 relevant articles and after screening and reviewing full manuscripts, 21 articles met the inclusion criteria with 22 clinical studies [12–32]. The process of study selection is shown in Fig. 1.

The study design and participant characteristics of the included trials is shown in Table 1. Majority of studies (n = 14) used blinding and these studies took place between 1997 and 2007 in different centers around the world. There were a total of 8777 participants (range of participants in each study 30 to 1950) with an average age of 61 years and 70% were male participants. All studies took place in the setting of transradial access (TRA).

Table 2 shows the different treatments that have been used as intra-arterial vasodilators and results from the studies. Many agents were evaluated including verapamil, magnesium sulphate, nitroglycerin, nicorandil, diltiazem, isorobide mononitrate, petolamine, isosorbide

Table 1
Study design and participant characteristics of studies which evaluated intra-arterial vasodilators.

Study ID	Design	Year	Country	No. of participants	Mean age	% male	Participants
Abe 2000 [12]	RCT	1997	Japan	100	64	64	Transradial catheterization.
Boyer 2013 [13]	Blinded RCT	NR	USA	121	61	65	Transradial catheterization.
Byrne 2008 [14]	Double blind RCT	2007	Researchers from Canada and UK.	86	NR	NR	Transradial catheterization.
Carrilo 2011 [15]	Double blind RCT	NR	Spain	30	63	77	Transradial catheterization.
Chen 2006 [16]	Blinded RCT	2002–2003	Taiwan	361	64	68	Transradial catheterization.
Cho 2008 [17]	RCT	2007	Korea	142	64	74	Transradial catheterization.
Coppola 2006 [18]	Double blind RCT	NR	NR	379	57	83	Transradial catheterization.
Dalal 2011 [19]	Single blind trial	NR	India	200	NR	NR	Transradial catheterization.
Dharma 2012 [20]	Double blind RCT	NR	Indonesia	150	58	72	Transradial catheterization.
Hizoh 2014 [21]	Double blind RCT	NR	Hungary	591	62	64	Transradial catheterization.
Kiemeneij 2003 [22]	Non-randomized, non-blinded trial	NR	Netherlands	100	64	75	Transradial catheterization.
Kim 2007 [23]	Double blind RCT	2005	Korea	150	60	53	Transradial catheterization.
Manickam 2011 [24]	Non-randomized, non-blinded trial	NR	India	600	NR	NR	Transradial catheterization.
Mont'AlverneFino 2003 [25]	Double blind RCT	2000–2001	Brazil	51	56	74	Transradial catheterization.
Rosencher 2012 [26]	Double blind RCT	NR	France	332	NR	NR	Transradial catheterization.
Rosencher 2013 SPASM 3 [27]	RCT	NR	France	731	NR	NR	Transradial catheterization.
Ruiz-Salmeron 2005 [28]	Double blind RCT	2003–2004	Spain	500	63	76	Transradial catheterization.
Sakai 1999 [29]	Non-randomized, non-blinded trial	NR	Japan	186	NR	NR	Transradial catheterization.
Varenne 2006 SPASM 1 [30]	Double blind RCT	2003	France	1219	60	75	Transradial catheterization.
Varenne 2006 SPASM 2 [30]	Double blind RCT	2004–2005	France	618	62	70	Transradial catheterization.
Varenne 2014 [31]	RCT	NR	France	1950	NR	NR	Transradial catheterization.
Xiaolong 2012 [32]	RCT	NR	China	180	NR	54	Transradial catheterization.

RCT = randomized controlled trial, NR = not reported.

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