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[Intervention Review]

Totally implantable vascular access devices for cystic fibrosis

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ABSTRACT

Background

Totally implantable vascular access devices are widely used in people with cystic fibrosis to provide intermittent venous access for therapeutic infusions. Their use is associated with some complications such as thrombosis, embolism and infection.

Objectives

To assess if totally implantable venous access devices provide a safe and effective route for venous access for intermittent administration of intravenous antibiotics in people with cystic fibrosis. Also to assess strategies to reduce possible complications of totally implantable venous access devices (e.g. anticoagulants to reduce the risk of thrombosis).

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Trials Register which comprises references identified from comprehensive electronic database searches, handsearches of relevant journals and abstract books of conference proceedings.

Date of the most recent search: 05 April 2012.

Selection criteria

Randomised and quasi-randomised controlled trials which compared the use of totally implantable venous access devices in people with cystic fibrosis to other means of vascular access, trials which compared the different types of these devices against each other and trials which assessed strategies to reduce complications of these devices.

Data collection and analysis

No relevant trials were identified.

Main results

No trials were included in this review.

Authors' conclusions

Totally implantable vascular access devices are widely used in people with cystic fibrosis to provide intermittent venous access for therapeutic infusions. Reports of their use in people with cystic fibrosis suggest that they are safe and effective. These reports also suggest that certain interventions might reduce the risk of complications; however, it is disappointing that these reports have not been assessed by randomised controlled trials. This systematic review identifies the need for a multicentre randomised controlled trial assessing both efficacy and possible adverse effects of totally implantable venous access devices in cystic fibrosis.

PLAIN LANGUAGE SUMMARY

A tube fitted inside a vein to allow drug injections for people with cystic fibrosis

Cystic fibrosis blocks the lungs with mucus and causes frequent infections and lung damage. Infections are often treated by giving drugs intravenously (through a vein), but regular injections can damage veins. Another option is to use a totally implantable vascular access device (TIVAD). There are different types of device and people with cystic fibrosis or their families can be shown how to administer drugs through them. TIVADs have no external portion attached when not in use and long-term maintenance is quite easy. Some people feel that the devices improve their self-image while others do not like the way they look. Sometimes TIVADs cause blood clots and infections. We looked for randomised and quasi-randomised controlled trials of these devices in people with cystic fibrosis. The review found no trials to include. Reports of the use of TIVADs in people with cystic fibrosis suggest that they are safe and effective. They also suggest that certain interventions might reduce the risk of complications; however, these issues have not been examined by randomised controlled trials. We think a multicentre randomised controlled trial is needed to assess the efficacy and possible adverse effects of TIVADs in cystic fibrosis.

BACKGROUND

Description of the condition

Cystic fibrosis (CF) is the most common genetic disorder in Caucasians (Connor 1997). People with CF usually become colonised with bacteria such as *Pseudomonas aeruginosa* and often suffer exacerbation of their chest disease requiring frequent, regular courses of intravenous antibiotics. Over time, people with CF often lose peripheral venous access and require an indwelling central venous catheter for the rest of their lives. Totally implantable vascular access devices (TIVAD) have emerged as an effective means for intermittent venous access for therapeutic infusions.

Description of the intervention

TIVAD consist of a subcutaneously placed reservoir attached to a silastic catheter placed in a central vein (Morris 1990). Different kinds of devices exist. The commonest device used in people with CF is the Port-a-cath® system. This consists of a silicone catheter attached to a stainless steel portal with a self-sealing silicone septum (Ball 1989). The chamber is accessed with a Huber needle, which has a specially designed tip to avoid damaging the silicone septum. Other types of TIVAD such as peripheral access systems (PAS), bared access systems (such as Groshongs, Hickman lines and Broviacs) are also used. People with CF or their carers can be trained, under appropriate instructions from CF specialist nurses, to use the system for administering antibiotics in the home.

How the intervention might work

TIVAD have many advantages when compared to external indwelling catheters: there is no external portion attached when the device is not in use so physical activity is not limited; long-term maintenance is relatively easy and is done by flushing with heparinized saline once every four to six weeks (Morris 1990). People with CF have different attitudes towards the cosmetic appearance of these devices and the subsequent effect of these on their self-image. Some people feel that the devices improve their self-image while others perceive them as cosmetically unsatisfactory (Rodgers 1998).

Why it is important to do this review

There has been research looking into whether these devices are effective in improving clinical outcomes in people with CF and this suggests that they may be an effective and safe way of administering intravenous antibiotics (Aitken 2000; Ball 1989; Burdon 1998; Morris 1990; Rodgers 1998; Yung 1996). A number of complications have been associated with the use of these devices including thrombosis, embolism, infection, pneumothorax and air embolism. A retrospective analysis of 452 TIVAD in 36 CF centres showed a complication rate of 42% which was mainly due to occlusion (Munck 2004). This study identified the use of polyurethane (versus silicone) and the routine use of devices for blood sampling as significant risk factors for causing complications leading to removal of the device (Munck 2004). It is unclear if there are other factors associated with a higher risk of complications; or if there are any interventions which may reduce the incidence of complications and prolong the survival of these devices.

OBJECTIVES

The aim of this review is to assess if TIVAD are a safe and effective route for providing venous access for intermittent administration of antibiotics in people with CF. The review will also assess strategies to reduce possible complications of TIVAD (e.g. anticoagulants to reduce the risk of thrombosis).

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) and quasi-randomised controlled trials.

Types of participants

Participants with CF of any age and severity, diagnosed clinically by sweat testing or genetic analysis.

Types of interventions

We planned to investigate the use of TIVAD compared to other means of vascular access such as peripheral long lines, cannulae or other types of central lines. We planned to include trials comparing different types of TIVAD to each other and trials assessing strategies to reduce the complications of TIVAD.

Types of outcome measures

Primary outcomes

1. Duration of survival of TIVAD
2. Assessment of complications associated with TIVAD (such as thrombosis, embolism, infection, pneumothorax, air embolism and mechanical problems)

Secondary outcomes

1. Access of health resources
 - a. Number and duration of hospitalisations
 - b. Frequency of out-patient visits
2. Participant preference
 - a. Quality of life (QOL) (as measured by stated QOL assessment tool)
 - b. Satisfaction with the cosmetic appearance of the device

Search methods for identification of studies

Electronic searches

Relevant trials were searched for in the Group's Cystic Fibrosis Trials Register using the terms: intravenous access device AND implantable.

The Cystic Fibrosis Trials Register is compiled from electronic searches of the Cochrane Central Register of Controlled Trials (Clinical Trials) (updated each new issue of *The Cochrane Library*), quarterly searches of MEDLINE, a search of EMBASE to 1995 and the prospective handsearching of two journals - *Pediatric Pulmonology* and the *Journal of Cystic Fibrosis*. Unpublished work is identified by searching through the abstract books of three major cystic fibrosis conferences: the International Cystic Fibrosis Conference; the European Cystic Fibrosis Conference and the North American Cystic Fibrosis Conference. For full details of all searching activities

for the register, please see the relevant sections of the [Cystic Fibrosis and Genetic Disorders Group Module](#).

A search of EMBASE from 1995 to March 2006 has been completed.

Date of the most recent search of the Group's Cystic Fibrosis Trials Register: 05 April 2012.

Data collection and analysis

The authors did not apply the process described below since no trials were identified. However, if trials are identified in future updates of this review, the authors will apply the following methods.

Selection of studies

Two authors will identify and independently review relevant trials, in order to select the trials for inclusion in the review. The authors will resolve any disagreement by discussion and by involving a third party if needed.

Data extraction and management

Each author will independently extract data using standard data acquisition forms. The authors will resolve any disagreement by discussion and by involving a third party if needed.

We will compare outcomes at one, three, six and twelve months or other relevant time points identified.

Assessment of risk of bias in included studies

The authors will assess the methodological quality of each trial using criteria described by Jüni ([Jüni 2001](#)). They will use their findings to estimate a potential risk of bias for each trial. In particular, authors will examine details of the randomisation method, whether the trial was blinded and who was blinded. Assessment of blinded trial quality will be made according to generation of allocation schedule; measures taken to conceal treatment allocation; measures taken to implement double blinding; whether intention-to-treat analyses were possible from the available data; and if the number of participants lost to follow up or subsequently excluded from the trial was recorded. If we judge these criteria to have been adequately addressed, we will attribute a low risk of bias to them; if these are not adequately addressed, they will be recorded as having a high risk of bias. If these criteria are not discussed, the risk of bias will be judged as unclear.

Measures of treatment effect

For binary outcome measures, we aim to calculate a pooled estimate of the treatment effect for each outcome across trials using the odds ratio, (the odds of an outcome among treatment allocated participants to the corresponding odds among controls).

For continuous outcomes, we plan to record either mean change from baseline for each group or mean post-treatment/intervention values and standard deviation for each group. Then, where appropriate, we will calculate a pooled estimate of treatment effect by calculating the mean difference.

Dealing with missing data

In order to allow an intention-to-treat analysis, we will seek data on the number of participants with each outcome event by allocated

treatment group, irrespective of compliance and whether or not the participant was later thought to be ineligible or otherwise excluded from the treatment or follow up.

The review authors will request any missing data from the primary authors if appropriate.

Assessment of heterogeneity

Heterogeneity between trial results will be tested for using a standard chi-squared test.

Data synthesis

We plan to use a fixed-effect model in our analysis. If any significant heterogeneity is detected, we plan to reassess the significance of the treatment effect by using a random-effects model.

Sensitivity analysis

We plan to perform a sensitivity analysis based on the methodological quality of the trials, including and excluding quasi-randomised trials.

RESULTS

Description of studies

No trials were found that were eligible for inclusion in the review.

Risk of bias in included studies

No trials were found that were eligible for inclusion in the review.

Effects of interventions

No trials were found that were eligible for inclusion in the review.

DISCUSSION

It is disappointing that despite the wide use of TIVAD in people with CF, there are no RCTs to rigorously evaluate their use in this group of people. These devices, though very effective in providing long-term venous access, have potential for causing serious complications such as thrombosis, embolism, occlusion and infection. It would be valuable to assess the use of TIVAD in comparison with other means of delivering intravenous therapy in people with CF. A recent study by Munck concluded that TIVAD are relatively safe and reliable for providing long-term venous access; they identified catheter material and blood sampling as some of the risk factors leading to removal of these devices ([Munck 2004](#)). They also concluded that the insertion site significantly influenced incidence of vascular thrombosis ([Munck 2004](#)). As we believe this subject is important, we think that a multicentred RCT looking at these devices to explore the optimal management of such devices and the possible use of anti-platelet drugs and heparin to reduce the risks of vascular complications will provide useful information for both clinicians and people with CF. Such a trial will also allow people with CF to make informed decisions when they consider having these devices implanted.

A wide range of trials has been performed regarding the use of these devices in people with cancer. Although this might provide useful information, it is difficult to generalise these trials to people with CF since there are significant differences between the groups.

AUTHORS' CONCLUSIONS

Implications for practice

No conclusions can be made about the use of TIVAD in people with CF from the information currently available. Clinicians must balance potential benefit against the possible risk of complications in each case.

Implications for research

This systematic review has identified the need for a well-designed, adequately-powered, multicentre, RCT to assess the efficacy and safety of the use of TIVAD in people with CF compared to other means of vascular access, to compare the different types of these devices with each other and to assess strategies to reduce any complications of TIVAD.

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WHAT'S NEW

Date	Event	Description
23 April 2012	Review declared as stable	This review will no longer be regularly updated. Searches will still be undertaken on a two-yearly basis by the Cochrane Cystic Fibrosis & Genetic Disorders Group. If, in future, relevant trials are identified, the review will be updated again.

HISTORY

Protocol first published: Issue 1, 2003

Review first published: Issue 3, 2003

Date	Event	Description
10 April 2012	New citation required but conclusions have not changed	No trials have been added to this review, so the conclusions remain unchanged.
10 April 2012	New search has been performed	A search of the Group's Cystic Fibrosis Trials Register did not identify any new references potentially eligible for inclusion in this review.

Date	Event	Description
7 July 2010	New search has been performed	A search of the Cystic Fibrosis Trials Register did not identify any references which were potentially eligible for inclusion in this review.
12 August 2009	Amended	Contact details updated.
1 July 2008	New search has been performed	A search of the Group's Cystic Fibrosis Trials Register did not identify any new references which were potentially eligible for inclusion in the review.
10 April 2008	Amended	Converted to new review format.
21 May 2007	New search has been performed	A search of the Group's Cystic Fibrosis Trials Register identified no additional trials eligible for inclusion in this review.
26 April 2006	New search has been performed	A search of the Group's Cystic Fibrosis Trials Register identified no additional trials eligible for inclusion in this review.
17 May 2005	New search has been performed	A search of the Group's Cystic Fibrosis Trials Register identified no additional trials eligible for inclusion in this review.
23 April 2004	New search has been performed	A search of the Group's trials register identified no additional trials eligible for inclusion in this review.

CONTRIBUTIONS OF AUTHORS

Dr Amel A-Rahman wrote the initial drafts of the protocol and the review with advice and comments from Dr Spencer. Dr Amel A-Rahman is responsible for the update of the review.

Dr A-Rahman acts as guarantor of the review.

DECLARATIONS OF INTEREST

None known.

INDEX TERMS

Medical Subject Headings (MeSH)

Catheters, Indwelling [*adverse effects]; Cystic Fibrosis [*therapy]

MeSH check words

Humans