Do the Y-set and double-bag systems reduce the incidence of CAPD peritonitis?

A systematic review of randomized controlled trials

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Abstract

Background. Peritonitis is the most frequent serious complication of continuous ambulatory peritoneal dialysis (CAPD). It has a major influence on the number of patients switching from CAPD to haemodialysis and has probably restricted the wider acceptance and uptake of CAPD as an alternative mode of dialysis. This systematic review sought to determine if modifications of the transfer set (Y-set or double-bag systems) used in CAPD exchanges are associated with a reduction in peritonitis and an improvement in other relevant outcomes.

Methods. Based on a comprehensive search strategy, we undertook a systematic review of randomized or quasi-randomized controlled trials comparing double-bag and/or Y-set CAPD exchange systems with standard systems, or comparing double-bag with Y-set systems, in patients with end-stage renal disease (ESRD) treated with CAPD. Only published data were used. Data were abstracted by a single investigator onto a standard form and subsequently entered into Review Manager 4.0.4. Its statistical package, Metaview 3.1, calculated an odds ratio (OR) for dichotomous data and a (weighted) mean difference for continuous data with 95% confidence intervals.

Results. Twelve eligible trials with a total of 991 randomized patients were identified. In trials comparing either the Y-set or double-bag systems with the standard systems, significantly fewer patients (133/363 vs 158/263; OR 0.33, 95% CI 0.24–0.46) experienced peritonitis and the number of patient-months on CAPD per episode of peritonitis was greater. When the double-bag systems were compared with the Y-set systems significantly fewer patients experienced peritonitis (44/154 vs 66/138; OR 0.44, 95% CI 0.27–0.71) and the number of patient-months on CAPD per episode of peritonitis was also greater.

Conclusions. Double-bag systems should be the preferred exchange systems in CAPD.

Keywords: CAPD; double bag; peritonitis; randomized controlled trials; systematic review; Y-set

Introduction

Continuous ambulatory peritoneal dialysis (CAPD) has been an alternative to haemodialysis for patients with end-stage renal disease (ESRD) since 1976 [1]. It may be the first-choice dialysis therapy and in a number of countries, including the United Kingdom, a significant proportion of the ESRD population are treated by this modality in preference to chronic haemodialysis [2]. Peritonitis is the most common serious complication of peritoneal dialysis and is the leading cause of technique failure requiring a switch to haemodialysis [3]. Undertaking a peritoneal dialysis exchange is one of the key points during CAPD when micro-organisms can be inadvertently transferred via the lumen of the peritoneal catheter into the peritoneal space (intraluminal route), causing peritonitis. The CAPD transfer system used may therefore have an important bearing on both the incidence of peritonitis and CAPD technique failure.

There are three main types of catheter connecting systems. In the standard or straight connecting system the catheter is connected to the dialysate solution bag using a straight piece of tubing and a ‘spike’ or a luer lock device. At each exchange a new connection is made and the bag is drained. The empty bag is rolled up and remains attached until the next exchange when the process is repeated. The second type of transfer system is the Y-set in which the patient disconnects.
from the bags between exchanges (disconnect system). When a new exchange is due a Y-connection with one limb connected to an empty bag and one to a bag containing fresh dialysate is used [4–6]. During an exchange the peritoneal dialysate is first drained from the peritoneal cavity into the empty bag. Before introducing the fresh dialysis solution into the peritoneal cavity the Y-connecting system is first flushed with fresh dialysis solution and drained into the drainage bag. This allows any bacteria to be flushed into the spent fluid. The fresh fluid is then introduced into the peritoneal cavity and the Y-connector is disconnected from the CAPD catheter. The early Y-set technique, in addition, flushed the system with a disinfectant, a hypochlorite, during each exchange [7]. The third system, the double-bag (twin-bag) system, was a further development of the Y-set disconnect systems. With this system the connection with the fresh dialysis solution bag is already made and the patient has to perform one less connection procedure [8–10]. It has been suggested that use of the Y-set transfer or double-bag systems will lead to a reduced frequency of CAPD peritonitis [7] and some [11,12] but not all [13] observational studies have indicated an association between use of the standard connect system and a significantly increased risk of peritonitis. At present a considerable proportion of CAPD patients, including those in the UK, continue to use the standard system [14,15].

Other techniques such as the ultraviolet germicidal system [16,17], in-line bacteriological filters [17,18], and heat sterilization [17,19] have been developed and used in an attempt to reduce peritonitis rates; they were not considered as part of this review.

We undertook a systematic review of rigorous trials to determine if Y-set (and modifications) and double-bag systems are associated with an improvement in CAPD peritonitis and other relevant outcomes.

**Subjects and methods**

**Identification of trials**

We attempted to identify all eligible trials which compared (i) double-bag (experimental group) and/or Y-set (experimental group) compared to all this review

Data abstraction

Data on predetermined outcome measures were abstracted from included studies using a standard form, by a single assessor and were entered onto Review Manager 4.0.4 software. All data were independently checked from the original papers by a second person. Only published data were used: no raw data were sought. The outcome measures were: (i) number of patients experiencing peritonitis and its frequency (primary outcome), (ii) number of patients experiencing exit-site infections and their frequency, (iii) number of patients in whom CAPD catheters were removed, (iv) number of patients switching to haemodialysis, (v) number of patients hospitalized and average number of days of hospitalization, (vi) measures of quality of life and patient preference, (vii) mortality.

**Data analysis**

Quantitative data were analysed, where appropriate, using the meta-analysis package of Review Manager 4.0.4, Metaview 3.1, to calculate a Peto’s odds ratio for dichotomous variables and a weighted mean difference for continuous variables, with 95% confidence intervals. The methods are discussed in detail in Campbell et al. [20].

**Results**

We identified twelve RCTs comparing double-bag, Y-set, and standard transfer systems with a total of 991 randomized patients (Table 1). One study [32] compared all three system types, seven compared only Y-set with standard systems [21–30], one compared only double-bag with standard systems [31] and three compared only double-bag with Y-set systems [33–35]. Some of the trials’ reports did not include data relevant to all this review’s outcomes or reported these data in a manner that precluded inclusion in the meta-analyses (e.g. standard deviations or exact P-values were omitted). As a consequence, some of the meta-analyses include fewer studies and fewer patients than might be expected. The publication of the studies were fairly evenly spread over a 16-year period from 1983 (Maiorca et al. [21,22]) to 1999 (Li et al. [35]). Details of the methodological quality of the included RCTs are outlined in Table 1. The method of randomization should ensure that treatment allocation remains unknown until a patient is irrevocably recruited to a study. Only four studies described the method of randomisation. One [32] described a probably secure method of random allocation (central list of random numbers with order of allocation sent to participating centres in sealed envelopes). Two did not completely
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describe their method of random allocation: Churchill [26,27] (used ‘a variable blocking factor, by the coordinating centre’ no other details given), Maiorca et al. [21,22] (‘closed envelope system’, no other details given). Cheng et al. [29] described an insecure method of random allocation (random number tables but ‘investigators were not blind to treatment previously recruited patients received’ and next treatment could be anticipated). All 12 had parallel designs. Only two [25,29] failed to describe withdrawals and dropouts. None of the study reports clearly stated that data were analysed on an intention-to-treat basis, although for only four [21,22,32,34,35] was it clear that analysis was not on an intention-to-treat basis. Blinding or masking was infrequently described and none of the studies stated specifically that patients, healthcare providers, or outcome assessors were masked/blinded.

### Peritonitis

Significantly fewer patients (133/363 vs 158/263) experienced peritonitis when using either the Y-set or double-bag systems compared with the standard systems (OR 0.33, 95% CI 0.24–0.46) (Figure 1). Analyses limited to trials comparing double-bag systems with standard and then Y-set systems vs standard were consistent with this, significantly favouring the newer methods. When the two newer methods were compared, significantly fewer patients using the double-bag system experienced peritonitis (44/154 vs 66/138; OR 0.44, 95% CI 0.27–0.71) (Figure 1). Data describing the number of patient-months on CAPD per episode of peritonitis were consistent with this (Table 2). All trials comparing either Y-set or double-bag to standard systems favoured the newer systems, and all trials comparing double-bag with Y-set systems [32–35] consistently reported greater numbers of months per episode of peritonitis with the double-bag systems.

### Exit-site infections

Three studies reported the number of patients who experienced exit-site infections [26,27,28,31] (Figure 2). The meta-analyses found no significant differences when both the Y-set and double-bag systems were compared with the standard systems (overall, 39/131 vs 40/133; OR 0.99, 95% CI 0.57–1.72). None of the studies comparing the double-bag with the Y-set systems reported the number of patients experiencing exit-site infections. Apart from Kiernan [33], who favoured the double-bag system, none of the four RCTs reporting the number of months per episode of exit-site infection showed any difference (Table 3).

### Additional secondary outcomes

There was no convincing evidence from meta-analyses of any consistent differences between the systems in...
Fig. 1. Number of patients suffering peritonitis comparing double bag, Y-set and standard transfer systems in CAPD: meta-analyses of RCTs.

relation to technique failure, need for CAPD catheter removal, hospitalization, quality of life, or reported mortality (data not shown).

Discussion

This review generated clear evidence of benefit in terms of a reduction in the number of patients experiencing peritonitis when Y-set or double-bag systems were compared with standard systems (OR 0.33, 95% CI 0.24–0.46). Although the numbers were smaller and the confidence intervals wider, there was also additional benefit from the use of the double-bag systems in comparison with the Y-set systems (OR 0.44, 95% CI 0.27–0.71). The included RCTs also consistently reported greater numbers of patient-months on CAPD per episode of peritonitis when comparing either Y-set
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Comparison: 01 Y-set systems vs standard systems

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Churchill 1989</td>
<td>22 / 161</td>
<td>23 / 163</td>
<td></td>
<td>65.7</td>
<td>0.98 [0.47, 2.03]</td>
</tr>
<tr>
<td>Owen 1992</td>
<td>14 / 30</td>
<td>13 / 30</td>
<td></td>
<td>34.3</td>
<td>1.14 [0.42, 3.13]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>36 / 161</td>
<td>36 / 163</td>
<td></td>
<td>100.0</td>
<td>1.03 [0.57, 1.87]</td>
</tr>
</tbody>
</table>

Chi-square 0.30 (df=1): P = 0.97, z = 0.11, P = 0.9

Comparison: 02 Double bag systems vs standard systems

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dryden 1992</td>
<td>3 / 40</td>
<td>4 / 40</td>
<td></td>
<td>100.0</td>
<td>0.73 [0.16, 3.43]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>3 / 40</td>
<td>4 / 40</td>
<td></td>
<td>100.0</td>
<td>0.73 [0.16, 3.43]</td>
</tr>
</tbody>
</table>

Chi-square 0.00 (df=0): P = 1.00, z = 0.39, P = 0.7

Comparison: 03 Y-set or double bag systems vs standard systems

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Churchill 1989</td>
<td>22 / 161</td>
<td>23 / 163</td>
<td></td>
<td>57.3</td>
<td>0.98 [0.47, 2.03]</td>
</tr>
<tr>
<td>Dryden 1992</td>
<td>3 / 40</td>
<td>4 / 40</td>
<td></td>
<td>12.8</td>
<td>0.73 [0.16, 3.43]</td>
</tr>
<tr>
<td>Owen 1992</td>
<td>14 / 30</td>
<td>13 / 30</td>
<td></td>
<td>25.9</td>
<td>1.14 [0.42, 3.13]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>39 / 131</td>
<td>40 / 133</td>
<td></td>
<td>100.0</td>
<td>0.98 [0.57, 1.72]</td>
</tr>
</tbody>
</table>

Chi-square 0.22 (df=2): P = 0.97, z = 0.04, P = 1

Fig. 2. Number of patients suffering exit-site infections comparing double bag, Y-set and standard transfer systems in CAPD: a meta-analyses of RCTs.

Table 2. Number of patient-months on CAPD per episode of peritonitis reported in individual RCTs

<table>
<thead>
<tr>
<th>Study and Year</th>
<th>Double-bag systems</th>
<th>Y-set systems</th>
<th>Standard systems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheng et al. 1994 [29]</td>
<td>30.8</td>
<td>21.5</td>
<td></td>
</tr>
<tr>
<td>Li et al. 1996 [30]</td>
<td>17.0</td>
<td>11.4</td>
<td></td>
</tr>
<tr>
<td>Lindholm et al. 1988 [25]</td>
<td>22.0</td>
<td>8.0</td>
<td></td>
</tr>
<tr>
<td>Maiorca et al. 1983 [21,22]</td>
<td>33.0</td>
<td>11.3</td>
<td></td>
</tr>
<tr>
<td>Owen et al. 1992 [28]</td>
<td>13.4</td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td>Rottenbourg et al. 1987 [23,24]</td>
<td>23</td>
<td>12.3</td>
<td></td>
</tr>
<tr>
<td>Monetteon et al. 1998 [32]</td>
<td>24.8</td>
<td>11.8</td>
<td>6.1</td>
</tr>
<tr>
<td>Harris et al. 1996 [34]</td>
<td>46.4</td>
<td>14.0</td>
<td></td>
</tr>
<tr>
<td>Kiernan et al. 1995 [33]</td>
<td>33.9</td>
<td>11.7</td>
<td></td>
</tr>
<tr>
<td>Li et al. 1999 [35]</td>
<td>33.5</td>
<td>29.4</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Number of patient-months on CAPD per episode of exit-site infection reported in individual RCTs

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<th>Y-set systems</th>
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<td>Li 1999 [35]</td>
<td>17.4</td>
<td>16.0</td>
<td></td>
</tr>
</tbody>
</table>

or double-bag with standard systems, and additional benefit from the double-bag systems when compared with the Y-set systems (Table 2). No benefit was demonstrated in terms of a reduction in exit-site infections with either the Y-set or double-bag systems. The proposed mechanisms for peritonitis reduction with Y-set and double-bag systems (decrease in intraluminal bacterial contamination because of decreased number of connections/disconnections and flush before fill procedure) would be consistent with this failure to reduce exit-site infections.

This review considered the data from all RCTs that have compared Y-set, double-bag and standard systems. It was difficult to assess the quality of the 12 RCTs identified. The descriptions of the method of random allocation, of whether data were analysed on an intention-to-treat basis and of whether patients, healthcare providers, and outcome assessors were masked were often incomplete (Table 1). A clear description of trial methodology, such as through wider use of the CONSORT statement guidelines [36], would greatly assist validity assessment and exploration of heterogeneity between studies.

The review was facilitated by the primary outcome, peritonitis, being consistently reported and similarly
defined throughout all the included studies. In contrast, relatively few of the included RCTs reported data relevant to other outcomes. The review was unable to determine clearly if the Y-set and double-bag systems were beneficial or harmful in terms of the number of CAPD catheters removed, technique failure, or hospitalization. Similarly, while the available quality of life data appear to support the use of double-bag in preference to Y-set systems [27,28] the data are limited. This review found no differences in mortality when the three systems were compared.

The interventions within each group were not identical. For example, in the early Y-set studies, sodium hypochlorite disinfectant was left in components of the Y-system between exchanges [4–7]. It was initially assumed that the use of disinfectant contributed significantly to the reduction in peritonitis rates. However, subsequent trials showed equal benefit using the Y-modification without disinfectant and the use of disinfectant was later associated with chemical peritonitis and the development of sclerosing peritonitis, and hence the practice was discontinued. Assessing a number of different modifications in a single standard RCT risks failing to identify which change(s) contributed to any beneficial or adverse effects.

Peritonitis was the primary outcome of this review. There is clear evidence that use of either the Y-set or the double-bag systems compared with the standard systems is associated with a statistically and clinically significant reduction of peritonitis. There is also evidence that the double-bag system is superior to the Y-set system in this respect.

Implications for practice

From the purely clinical perspective, the standard systems (spike or luer lock) should no longer be used because of the clearly increased risk of peritonitis. The additional benefit the double-bag has over the Y-set systems suggests that where resources permit, the double-bag CAPD exchange systems should be used routinely in clinical practice. Policy-makers need to decide whether the necessary resources can be made available to allow this routine adoption of the double-bag system.

Implications for research

Peritonitis is the most frequent serious complication of CAPD. It is essential that innovations in CAPD technique or technology designed to reduce peritonitis rates are subject to rigorous assessment by well-designed RCTs. The double-bag system should be the standard against which future design modifications in CAPD transfer technology are compared. It should also be the routine best practice treatment when trials concerning any aspect of CAPD are being undertaken. If more than one intervention is being considered, clinical trials should be designed to identify clearly to which intervention any beneficial or adverse effects can be attributed. There is likely to be no additional research benefit in further trials comparing double-bag, Y-set, and standard CAPD exchange systems. A health economic evaluation of the use of double-bag or Y-set compared with standard systems needs to be undertaken. This should allow health care purchasers to decide if the additional benefits of double-bag and Y-set systems are worth any potential extra cost.

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