SHORT REPORTS

United Kingdom Survey of Culture-Negative Peritonitis and Dialysate Sampling Practice

Peritonitis is a major cause of technique failure in peritoneal dialysis (PD) and accurate diagnosis ensures successful management and avoids unnecessary antibiotic exposure. United Kingdom (UK) registry data on peritonitis rates are not routinely reported. We conducted an electronic survey amongst senior PD nurses and microbiologists to obtain information about PD effluent sampling and processing practices in the UK. The survey was completed by 53 of 79 centres (67% response rate). The median annual culture-negative rate was 15% (range 5 – 38%). The main findings were wide variation in reported sampling volumes and processing methods that may in part explain the variation in culture-negative rates. Adherence to guidelines might reduce culture-negative rates informed by reporting data into national registries.

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Peritonitis is a major cause of technique failure in peritoneal dialysis (PD), and accurate diagnosis ensures successful management and avoids unnecessary antibiotic exposure. International guidelines recommend PD centers aim for culture-negative peritonitis rates of < 20% per year and suggest < 10% is achievable in centers of excellence (1). The most accurate and cost-effective way of achieving this is not known, and United Kingdom (UK) registry data on peritonitis rates are not routinely reported. We aimed to obtain information about PD effluent sampling and processing practices in the UK.

METHODS

After a piloting step, electronic surveys specific to PD nursing staff and microbiologists were distributed to 80 UK renal centers in February 2014. Culture-negative peritonitis was defined according to the International Society for Peritoneal Dialysis (ISPD) Guidelines as:

- Clinical features of peritonitis (abdominal pain or cloudy dialysate)
- Dialysate leucocytosis (white blood cell count > 100/mL with > 50% neutrophils)
- Negative dialysate culture result (1).

Follow-up email and telephone communications were used to maximize the response rate.

RESULTS

Paired returns from a microbiologist and PD nurse were received from 53 of the 80 centers (66% response rate). Continuous variables were non-normally distributed and are reported as median (range). Discrete data are reported as counts (percentage).

PD NURSING STAFF

The median self-reported annual culture-negative rate was 15% (5 – 38%) and is summarized in Figure 1. The total sampled effluent volume sent in a sterile container for analysis ranged from 10 to 90 mL amongst 68% (36/53) of respondents, with 32% (17/53) sending the entire bag. In these instances, the volumes sampled were verified from the microbiology survey and are summarized in Figure 2. The effluent volume was equally divided between a sterile container and blood culture bottles, with the most common combination being 10 mL in each of 2 blood culture bottles and 20 mL in a sterile container. There was no significant correlation between self-reported culture-negative rates and processed effluent volume whether by sterile container (Spearman's rank correlation coefficient $r = -0.1$, $p = 0.53$), blood culture bottles ($r = 0.1$, $p = 0.4$), or both ($r = 0.09$, $p = 0.9$). There was no correlation between the

Figure 1 — Self-reported annual culture-negative peritonitis rate in 53 centers in the UK (median 15%, range 5 – 38%).

number of patients at each center and culture-negative rates ($r = -0.1$, $p = 0.5$, and Figure 3). In normal office hours, PD effluent was most commonly sampled by a specialist PD nurse (85%, 45/53), whilst a general renal nurse or clinical support worker took the sample evenings and weekends. There was variability in how laboratories processed samples outside of office hours. Nurse respondents in 78% of centers (41/53) sent the sample in the same way as in office hours, 11% (6/53) had samples stored in a ward or laboratory fridge, 11% (6/53) were unaware of how samples were stored outside office hours.

MICROBIOLOGY STAFF

All laboratories provided a service on request outside office hours with samples otherwise stored in a refrigerator at 4°C. Such samples were processed identically to normal office hours in 75% (40/53) of centers, whilst (13/53) 25% of centers performed a white cell count, then stored the sample to complete analysis in office hours. Total and differential white cell counts were routinely reported in 47% (25/53) of centers whilst the remaining 53% (28/53) performed differential cell

counts upon request. Gram stain was routinely performed on centrifuged deposits in 75% (40/53) of centers. A further 19% of centers (10/53) restricted the use of gram stain to effluent with white cell count $> 100 \times 10^6/\text{mL}$. A single center (2%, 1/53) performed the gram stain if requested and 2 centers (4%, 2/53) do not perform the gram stain.

To improve diagnostic yield of sediment culture, 43% of centers (23/53) used a concentration method, 49% (26/53) used a water-lysis method, 4% (2/53) used saponin lysis, and 4% (2/53) do not culture sediment at all. Each center employing sediment culture used between 1 and 5 different culture media under aerobic and anaerobic conditions; the data are summarized in Figure 4. Blood agar was the most frequently used general media (82%, 42/51) whilst Sabouraud and Maconkey agar were jointly the most frequently used selective media (24%, 12/51). There was a trend ($p = 0.1$) toward lower self-reported culture-negative rates in centers that use general and selective media compared to centers that used only general media (Figure 5).

Figure 2 — Self-reported sediment and blood-culture volumes of processed peritoneal dialysis effluent in 53 UK centers. In one-third of centers, the entire bag of effluent was sent to the laboratory and processed volumes were obtained from the microbiologist survey.

Figure 3 — Self-reported annual culture-negative peritonitis rate in 53 centers in the UK by the number of patients per center. Each black circle represents a PD center with the total effluent volume processed by both sediment and blood culture expressed in the size of the circle. There was no significant correlation of the culture-negative rate to either the total effluent volume sent ($r = 0.09$, $p = 0.9$) or the number of patients in each center ($r = -0.1$, $p = 0.5$). PD = peritoneal dialysis.

Figure 4 — Routinely used culture media for sediment culture of PD effluent in 51 of 53 UK centers. Each center used between 1 and 5 of these media. Two of 53 UK centers do not use sediment culture. FAA = fastidious anaerobic agar; CLED = cysteine lactose electrolyte deficient. PD = peritoneal dialysis.

Figure 5 — Self-reported culture-negative rates in 51 UK centers stratified by whether the centers use general media ($n = 24$) or general and selective culture media ($n = 27$) for centrifuged sediment culture of PD effluent. Mann-Whitney test showed a trend to lower culture-negative rates in centers using both general and selective media ($p = 0.1$). PD = peritoneal dialysis.

All centers inoculated effluent into blood-culture bottles, with 66% (35/53) using BacT/Alert, 21% (11/53) using BACTEC with resins, 8% (4/53) using brain and heart infusion broth, and 6% (3/53) using BACTEC without resins. Three microbiologist respondents noted in free text comments that they did not have the facility to centrifuge more than 25 mL of effluent as a single volume. All respondents were emailed to clarify this issue, with a lower response rate of 41% (33/80) for this additional question. Of the respondents, 85% of centers (28/33) have PD effluent volumes limited by the design of the centrifuge machine to a capacity of 20 – 30 mL whilst 15% (5/33) circumvent this limitation by requesting complete filling of two 20 – 30 mL sterile containers.

DISCUSSION

The main findings of this survey were of significant variation in PD effluent sampling and processing practice in the UK. The self-reported median annual culture-negative rate of 15% was similar to previously published reports of 19% and 25% from regions of the UK (2,3). As in prior reports, culture-negative rate ranged widely from 5 – 38% and this might in part be explained by the variation in sampling practices. The ISPD guidelines recommend that culture-negative rates are minimized by:

- Sending PD effluent samples to the laboratory within 6 hours of sampling
- Centrifugation of 50 mL of PD fluid for sediment culture and
- Bedside inoculation of 5 – 10 mL effluent in 2 blood culture bottles (1).

There was variation in each stage of sample acquisition and processing. A wide range of PD fluid volumes are typically inoculated into blood culture bottles and sterile containers. The inoculation occurs at the bedside in two-thirds of units and in the laboratory in one-third. There was also a range of procedures to deal with effluent samples off-hours. Furthermore, different techniques are used for sediment culture with 53% (27/51) of respondents using an additional water-lysis or saponin-lysis step that was shown in 1 study to improve diagnostic yield (4). Szeto and co-workers previously demonstrated that higher rates of culture-negative peritonitis were associated with sampling by a non-specialist nurse and previous antibiotic exposure (5). All centers use blood-culture bottle media of varying types. Whilst nearly all centers routinely use sediment culture, only 9% (5/53) of centers routinely culture volumes of 50 mL effluent as per ISPD guidelines. This was apparently due to many UK laboratories lacking the facility to centrifuge large volumes of effluent without resorting to multiple sterile containers.

Whether all centers need to use both sediment culture and blood culture bottles is not clear. Many studies show that automated blood-culture bottle systems have greater diagnostic sensitivity than sediment culture but this might be at the expense of specificity and there has been no systematic review. In resource-limited healthcare systems, using a single diagnostic technique might be more cost efficient. This survey did not query whether any centers routinely use novel methods

based on polymerase chain reaction that have shown promise in single-center studies. Their role might be justified particularly in culture-negative cases. Further data to clarify clinical and cost efficacy of established and novel diagnostic techniques are needed. Whilst recent data have shown culture-negative peritonitis is associated with more benign outcomes than if the causative organism is identified, there are multiple benefits to achieving diagnostic accuracy. Inappropriate antibiotic exposure is prevented, and the most sensitive techniques might differentiate truly sterile peritonitis due to inflammation from that associated with infection.

LIMITATIONS

The survey was not designed as a formal audit. The data cannot be verified, and surveying different staff within the same centers and non-respondents may have altered the results. The survey did not verify whether the port on the dialysate bag was cleaned prior to sampling or what cleaning substance was used and may have missed further practice variation. Utilizing the infrastructure of national renal registries to collect PD peritonitis data and share best practices for the UK is an appropriate future step. This is pertinent given that Australia and New Zealand dialysis registry data have shown that strict adherence to ISPD guidelines is associated with better outcomes from peritonitis (6).

CONCLUSION

There is wide variation in reported sampling volumes and processing methods for PD effluent in the UK, and this may in part explain the variation in PD culture-negative rates. Adherence to national or international recommendations on diagnostic methods might reduce culture-negative rates, informed by reporting of peritonitis data into national registries.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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