Y Connectors In CAPD Patients: Do Subtle Important Modifications Have Potential Role In Reducing Contamination And Rate Of Infective Peritonitis?

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Abstract: Continuous Ambulatory Peritoneal Dialysis (CAPD) involves transfer of dialysate into and out of peritoneal cavity several times a day with the help of a permanent catheter and connection system. Connection and disconnections during the exchange lead to entry of various organisms into peritoneal cavity and therefore intraluminal infections account for approximately one-third to one-half of all episodes of peritonitis. It is essential that innovations in technology of peritoneal dialysis delivery system should aim at protecting critical areas of the connectors from accidental contamination and incorporating effective bacterial flushing techniques. Thus the design of the connectors and Y-junction is extremely critical in influencing efficiency of any delivery system. Y junction plays a critical role in fluid flow path, especially in terms of convective bacterial removal. Central junction of symmetric Y set can induce nonlinear turbulent flow and obstruct the flushing process leading to fibrin blockage. Hence, a variation of Y system, known as asymmetric Y set, was developed with an idea to reduce contamination and rate of peritonitis. Asymmetric Y set essentially has straight transparent line to drain the bag combined with short distance between the Y set and patient line. Various single center and small multicentric studies using twin bag with asymmetric Y and advanced connectors have shown significant improvement in peritonitis rates. Further, it is essential to assess these innovations by large well-designed RCTs for their usefulness, cost advantage and impact on quality of life.

Keywords: CAPD, asymmetric Y set, CAPD connection system, peritonitis, Y junction

Introduction:
Continuous Ambulatory Peritoneal Dialysis (CAPD) has been an important modality of treatment for end stage renal disease (ESRD) since the last three and half decades. It offers advantages of hemodynamic stability, steady-state chemistries, lower cost, and improved quality of life with convenience of home therapy, a flexible schedule, and increased freedom. But peritonitis still remains a major complication of CAPD. Hospitalization rates for peritonitis range from 13.5% to 23% of admissions among peritoneal dialysis (PD) patients. It is an important reason for patient dropout, morbidity, and mortality as well. It is also the leading cause of transfer to hemodialysis. Various possible factors which may be implicated for peritonitis with CAPD are compromised host defenses, improper training programme management and dialysis system development including fluids and connectology.

CAPD involves transfer of dialysate into and out of peritoneal cavity several times a day with the help of a permanent catheter and connection system. The possible routes for transfer of organism into peritoneal cavity can be intraluminal (through the catheter), periluminal (around the peritoneal catheter), transmural (visceral perforation or migration of bacteria across the bowel wall), hematogenous and other endogenous infections such as the retrograde vaginal route. Out of these, intraluminal infections account for approximately one-third to one-half of all episodes of peritonitis. Adequate hand hygiene measures prior to bag exchange procedure have major impact on touch contamination levels. Miller et al., in 1997 studied the numbers of micro-organisms entering the dialysis bag during a touch-contamination event in patients undergoing CAPD, so as to identify the level of bacterial contamination associated with touch contact of a connector set. Ten subjects from each of the PD and control groups rolled the artificial spikes lightly between their fingertips for 5 seconds to simulate a touch-contamination event. Approximately 500 or fewer
micro-organisms were transferred to the connector device, if it is accidentally touched by unwashed hands (Unprepared hands). Furthermore, if the hands are wet at the time of contact, the number of translocating organisms were as high as 4500. Thus the process of connection and disconnections during the exchange can be an important cause of intraluminal contamination. This facilitates various organisms to enter into peritoneal cavity leading to peritonitis. In order to minimize this risk, improvements of PD delivery systems have aimed at both protecting critical areas of the connectors from accidental contamination and incorporating effective bacterial flushing techniques to remove existing intraluminal contamination. Advancement in this field include double-bag, Y disconnect systems and advanced connector systems. The design of the connectors and Y-junction are both extremely critical to the effective performance of any delivery system in these respects.

Minimizing exposure of dialysate flow pathway to touch contamination and mechanisms to eradicate contamination before initiating the infusion of dialysate may reduce the incidence of peritonitis. The reduction in the peritonitis rate itself is sufficient to justify the use of the new systems because repeated infections reduce the capacity of peritoneum for dialysis in future. This article reviews specific developments in design of exchange systems for CAPD, highlights importance of asymmetric Y design connector set and its potential role in reducing risk of contamination and peritonitis.

Evolution and Development of CAPD exchange systems: Trends in connectology

Basic components of CAPD exchange systems include bag containing dialysate, tubing from bag to connector assembly and specialized connectors required to connect these to each other and to patients PD catheter and drain bag. This can be a united with all components together or separate components need to be assembled during exchange procedure.

After initial discovery of ambulatory PD by Popovich, first important technological innovation on PD exchange system was replacement of glass bottles by collapsible plastic bags. In this straight connecting system, the dialysate solution bag and peritoneal catheter was connected using a straight piece of tubing and a “spike” or a luer lock device. The empty bag after infusing dialysate was rolled up, which remain attached until the next exchange. Hence, in this system the patient had to continuously carry all the plastic elements on his/her body, and was called as wearable system (Fig 1).

Figure 1: The Wearable Straight Connecting System with Rolled up Bag

Symmetric Y connector set

Initially developed Y-set consisted of three tubes (Fig 1). The short limb of Y set was connected to the titanium adapter of the peritoneal catheter by means of a ‘Luer-lock’. One limb of Y-set was connected to an empty bag and other to a bag containing fresh dialysate (Fig 2). During each bag exchange
procedure the spent dialysate was drained into the empty bag. Y tubing was then flushed with a small volume of fresh dialysate, followed by introduction of fresh dialysate solution into peritoneal cavity.

A number of variants of Y-set were then introduced into the clinical practice. The most widely used were the long Y set (Y set with long limbs), and the O-set (named from the shape it takes when two free limbs are connected to each other during the dwell phase). In both systems the patient can disconnect from the bags between exchanges i.e disconnect systems. In the early years of development Y or O set was filled with disinfectant during the dwell time and reused in the next exchange.13

However, this had an inherent risk of accidental introduction of the disinfectant agent into the peritoneum. To further reduce the incidence of intraluminal contamination, various alternative approaches such as in-line bacterial filters, UV light or heat had been tried at the points of connection. Efforts were also made to improve the ergonomics and ease of use of the equipment.

**Symmetric Y sets with integrated disconnect system**

In the earlier systems, minimum two connections were needed, one between the Y set and the fresh dialysate container, the other between the Y set and the peritoneal catheter or the catheter extension line. To reduce one connection between the Y set and the fresh dialysate and to avoid touch contamination, the concept of integrated disconnect system (IDS) was introduced. IDS consisted of a twin bag, one prefilled with dialysate and other empty for collection of drainage fluid from peritoneal cavity with help of a Y set. Sterility of the IDS “dry side” (drainage line and bag) was maintained solely by the steam sterilization process without need of ethylene oxide or other agents like gamma radiation. Also there was no need of any disinfectant fluid for the drainage bag and line to ensure their sterility.

**Importance of drain-flush-fill sequence for the bag exchange procedure**

A drain-flush-fill sequence for the bag exchange procedure is based on identification of a backflow phenomenon taking place during the first seconds of the drainage phase. This backflow is a secondary flow starting at the Y junction of the set and going up the line to the fresh solution container. The concept utilizes the simple principle of physically removing organisms convectively with the flow of dialysis solution. During an exchange process 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 empty 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. Flushing from the fresh solution container to the drainage container helps to eliminate any contamination.

**Nonlinear, turbulent flow dynamics with symmetric Y sets**

Integral to the effective removal of bacteria by “convective flushing” or “draining of fluid” is the design of the fluid flow path. The most critical aspect of the fluid flow path, in terms of convective bacterial removal will be the Y junction. One frequently encountered problem with Y set is fibrin blockage of drained bag. This is due to the design of central junction of Y set which can induce nonlinear turbulent flow and can obstruct the flushing procedure.1415 This can also increase the probability of spillage and stasis at the end junction point of Y set. The degree of turbulence and the number of entrapment areas present in any given design will likely reduce the efficiency of drain-flush-fill sequence concept and bacterial removal. However, straight path to drain bag may decrease chances of fibrin blockage. So a variation of Y system, known as asymmetric Y set, was developed with an idea to reduce contamination and rate of peritonitis.

**Asymmetric Y Set Disconnect System with Twinbag**

This system is an IDS with modifications of standard Y-set. It consists of a double bag (twin bag) having a specific geometry of Y junction i.e a shape of asymmetric Y (Fig 3). Asymmetric Y set essentially has straight transparent line to drain the bag combined with short distance between the Y set and patient line. Straight drainage path facilitates the faster outflow and less chances of fibrin blockage. Asymmetry at central junction ensures continuous strong linear flow without any turbulence and convective removal of bacteria by flushing of dialysis solution. Absence of entrapment site and no recirculation or back-flow further decreases the chances of bacterial contamination. Transparent line also allow for visual inspection of the effluent. Patient convenience is increased further by including color-coded frangible seals to differentiate and separate inlet and outlet fluid paths.

Another critical design principle which avoids the possible exposure of fluid flow path to touch contamination is
improvement in the connectology of the asymmetric Y disconnect system\textsuperscript{16}. The male luer is recessed within the connector shroud, making touch contamination virtually impossible and a female counterpart on the patient connector side is such that when the male and female connectors are mated, the surfaces of both connectors are outside the fluid path (Fig 4). In this system even if patient accidentally touch any of these connectors, the design keep that contaminated area outside the fluid path. Thus it is also plausible to assume that the shorter distance between the Y set and patient side, superior flushing technique along with advanced connectology may play an important role in reducing the chance of infection and incidence of peritonitis. The “Y set” in twin bag system of Baxter has asymmetric configuration, which causes flow of contamination directly to the drain instead of recirculation and possibly flowing back to the patient\textsuperscript{13}.

In another type of double-bag system, Stay-Safe (SS; Fresenius Medical Care), two bags are connected to tubing catheters by means of a special switch disc device, which controls and regulates all three phases of exchange: outflow, flush, and inflow. The Y-tubing connection is built into the control disc that consists of a PIN system; turning the knob in the control disc from position 1 to 4 will complete the CAPD exchange cycle. In the Stay-Safe System, the tip of the male luer extends to very near the connector shroud and can be easily touched. In addition, the male luer becomes part of the fluid path when the male and female connectors are mated. Therefore, if the tip of the male luer is contaminated during the connection process, it is possible for bacteria to be introduced into the fluid path and therefore into the peritoneum. The tip of the female connector by design is excluded from the fluid path and is unlikely to contribute to contamination\textsuperscript{16}.

**Impact of PD exchange system modifications on peritonitis rate.**

Buoncristiani et al., of Perugia, Italy introduced the Y or the Perugia system in 1980, which prominently reduced peritonitis rates, but it took a long time to satisfy rest of the world regarding efficacy of this simple modification of the original technique. Now, all nephrologists agree with the functioning each new bag exchange and the concept of “flush before fill” was recognized as the the key to the success of the Y – system\textsuperscript{17}. With the advent of Twinbag systems with asymmetric Y, the focus is shifting to the convective efficiency of the patient drain to remove organisms from the patient transfer set connector to the drain bag than the earlier used flush before fill method to remove contamination\textsuperscript{18}.

In a systematic review of 12 RCTs\textsuperscript{19}, the use of the symmetric Y-set compared to standard spike systems was associated with a significantly lower risk of peritonitis (7 trials, 485 patients): RR 0.64, 95% CI 0.53 to 0.77) and peritonitis rate (8 trials, 7417 patient-months): RR 0.49, 95% CI 0.40 to 0.61). Similarly, a single center study on 240 subjects showed that, after beginning use of Y disconnect systems in the year 1988, peritonitis rates decreased from 1 episode per 5 to 12 pt-months in initial years, to 1 episode per 68 pt months after 10 years of usage\textsuperscript{20}. In a two year prospective randomized trial comparing symmetric Y connection versus conventional technique of spike systems in prevention of peritonitis episodes, new patients (n=27) with Y connection had 1 episode every 23 patient-months as compared
to 12.2 patient-months (p<0.02) in those on the conventional system (n=28)\textsuperscript{21}.

**Y set with disinfectant - Peritonitis rates**  
In a prospective controlled trial performed in two centers on 62 new CAPD patients, the peritonitis rate of patients using Y set with disinfectant was one episode every 33 patient-months (11 episodes; 10 patients; 363 months) compared to one episode every 11.3 patient-months (31 episodes; 17 patients; 351 months) in those using the standard method\textsuperscript{22}. Many Italian groups have demonstrated that use of same Y system or comparable systems is associated with a very low incidence of peritonitis. Maiorca et al.,\textsuperscript{21} studied a rate of one episode every 50 patient-months, furthermore exclusion of diabetics resulted in decrease in peritonitis rate with patient experiencing one episode every 155 patient-months. Another study by Cantaluppi et al.,\textsuperscript{24} revealed that incidence of peritonitis rate decreased from one episode every 52.5 patient-months to one episode every 76 patient-months, when the diabetics were excluded. Similar findings have also been reported by Bazzato\textsuperscript{25}.

**Y set without disinfectant and effectiveness of flush-before-fill**  
In a study four disconnect systems were used without disinfectant. 58 new patients including 19 insulin dependent diabetic patients (33%) were randomized. The peritonitis incidence was statistically reduced in this prospective study comparing disconnectable systems and conventional systems with 1/23 patient-months compared to 1/12.2 patient-months (p<0.02). The patients with high incidence of peritonitis had 1 peritonitis episode per 10 patient-months before and 1 peritonitis episode per 24 patient-months after their transfer to the y connection (p < 0.001). Conventional CAPD patients (n=43) had one peritonitis episode per 11.7 patient-months\textsuperscript{21}.  
An in vitro study by Verger and Luzar explained that a 100 ml flush with dilysate is effective in sterilizing lines contaminated with common microorganisms responsible for touch contamination related infections with low adhesiveness such as *S. epidermidis*\textsuperscript{26}. However, the flush is only partially effective when *S. aureus* and *Pseudomonas species* were present. In another prospective controlled study, Verger et al compared the efficacy of CAPD Y-lines without disinfectant and standard CAPD systems with and without disinfectant\textsuperscript{27}. It was concluded that Y-set CAPD systems are significantly more effective than standard CAPD in preventing peritonitis, even when an antiseptic is used with the latter. Enhancing efficacy of the flush-before-fill technique will require larger volumes being used at the flushing time. Thus it would be necessary to increase the initial volume of the bag to avoid a decrease in the inflow volume.

**Twin bag system with asymmetric Y set vs. other PD exchange systems: Peritonitis rates**  
Although a number of devices are available currently, but, among them, use of twin-bag disconnect systems appear to be associated with the lowest rates of infection. Similar result was observed by Kiernan and colleagues, in a recent prospective randomized clinical trial in 82 patients, authors reported significantly lower rates of peritonitis with a twin-bag (Ultra Twin; Baxter Healthcare, Round Lake, IL) versus a single-bag (Ultra Y-set; Baxter Healthcare, Round Lake, IL) system\textsuperscript{28,29,30,31,32,33}. Similarly out of 680 incident CAPD patients from 14 centers in the CANUSA study\textsuperscript{34}, 37 used a twin-bag system and 279 used standard Y-set; the 1-yr peritonitis-free rate was 79% with a twin-bag system and 66% with the standard Y-set.

The recent systematic review of 12 randomized controlled trial by Daly C et al found a significant reduction in the risk of peritonitis on comparison of combined analysis of standard Y-set or double bag systems with asymmetric Y set and standard systems (8 trials, 626 patients): RR 0.58, 95% CI 0.49 to 0.68) and peritonitis rate (11 trials, 10082 patient-months): RR 0.55, 95% CI 0.42 to 0.32. Authors also observed that though use of twin bag systems with asymmetric Y set was associated with fewer episodes of peritonitis when compared to standard Y-systems, but there was no statistically significant advantage (P =0.05). In a previous systematic review by the same author, a significantly lower risk of experiencing peritonitis episodes with double bag systems with asymmetric y set compared with standard Y-systems (odds ratio 0.44, 95% CI 0.27 to 0.71) was reported\textsuperscript{19}.

In another prospective controlled trial\textsuperscript{35}, 147 patients commencing CAPD were randomly assigned to one of three groups: the conventional (n=29), standard the Y-set (n=57), and the twin bag systems with asymmetric Y set (n=61). They were followed up for an average of 11.3 months. The maximum average peritonitis-free interval was seen in twin bag (24.8 months (P < 0.001)) followed by the Y system (12.0 months) and then conventional group (6.1 months). Multivariate analysis further revealed CAPD system to be only factor associated with peritonitis. Peritonitis-related hospitalization
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was seen most in conventional system (5.3±2.0 days/patient/year) when compared to Y system (2.7±1.0 days/patient/year) and twin bag system (1.5±0.9 days/patient/year). There was a 50% reduction in peritonitis incidence with the Y-set and a 75% reduction with the twin-bag configuration as compared with standard-bag systems.

The effect of asymmetric Y system on peritonitis incidence and patient morbidity was also evaluated in a comparative, retrospective single-center analysis over a period of 5 years. Introduction of IDS with asymmetric Y led to improvement in the peritonitis-free period from 1:11 patient-months (conventional system), to greater than 1:50 patient-months (asymmetric -Y system). The rate of hospitalization was also decreased by 45%.

Another single-center randomized study performed in 63 adult patients compared the efficiency and total cost of Freeline Solo (FS, twin-bag) and Basic V (BY, single-bag) systems. After a total follow-up of 631 patient months, cumulative incidence of peritonitis was 1 per 14.0 patient months with BY and 1 per 46.5 patient months with FS (odds ratio, 3.6; 95% CI 1.5 to 8.5; P = 0.004).

Similarly, 15 CAPD patients were studied using two different types of exchange systems: a snap-disconnect Y-set system and the Baxter UltraBag system with asymmetric Y set. The incidence of peritonitis in patients using snap-disconnect Y-system was found to be 32 cases in 187 months, or a rate of 1 case of peritonitis episode every 5.8 months. Switching these patients to the Baxter UltraBag system, resulted in highly significant decrease in incidence of peritonitis to 4 cases in 175 months, or 1 case every 43.8 months. In another study the peritonitis rate for the standard "Y" set (Freeline 1 and 2 T.M., Baxter UK) and "twin-bag" with asymmetric Y set (Freeline Solo T.M., Baxter UK) systems were compared over a period of one year. Peritonitis rates were 1/21.2 pt months and 1/31.8 pt months with freeline and Solo system respectively. Similar peritonitis rates were observed in comparison of the UltraBag (UB) with asymmetric Y set from Baxter Healthcare (Deerfield, IL) and double-bag system, Stay-Safe system (SS; Fresenius Medical Care, Deutschland GmbH).

A multicenter (6 centers), open-label, parallel-group, randomized trial was conducted over a period of 12 months (April 2002 to May 2003) with 270 new or existing CAPD patients using a single-bag system, 212 patients (ANDY-Disc 102, UltraBag 110) completed the trial. The overall peritonitis rate for all centers combined was 22.9 patient-months/episode for ANDY-Disc and 35.0 patient-months/episode for UltraBag (P=0.033). The risk of peritonitis was 53% greater for ANDY-Disc compared to UltraBag.

Asymmetric Y system with twin bag: Cost-effectiveness & Quality of life

Use of all the disconnectable systems is associated with the increased cost of the supplies. But, it is of little matter of concern when compared to benefits of the Y set: decrease in peritonitis, less hospitalization, decrease in protein losses, no additive cost of antibiotics, etc. Monton et al 1998 found the cost per bag as similar for the conventional and Y system, but higher for the twin bag. However, the total costs of treatment (pesos/patient/year) were lower for twin bag (62,159 for the conventional, 70,275 for the Y system, and 54,387 for the twin bag), due to the lower peritonitis incidence, decreased usage of antibiotics and fewer hospitalizations. Thus the reduction in the peritonitis rate itself is sufficient to justify the use of the new systems on economic grounds.

Better connectology and subtle important modifications in Y connector systems may also lead to better quality of life. Only two studies comparing double bag with a standard Y-set system reported quality of life data. Harris 1996, using a Lickert scale, reported significantly greater “ease of use” and Li 1996, using a 6-item questionnaire, reported significantly greater “patient acceptability” with the double bag system. However, these instruments of assessment still need to be validated in this particular setting.

Implications for clinical practice & future research

Continuous quality initiatives in CAPD exchange systems can significantly reduce peritonitis rates, thereby reducing cost and need for hospitalization, improving ability to maintain patients on PD, and enhancing patients' quality of life. The studies show a significant benefit of using twin bag systems with asymmetric Y set. However, measures like aggressive patient training and periodic retraining every six months, using equipment from a single reliable PD manufacturer for all patients and other organized initiatives towards preventing infections can add to peritonitis reduction considerably.

Though many single centre and multicentric studies have shown the benefit of using twin bag with asymmetric Y and advanced connectors, for CAPD, it is essential that innovations in technology designed to reduce peritonitis rates should...
be assessed by well-designed RCTs. The double bag with asymmetric Y set should be further tested in large scale trials in India to assess the significance of reducing peritonitis rates in terms of cost advantage and quality of life. Trials should be designed in a way to clearly identify the beneficial intervention or adverse effects amongst the various advances in CAPD exchange systems. This may help in guiding the PD therapy and further improving patient outcomes.

References


