Research Article

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Improving Peritoneal Dialysis Effluent Sample Collection Techniques to Lower Culture-Negative Peritonitis Rate: A Single-Center Experience

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ABSTRACT

Background : Peritonitis remains the most feared complication of End Stage Renal Disease (ESRD) patients on peritoneal dialysis (PD), but cultures are often negative. Our study was aimed to determine if improving the collection techniques of peritoneal fluid would reduce the rates of Culture Negative Peritonitis (CNP) as recommended in the 2020 ISPD guidelines.

Methods : We implemented a policy to standardize the collection techniques of PD effluent by introducing an additional step that increased the concentration of organisms in the PD effluent. This additional step consisted of culturing resuspended pellet obtained from 50 cc of centrifuged peritoneal fluid onto agar plates in addition to routinely culturing 5-10 cc of their peritoneal fluid in aerobic and anerobic blood culture bottles. We analyzed the differences in the rates of CNP from 01/01/2009 to 07/30/2013 representing patients prior to the new policy and compared it the CNP rates from 08/01/2013 to 12/31/2018 representing patients in the post policy period.

Results : We noticed a remarkable decline in the number of CNP rate from 0.40 (CI 95% 0.37-0.42) to 0.20 (CI 95% (0.19-0.22) and a total decline in all cases of peritonitis from 0.87 (CI 95% 0.83-0.92) to 0.24 (CI 95% 0.22-0.25) in the post policy period even though patients in the post policy period had more comorbidities [60.9% versus 94.1%], p=0.02. In both the eras, most patients were black and of female gender.

Conclusion : Our study validated the effectiveness of the new PD fluid culture policy based on the 2010 ISPD guidelines.

BACKGROUND

Peritoneal dialysis is one form renal replacement therapy (RRT) which is associated with improved quality of life at a lower cost as compared to hemodialysis.[1] In 2019, the number of End-Stage Renal Disease (ESRD) patients who initiated in-center hemodialysis (HD) had decreased by 6% since 2009, and the number of patients who started with peritoneal dialysis (PD) almost doubled, from 6% to 11%.[2] PD is also the most common modality of RRT among pediatric patients.[3] While the increase in the utilization of PD is encouraging, peritonitis related to PD remains a major concern for clinicians and patients.

The International Society for Peritoneal Dialysis (ISPD) released updated recommendations in 2010 and then updated it in 2022 regarding the acceptable culture detection rate and methodology for the optimal culture yield. These recommendations included: inoculation of effluent into blood culture bottles, centrifugation of effluent and re-suspension of pellet onto culture agar plates to increase the concentration of organisms, limiting delays from collection to plating and optimizing the growth conditions, avoiding antibiotics prior to collection, etc.". The recommendation from that article is, "Culture-negative peritonitis should not be greater than 20% of episodes. The standard culture technique is the use of blood-culture bottles but in addition a large-volume culture (e.g., culturing the sediment after centrifuging 50 mL of effluent) could further improve the recovery of organisms (Evidence).

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An optimal culture technique is the bedside inoculation of 5 – 10 mL effluent in two blood-culture bottles and the combination of culturing the sediment of a 50 mL centrifuged effluent onto agar plates. Culture-negative peritonitis (CNP) can lead to exposure to multiple antibiotics randomly, fungal peritonitis from multiple antibiotic exposure, catheter loss or conversion to hemodialysis (HD)[4-6]. The symptoms of peritonitis can be very vague especially among older and pediatric patients for a clinical suspicion of peritonitis. The clinical suspicion criteria differ from the definitive laboratory criteria for a diagnosis of PD related peritonitis which rely heavily on effluent sample culture, gram stain and PD cell count. While effluent culture results are essential for precise antibiotic treatment, the rate of culture-negative peritonitis (CNP) – "infectious peritonitis without a causal organism" restricts clinicians from practicing precision-based treatment. CNP should not be greater than 20 % with standard bedside collection techniques.[7-10]

Fahim et al. proposed that wide variation in CNP was due to receival of antibiotics prior to culture collection.[10] The ISPD guidelines released in 2010 recommended several approaches for sample collection to improve the identification of organisms within the sample.[14] These included but were not limited to collecting samples before antibiotic use, collecting at least 50 ml of PD fluid for analysis which is centrifuged for 15 minutes, and the resuspended pellet or sediment is used for culture on an agar plate.[14] Despite these recommendations, a variability in technique to sample and culture PD fluid is documented extensively in various studies and one reference showed that the yield from large volume fluid cultures were about the same to other methods (BACTEC blood culture bottles) but were less expensive..[11,15] The Standardizing Care to Improve Outcomes in Pediatric End Stage Kidney Disease (SCOPE) collaborative study surveyed 32 U.S. dialysis centers from 2010 to 2019 and noted significant variability in collection and processing of effluent samples, though no consistent practice helped differentiate between low- and high-rate peritonitis centers. The recommendations from the ISPD and the SCOPE collaborative differ slightly in that ISPD allows using one or both culture methods (centrifuging sample and plating and/or inoculation into blood culture bottles); while SCOPE recommends using both methods. SCOPE trial noted that collection techniques were inconsistent with ISPD recommendations and varied by the duration of dwell times prior to sample collection. This study also identified that many centers affiliated with SCOPE collaborative had a CNP rate above 20% (cut off recommended by ISPD 2010). This has also been identified in other countries.[11-13] There has been no correlation established to show high CNP rates when variabilities in antibiotic administration exist prior to culture, or when there is variability among centers in CNP rates and collection methods, or when using only one culture method to detect CNP detection rate.[10,11,16].

We implemented a new policy for PD effluent culture techniques that was consistent with ISPD 2010 guidelines.14 to determine differences in culture positivity. This was a quality improvement (QI) project between 2013 and 2018. We hypothesized that the techniques recommended by ISPD guidelines in 2010 would improve the utility in isolating organisms that were missed in CNP so that more appropriate tailoring of antibiotic coverage could be achieved in patients with peritonitis. [17]

METHODS

This study was a retrospective project which included adult ESRD patients who received care for PD between 2009 to 2018, before and after implementation of a change in effluent collection and processing as a part of a QI initiative. We designed this study to evaluate the effectiveness of the new peritoneal effluent culture policy after the change on 7/30/2013. We excluded patients younger than 18 years old, pregnant, and excluded for some computations, patients who never had a peritoneal culture tested. As per ISPD, the diagnosis of peritonitis requires two of the following three criteria: clinical symptoms (abdominal pain, fever, cloudy PD effluent), PD effluent white blood cell count of > 100 cells / mm3 with >50% polymorphonuclear (PMN) leukocytes, and culture positivity or a gram stain positivity of dialysis effluent from a 2–4-hour dwell7. The Institutional Review Board (IRB) approved a full waiver of consent. 40 patients' records were screened and reviewed. For all patients, basic demographic and clinical characteristics were collected. Data on antibiotic administration prior to peritoneal fluid culture was not available and is likely a source of confounding. Peritoneal effluent cell counts, and culture results of these patients were exported from the hospital electronic medical records (EMR) system.

Peritoneal Dialysis Effluent Culture Policy

The new policy since July 30, 2013, specified that the PD effluent fluid culture on agar plate should be done from a pellet of 50 ml effluent sample post centrifugation in addition to doing usual gram stains and culturing unspun 5-10 ml of effluent samples from aerobic and anaerobic blood culture bottles. Due to a higher-than-expected rate of CNP at our facility, we instituted the new policy of PD effluent culture techniques recommended by ISPD guidelines on 7/30/2013 14 as preliminary observations indicated that additional culture steps to increase the sensitivity of culture methods were necessary. In addition to sending two blood culture bottles (aerobic and anaerobic blood culture bottles containing 10 ml of effluent BACTEC blood culture bottles), cell counts of the

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effluents were being sent routinely. There were no other QI interventional changes done in the post interventional period. The procedural changes in the pre-intervention group were kept the same for the post interventional group such as giving antibiotics prior to culture collection or avoiding delays in transport of specimens, keeping dwell times the same for instilling dialysate in case of dry abdomen, etc. To avoid confounding, the new policy did not specify further education of PD nurses or their families about PD dwell times prior to sample collection, as we followed ISPD guidelines for peritoneal effluent culture which specifies best culture techniques. We also did not do any special culture methods to try to identify fastidious organisms when initial cultures of PD fluid were culture negative to not introduce further confounders post policy.

Diagnosis of Peritonitis

We used ISPD 2010 definition of infectious peritonitis and excluded non-infectious causes of peritonitis in this patient population. The clinical diagnosis was reached by chart documentation of clinical symptoms of peritonitis. These symptoms included fever, chills, abdominal pain, or cloudy peritoneal effluent.

Data Analysis

Forty adult patient's data were acquired and analyzed as pre- and post-policy change groups. They all received care at our dialysis center until they expired, were transferred to other facilities, or received kidney transplantation. Categorical data were presented as frequencies (%) and continuous variables as medians (range). Differences between categorical variables were compared using the chi-square tests. Continuous variables were compared using the Wilcoxon test.

The impact of the protocol change was computed by assessing the rate of cases per person year. Bootstrap resampling was used to calibrate the 95% confidence intervals and the p-value for the rates. To assess the impact of age, gender, co-morbidities, in addition to the protocol change, multivariable negative binominal regression models for counting variables were developed. The models were adjusted for the different follow up times of the patients. Overall duration of PD and patient survival were assessed using the Kaplan-Meier method. Outcome of groups were compared using the log-rank test. A p-value less than 0.05 indicated statistical significance. All computations were performed using SAS9.4 (Cary, NC).

RESULTS

The baseline characteristics of the 40 patients are reported in Table 1. As summarized in the table, the median age of the patients before and after the policy change decreased significantly from 54.0 [27-79] to 45 [22- 83]; Most patients were Black and of non-Hispanic ethnicity. Female patients were dominant with a ratio of 82.6% and 76.5%. Only 14 patients (60.9%) in the pre-policy group, but 16 patients (94.1%) in the post-policy group had documented comorbidities (P=0.02). The follow-up time of patients between the 2 periods was comparable (p=0.2) and no difference in the rate of PD failures was noted (p=0.18).

Table 1 : Baseline Characteristics of Patients Before and Post New Policy

	Pre – policy change	**Post-policy change**	**P-value**
Period	1/1/2009-7/30/2013	8/1/2013 – 12/31/2018	
# of patients	23	17	
Age	54 [27-79]	45 [22- 84]	0.04
African American	20 (87.0%)	16 (94.1%)	0.46
Non-Hispanic	20 (87.0%)	17(100%)	0.12
Female	19 (82.6%)	13 (76.5%)	0.63
With Comorbidities	14 (60.9%)	16 (94.1%)	0.02
FU time [Years]	2.2 [0.1 – 4.6]	3.0 [0.1 – 5.9]	0.20
PD Failure 1Yr 2Yr	 11% 16%	 6% 14%	0.18

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Table 2 shows the significant decline in cases of peritonitis per person year from 0.87 (CI95%: 0.83-0.92) in the pre-policy change era to 0.24 (CI95%: 0.22-0.25) during the post-policy change era. Amongst culture positive cases of peritonitis most infections were of bacterial nature (94%) and 6% were fungal. Amongst bacterial cases of peritonitis 58% were gram positive organisms and 36% were gram-negative organisms. No differences in the distribution of those organisms were found pre-policy and post-policy change (p=0.55).

Table 2 : Rates of peritonitis and culture results

	Pre-Policy Change	Post policy change	p
N of Patients	23	17	
N of cultures/Patient	2 (2-11)	2 (0-4)	
Peritonitis (cases/person Year)	0.87 (CI95%0.83-0.92)	0.24 (CI95%: 0.22-0.25)	<0.05
Total N of effluent culture tests	57	36	
N of effluent tests/person year	1.21 (CI95%: 1.16-1.26)	0.66 (CI95%0.63-0.69)	<0.05
CNP tests in positive Peritonitis (Cases /person year)	0.40 (CI95% 0.37-0.42)	0.20 (CI95%0.19-0.22)	<0.05
Negative Omission Rate	45%	24%	

This result was confirmed by the negative binominal regression model. Besides the policy change, the patients with reported comorbidities showed a lower rate of peritonitis (p=0.001). Patient age, gender and race had no impact on the number of peritonitis cases in this model (p>0.7). A significant decline in the numbers of effluent culture tests per person year was noted between pre- and post-policy change. Of special interest was the significant decline of culture negative tests in patients with a positive diagnosis of peritonitis (CNP) from 0.40 to 0.20 between pre- and post-policy change (p<0.05). The multivariable negative binominal regression model could not detect any impact of patient gender, race, or age on the overall, positive, or negative number the of effluent culture tests. It detected a significant decline in the number of overall and respectively the number of positive tests between pre-policy and post-policy change (p=0.05). Patients with preexisting comorbidities showed a lower rate of total number and number of positive tests. No negative binominal regression model could be fitted for the number of overall negative tests.

DISCUSSION

In summary, our findings prove that the new policy improved the yield of organisms from peritoneal effluent culture techniques and reduced the rate of culture negative peritonitis rates. The number of CNP tests in patients with peritonitis per person year were twice as high before policy change (p<0.05). This confirmed the validity of the new policy change. In addition, the number of tests performed were drastically reduced as overall rates of peritonitis were reduced which also reduced the costs of patient care.

Our results also revealed some interesting findings and trends. There was a statistically significant decrease in peritonitis cases per person year. The decreased incidence suggests that the patients' self-care or the care from their families and education from PD nursing had improved significantly, leading to better aseptic PD procedures.[20] The fact that patients in the post-policy change group are younger than patients in the pre-policy change group might have contributed to better self-care but did not show an impact on outcome. It is interesting that more and more younger patients were interested in and accepted peritoneal dialysis for ESRD management.

In terms of clinical suspicion of PD-associated peritonitis, it is important to collect PD effluent samples for culture appropriately. It can maximize the chances that the causative microorganism and its antimicrobial susceptibility pattern are identified accurately. This helps identify the possible source of infection, reduces the time needed to attain a positive culture, and guides antimicrobial therapy.[7] More focused therapy can be given to avoid systemic side effects of antibiotics, such as ototoxicity, renal toxicity, and the emergence of antimicrobial resistance.[16] CNP is a significant barrier to proper antimicrobial treatment, and the rate varies across PD centers in the United States.[11] Causes of CNP include improper collection techniques, recent exposure to antimicrobial agents, and infections caused by fastidious organisms.[18,19] Our study focused on the proper collection techniques for culture and its impact on the false culture-negative rate, namely the incidence of CNP.

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LIMITATIONS

This study represented the first report on the epidemiology and clinical course of culture-negative peritonitis. A significant percentage of the patients studied were from a medically underserviced African American population. This study was a small study with limited statistical power. In addition, the demographic pattern (with a predominantly underserviced African American population) might limit its generalizability to other populations.

CONCLUSION

Our data analysis confirmed our hypothesis that the new policy of recommended techniques would reduce the false culture-negative rate. We show that proper collection techniques did lower the CNP incidence in patients with a positive diagnosis of peritonitis. Of note, patient age, gender, and race did not influence the outcome.

Transparency Declaration

Declaration of conflicting interests : The Authors declare that there is no conflict of interest.

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Authors Contributions :

1. Conception and design of the study: Sandeep Sasidharan and Subodh J Saggi
2. Acquisition of Data: Sandeep Sasidharan, Subodh J Saggi and Tahir A Jatoi
3. Analysis and interpretation of data: Angelika Gruessner and Subodh J Saggi
4. Drafting the article or revising it critically for important intellectual content: Eugene K Yeboah, Salifu O Moro, Tahir A Jatoi and Subodh Saggi
5. Final approval of the version to be submitted: All authors

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