ISPD Asia-Pacific Chapter Newsletter, August 2021

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News from the ISPD

International Society for Peritoneal Dialysis 2022 Congress

11-14 August 2022

Suntec, Singapore

Abstract Submission Open: 1 October 2021

Abstract Deadline: 1 February 2022

Early Registration: 29 April 2022

Website: https://ispd2022.com/

10th International Society for Peritoneal Dialysis Asia Pacific Chapter meeting

22-24 September 2023, New Delhi, India

Call for Bids to Host ISPD 2024

The ISPD is looking for a host for the ISPD 2024 Congress. We are inviting our members to consider working together with the ISPD to bring the latest advances in PD to their home country. The only rotation condition in 2024 is that the host country has to be outside Europe.

You can download the request for proposals document HERE. It contains all the necessary information to prepare your bid for becoming the host of our next ISPD congress after Singapore.

Anyone interested in putting forward a bid should send an email with an expression of interest to our PCO (Professional Congress Organiser). They will be able to assist you during the whole process, and they will also carry on most of the work of celebration of the event.

We will decide on the host of our 2024 Congress by the end of this year; therefore we are expecting to **receive proposals by September 1st, 2021**. You can find all the deadlines in the RFP document.

ISPD Asia-Pacific Chapter Scholarship

This is a scholarship to support up to 3 months training in clinical PD for doctors and nurses from Asia-Pacific region. Deadline for application for each round: twice a year at 30 June or 31 December. **The next deadline is 31 December 2021.** Details and application procedures can be found under the Regional Chapters – Asia-Pacific Chapter, at the ISPD website.

ISPD Fellowships: call for applications open until September 30th

The ISPD offers an opportunity for eligible doctors and nurses to improve their knowledge and expertise in peritoneal dialysis by visiting, for a period of up to 3 months, an established PD center with experience in training new PD specialists.

Scholarships are awarded for a maximum amount of $5000, for up to 3 months of training. Eligible costs include travel and living expenses, and educational expenses during the visit to the host institution.

In 2021, the call for applications usually issued in March had to be postponed due to travel limitations linked to the COVID pandemic. We will therefore offer 11 ISPD Fellowships in September, for training periods to start in 2022. Because travel restrictions will likely continue in 2022 in some form, we advise applicants to take the situation into consideration when preparing the application. Rest assured, ISPD will be flexible to allow changing dates if necessary.

You can find all the information and the application form on www.ispd.org/ispd-fellows

Renew your membership !

Visit https://ispd.org/memberships/ to join the ISPD or renew your membership. Membership benefits of the International Society for Peritoneal Dialysis include:

- print and/or online subscription to Peritoneal Dialysis International
- Receipt of PD News
- Online access to ISPD Guidelines
- Special registration fees at ISPD Congress, Chapter Meetings and the Annual Dialysis Conference
- Application for ISPD Scholarships and Grants

Membership for developing countries can be done at advantageous rates, by grouping members by institution or region geographical area. Write to admin@ispd.org for more information.

Upcoming Meetings

19th Asian Pacific Congress of Nephrology

18-22 August 2021

Pattaya, Thailand

Website: http://www.apcn2021.com/

ISN World Congress of Nephrology 2022

24-27 February 2022

Kuala Lumpur, Malaysia

Abstract submission open: 15 April 2021

Abstract submission deadline: 22 September 2021

Website: https://www.theisn.org/wcn22/

Guideline Update

Implementation of PDOPPS in a middle-income country: what the rest of us can learn?

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The Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS) is a groundbreaking research initiative for understanding optimal practices for PD patients and identifying those associated with improved clinical outcomes across the globe. Arbor Research Collaborative for Health coordinates the study in collaboration with the International Society for Peritoneal Dialysis (ISPD). In the first phase of PDOPPS, 7629 patients from 215 dialysis facilities in 7 participating countries (Australia, Canada, Japan, New Zealand, Thailand, the United Kingdom, and the US) consented. The study extends data collection to South Korea in the second phase and is now in the midst of launching the third phase of PDOPPS in the forthcoming year. Findings from the first phase have been presented at numerous international conferences and symposia and have led to the acceptance of 14 articles, and the published data has been used for

stemming the 2020 ISPD Guideline “Prescribing high-quality goal-directed PD.”[1] Among 7 participating countries, Thailand is unique insofar as it is the only non-high income country and the only country with a “PD First” policy. Kanjanabuch et al. have published the first phase of Thailand PDOPPS in the PDI 2021 [2] and Kidney360 [3].

Study processes of Thailand PDOPPS

The study methodology comprised structurally 2 phases (Figure 1). The pilot phase recruited PD patients from 4 randomly selected PD facilities from May to November 2016 to assess the feasibility of implementing the study in Thailand. Implementation phase with minor revisions made to the questionnaire and a bilingual, web-based data collection tool (PDOPPSLink), PD patients from 22 PD centers from different geographic regions, sizes, and affiliations, representing Thailand PD facilities, have been enrolled (November 2017 to 1 February 2018). Demographic, clinical and laboratory data, medications, and patients’ outcomes were prospectively collected and analyzed. Clinical data were obtained by manual abstraction from the medical chart. Patient-reported information was captured annually. In Thailand, patients' specimens, including serum, PD effluents, and PD catheters, were collected and shipped to the central lab when peritonitis was suspected and whenever the PD catheter was removed. The specimen collections were done separately and independently from the global PDOPPS.

To help ensure the integrity of data collected and minimize the number of errors and missing data, both remote and on-site validation visits was employed. The remote validation ran the data through established quality control programs at Arbor Research Collaborative for Health. On-site validation visits were performed by clinical research associates (CRAs) from an external firm, the Medical Research Network (MedResNet).

Key Findings

In this first description of contemporary PD practices in Thailand after implementing the "PD First" policy, 848 PD patients [31% incident cases] from 5,090 patients in participating centers were enrolled. Thai PD facilities were large (median PD patients per facility of 132) with low APD penetration (5%). Most clinics had burgeoning workloads for the PD health workforce (87:1 PD patients-to-nephrologist ratio and a PD patient-to-nurse ratio of 70:1). Of note, 82% of patients on CAPD received 4 exchanges a day, with very few performing ≤3 exchanges a day. Around 90% of patients received 2 L daytime exchanges, and 9% of CAPD patients used < 2 L dwell volumes during their daytime exchanges. This information is consistent with high peritoneal Kt/V (1.6±0.5) and total Kt/V (2.1±0.8) [4].

Major problems specific to Thai PD patients have also been depicted, including a high proportion of late referral (as evidenced by low baseline residual kidney function and high rates of urgent start PD), malnutrition, and culture-negative peritonitis episodes (0.13 episodes/year, 28% of total episodes). In comparison, peritonitis rates (0.40 episodes/year) were acceptable according to the 2016 ISPD Peritonitis Guideline (Figure 1) [9]. Patients belonged to the Bangkok metropolitan region clinics had better socioeconomic status, educational levels, nutritional parameters, and peritonitis rates, emphasizing the center effect on key success factors in PD.

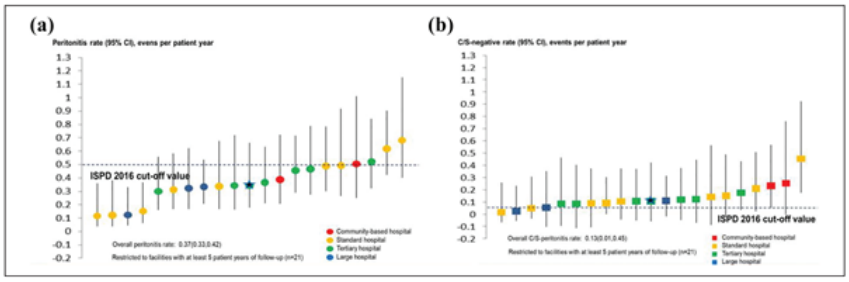

Figure 1. Peritonitis rate (a) and culture (C/S)-negative peritonitis rate (b) among 21 Thailand facilities demonstrated according to the size of the hospital, restrict to the facility with at least 5 patient-years of follow-up. (*represent median value. The dotted lines represent the cut-off value recommended by the 2016 ISPD Peritonitis Guideline. Numbers below the dotted line in (a) and above the dotted line in (b) mean passing the threshold)

In conclusion, the study highlights the feasibility of implementing a high-quality observational cohort study, PDOPPS, in a middle-income country with limited national resources like Thailand. Although the study emphasizes the limitations of infrastructure and poor clinical conditions of patients treated in PD centers, particularly in the provincial area, peritonitis rates were acceptable. In the short term, an improvement in PD supporting systems and equality in resource distribution is urgently needed to sustain the "PD First" policy and quality improvement of PD care in Thailand.

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Research News from Asia-Pacific Region

Antibiotics for the treatment of peritonitis in patients on automated peritoneal dialysis: A ‘one-size-fits-all’ or ‘individualized’ dosing?

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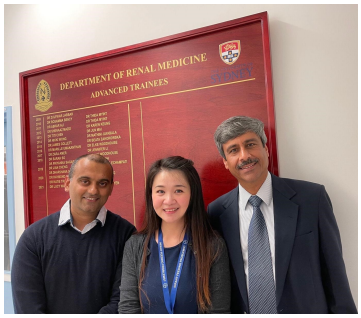

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Background

Peritonitis is one of the major and common complications in patients receiving peritoneal dialysis (PD). Repeated episodes of peritonitis can cause functional and structural changes to the peritoneal membrane which can, in turn, lead to technique failure, resulting in a permanent switch to haemodialysis (1).

Prompt treatment with intraperitoneal (IP) antibiotics as recommended by the International Society of Peritoneal Dialysis (ISPD) guidelines (2), is the cornerstone for therapy. However, antibiotic dosing regimens in the ISPD guidelines are largely derived from pharmacokinetic studies conducted in patients on continuous ambulatory peritoneal dialysis (CAPD), while data on automated peritoneal dialysis (APD) remains extremely scarce.

In CAPD, patients typically receive ‘standard’ two or three exchanges during the day and a night dwell (3). On the other hand, patients on APD typically have more frequent and rapid exchanges with shorter dwell times. Specifically, the APD regimens can vary in a number of exchanges conducted by the cycler at night to a dry day, day fill or manual exchanges performed during the day, all of which can potentially affect the pharmacokinetics of antibiotics in patients on APD. In practice, as per the ISPD guidelines, patients on APD and CAPD with peritonitis are treated with the *‘one-size-fits-all’* approach, where patients are recommended to be treated with the same IP antibiotics dosing regimens with antibiotics administered in a PD exchange with a minimum of 6-hour dwell. It is however, unclear whether this approach would produce similar local and systemic drug levels, leading to similar clinical response and treatment outcome to patients on

CAPD. However, outcomes of peritonitis in patients on CAPD and APD may not be similar. The analysis of the Australia New Zealand Dialysis and Transplant Registry (ANZDATA) showed a non-significant higher likelihood of 30-day mortality and hospitalisations in patients on APD as compared to CAPD, indicating possible poorer outcomes of peritonitis in patients on APD (4). Although the ISPD guidelines have recommended a minimum of 6-hour dwell time to allow adequate absorption of the antibiotics administered via the IP route, important factors such as peritoneal membrane permeability (that increases during acute phase peritonitis episodes, and possibly, reduces as the peritoneal inflammation begins to resolve (5), number of PD exchanges, and residual renal function (RRF), could also affect the clearance of the antibiotics.

Our recent systematic review (6) has highlighted that the available pharmacokinetic data supporting the use of intermittent culture-directed antibiotics (i.e. cefepime, meropenem and fosfomycin) in patients on APD would be valid in patients receiving APD exchanges with dwell times of 6 hours for cefepime, 15 hours for meropenem and fosfomycin. It is however, unclear whether these antibiotics administered in patients receiving nocturnal intermittent peritoneal dialysis, and multiple day exchanges will have similar outcomes. On the other hand, information on the therapeutic efficacy of other culture-directed antibiotics in patient on APD, was derived mainly from the case reports/series in individual patients, making it difficult to make firm dose recommendations.

Since patients on APD do not receive a standard 6 hour PD dwell time recommended for IP antibiotic administration, alternative approaches such as temporarily switching patients to CAPD for IP antibiotic dosing during peritonitis episodes have been employed(2). However, these approaches may be impractical due to the need to retrain users in the manual exchange technique, and CAPD supplies may not be immediately available especially if patients are being treated in the home environment. Furthermore, strategies such as administering antibiotics in addition to the day exchanges in patients on APD, while continuing APD exchanges at night have also been trialled. A cohort study by Ruger *et al* (7) reported a comparable success with gentamicin 20 mg/L administered in the first exchange followed by once daily in the long day dwell in patients on both CAPD and APD. However, the authors did not specify the number of APD exchanges used in the study, that could affect the clearance of the antibiotic. Therefore, it is unclear whether similar outcome will be achieved in (a) patients with variable APD regimens and shorter dwell times, (b) antibiotics that exhibit time-dependent killing where optimal bactericidal activity occurs when serum drug concentrations remains T>MIC (time intervals for which the antibiotics remain above the minimum inhibitory concentration of the susceptible organisms), and (c) presence of RRF.

Peritoneal inflammation during the acute inflammatory phase may lead to significant amount of IP antibiotics being absorbed from the peritoneal cavity (8). However, it is unclear whether the extent of drug absorption remains the same during the resolving phase, as multiple insults to the submesothelium due to repeated peritonitis may cause peritoneal sclerosis (9). Therefore, dose adjustment of the IP antibiotics may be necessary in patients with repeated peritonitis episodes, in order to enhance diffusion of antibiotics from the peritoneal membrane to the plasma in between exchanges, potentially allowing drug concentrations to remain above the MIC for optimal bactericidal activity.

An ‘individualized’ dosing strategy for managing APD-associated peritonitis: A better solution?

Peritoneal clearance and absorption of IP antibiotics can vary depending upon the presence of RRF, peritoneal membrane transport characteristics, and different stages of APD-associated peritonitis, in terms of peritoneal inflammation (i.e. acute [first 48 hours] and resolving phases [>96 hours]). However, these factors may pose a greater challenge in patients on APD with higher number of exchanges and shorter dwell times.

Elwell *et al* (10) reported higher peritoneal and total renal drug clearance in patients with higher RRF and renal Kt/Vurea, suggesting a need to individualize IP antibiotics dosing based on the patients’ most recent PD adequacy test (i.e. administer a higher dose of antibiotics in patients with greater creatinine clearance and renal Kt/Vurea, as opposed to the ‘*one-size-fits-all*’ antibiotics dosing), to achieve optimal clinical response and therefore, resulting in a better clinical outcomes. Although this theory requires further research, it remains an important consideration to provide a more accurate dosing for the treatment of APD-associated peritonitis.

Conclusions

The effective treatment of PD-associated peritonitis involves a combination of prompt treatment with appropriate IP antibiotics, and the knowledge of pharmacokinetic variations between APD and CAPD patients. Although a minimum dwell time of at least 6-hour is required for adequate absorption of IP antibiotics, important factors such as (i) peritoneal membrane permeability during the acute and resolving phases of peritonitis episodes, (ii) number of APD exchanges, (iii) presence of RRF should be taken into consideration when dosing antibiotics in patients on APD. Further studies are required to compare the pharmacokinetics of IP antibiotics administered in patients on APD receiving higher number of

exchanges with shorter dwells as compared to those on CAPD, with special considerations taken in those patients with RRF and the degree of peritoneal inflammation during the acute and resolving phases of the peritonitis episodes, which could potentially affect the clearance of the IP antibiotics.

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