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Evaluating the Value of Intraperitoneal Ceftazidime Prior to Colonoscopy in Reducing Peritonitis in End Stage Renal Disease Patients on Peritoneal Dialysis

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Abstract

The biggest burden in peritoneal dialysis is still peritonitis which increases the rate of mortality and hospitalization. The aim of our research was to address one of the ISPD (international society of peritoneal dialysis) guidelines 2016 which advocate the use of prophylactic antibiotic in peritoneal dialysis patients before going to colonoscopy, but this recommendation is class C which means a weak one. Our aim was to look at the effect of giving intraperitoneal ceftazidime before the procedure of colonoscopy in reducing the possible risk of peritonitis.

Patients and methods: Over a period of 2 years and 6 months, from January 2016 we managed to enroll 120 patients out of 163 whom we performed 120 colonscopies. Patients were randomized for Ceftazidime use by 1:1 method, ending up with 60 patients in group A who received the drug and 60 patients in group B who did not receive the drug.

Results: peritonitis occurred within 48 hours following the procedure. It was documented in 4 (6.7%) and 5 (8.3%) patients in groups 1 and 2 respectively (p =0.3243); the causative organisms were mainly gram-negative bacteria.

Conclusion: It appeared that giving intraperitoneal Ceftazidime prior to colonoscopy did not offer greater benefits in reducing the risk of peritonitis when compared with the group who did not receive it.

Keywords: *Peritoneal dialysis, peritonitis, colonoscopy, ESRD, colon cancer, ceftazidime.*

Introduction

The expansion of peritoneal dialysis uses in the late years as an option for renal replacement therapy (RRT) for end stage renal disease (ESRD) patients and the development of automated peritoneal dialysis (APD) have led to improved quality of life as well as increased survival among those patients. Maintaining patients on peritoneal dialysis for many years, however, has its own challenges that face nephrologists. These challenges based on the fact that most of ESRD patients are suffering from different comorbidities. Such challenges may require the need for other services namely cardiology, endocrinology, gastroenterology and others, each of which has its own diagnostic procedures that might harm patients if done without proper preparation. Colonoscopy is one of these procedures that may be required for both screening for and diagnosis of colon cancer as indicated. Colorectal cancer is still the third most prevalent cancer in USA general population. Although controversial, the overall incidence of cancer is reported to be higher in patients with ESRD than in the general population. An international study of cancer registries reported that, between the years 1980 to 1994, cancer occurred in 25,044 of 831,804 dialysis patients (compared with an expected number of 21,185), resulting in an overall standardized cancer incidence of 1.18. There are, however, no reported data concerning the prevalence of the disease amongst Saudi ESRD patients who are subjected to dialysis. Variable factors may influence the prevalence of colorectal lesions in this population in particularly diabetes, type and length on dialysis, statin use, immunosuppressive drugs and obesity. The current recommendations for colonoscopy screening in ESRD patients before renal transplantation are the same as those for the general population as detecting colorectal cancer may exclude patients from the transplant list for at least five years after clinical remission. The fear of developing peritonitis after colonoscopy is unjustified as few cases have been reported in the literature on post colonoscopy peritonitis in PD

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patients (Reference 19-23). A retrospective study (Reference 24) found that the risk of peritonitis after colonoscopy without antibiotic prophylaxis was 6.3%; colonic biopsy or polypectomy did not appear to further increase the risk and no peritonitis was observed in patients that received prophylactic antibiotics although the difference was not statistically significant. Few cases have been reported on the incidence of peritonitis following colonoscopy in CAPD patients. Those reports claimed that instrumental diagnostic procedures such as colonoscopy may play a significant role in the development of gram-negative peritonitis in CAPD patients (References 25, 26). Similar results were reported by Yip et al in 2007 (Reference 27). All reported cases about peritonitis following colonoscopy were on CAPD and there were no case reports in APD patients. The recent guidelines of the International Society of Peritoneal Dialysis (ISPD) showed evidence 2-C favoring the use of prophylactic antibiotics prior to colonoscopy; however there have been no controlled randomized studies to support these recommendations. In view of these challenges, our study aimed at investigating the need of prophylactic antibiotics prior to colonoscopy in APD patients undergoing this procedure.

Patients and methods

Between January 2016 throughout June 2018, 120 patients out of 163 were included in this study. Patients were randomized (1:1) into two groups; Group 1: 60 patients on APD with prophylactic antibiotic therapy before the flexible colonoscopy, Group 2: 60 patients on APD without prophylactic antibiotics (Table-1). Exclusion criteria were: history of colonic or rectal resection, neurologic deficit, pregnancy, ongoing sepsis, valvular or chronic heart disease, urinary tract infections, chronic liver disease, exit-site or tunnel infections, pneumonia or pulmonary tuberculosis, peritonitis or history of peritonitis for the last one year and unwillingness to give informed consent (Figure-1). All flexible colonoscopy examinations were performed by trained gastroenterology consultants. All Staff in the endoscopy unit were aware of the potential hazard of cross-infection and assiduous mechanical cleaning followed by disinfection was done. The following parameters: age, gender, duration on dialysis, diabetic state, use of antibiotics before the procedure, and indications for and findings of colonoscopy were studied. APD peritonitis episodes occurring within 1 week after colonoscopy, culture results and outcomes of peritonitis were recorded. At our center, the colonoscopy bowel preparation protocol included a low residue diet 2 day before the examination and patients are instructed to take a fluid diet the day before the procedure. Oral electrolyte lavage solutions or aqueous sodium phosphate solution were used as laxative for bowel preparation. Peritoneal dialysis effluent (PDE) was drained and the patient's abdomen was kept empty before the procedure. Prophylactic antibiotics were given for prevention of peritonitis if needed according to the 2010 ISPD guidelines (17). Prophylactic antibiotics for APD peritonitis prevention were not routine at our center. Peritonitis was diagnosed when abdominal pain and cloudy fluid occurred with or without fever, and when peritoneal fluid white blood cell (WBC) count was >100/mm3, with >50% neutrophils. Episodes with peritoneal eosinophilia but negative bacterial culture were excluded. The PDE was sent for hematological and microbiological examination when patients complained of abdominal pain or if the PDE was turbid. For the microbiological tests, 50 mL peritoneal fluid was centrifuged at 5000g for 15 minutes. The deposit was inoculated on 5% sheep blood agar, MacConkey agar, and Sabouraud agar and incubated aerobically at 35°C for up to 72 hours. All isolates were identified by standard biochemical methods and the identity of the isolates was confirmed using the Vitek Automicrobic System (bioMerieux, Vitek, Hazelwood, Missouri, USA). Antimicrobial susceptibility was tested by the Kirby–Bauer disk diffusion method and results interpreted according to the National Committee for Clinical Laboratory Standards criteria. Reappearance of signs of infection with the same organism(s) isolated in the dialysate within two weeks after the completion of antibiotic treatment was classified as relapse, and not as a new episode.

All Patients were on automated peritoneal dialysis (APD) and their dialytic prescription consisted of 1.36% and 2.27% glucose-based solutions Dianeal® over 9-10 hours night dwell and 7.5% icodextrin (Extraneal®, Baxter Castlebar, Ireland) 2 liters as the last fill for the day dwell. Total daily PD volume ranged between 10-12 liters with a fill volume ranging between 2.0-2.5 liters/cycle.

Colonoscopy procedure

In the procedure room, all patients were given supplemental oxygen (4 L/min) through a nasal cannula, and a 3-lead electrocardiogram, pulse oximetry, and blood pressure were monitored. Only the anesthesiologist certified in advanced life support and who completed a structured training program were permitted to administer propofol under the guidance of the endoscopist. The anesthesiologist who administered the sedative medications and physicians were present for the entire period of sedation and examination. The anesthesiologist attempted to achieve a level of sedation that allowed the patient to tolerate the procedure with minimal to mild pain while maintaining adequate cardiorespiratory function. Propofol induction of sedation was begun with an initial 40-mg bolus (20–30-mg for elderly and smaller patients at the discretion of the endoscopist and anesthesiologist) administered intravenously followed by titration with 10–20-mg boluses. After an initial bolus infusion of propofol, the patient was observed for 30–60 seconds before deciding to administer the next bolus. Fentanyl was administered intravenously in 12.5- or 25-g boluses and midazolam as 0.5–1.0-mg boluses. Additional medication was titrated at 1–3-minute intervals to achieve or maintain the desired level of sedation. An endoscopy technician was available to assist the Colonoscopy with technical maneuvers. This staffing pattern has been used in our endoscopy suite for all sedated procedures for several years and was not changed for the study. The following time points were recorded: initiation of sedation, full sedation (when the nurse and endoscopist mutually agreed the patient was sedated sufficiently to begin the procedure), colonoscope insertion, intubation of the cecum, and colonoscope removal from the anus. Interventional procedures like polypectomy were performed when indicated with disposable polypectomy snare G-Flex. Post polypectomy bleeding (if any) was managed by epinephrine injection, hemoclip and heat probe.

Biopsies were taken when indicated by disposable biopsy forceps (Endow by Olympus). After the procedure, both the physician and the nurse completed a questionnaire that assessed the patient's level of sedation, pain, and ability to cooperate. Any complications (decline in oxygen saturation to less than 85%, heart rate less than 50 beats per minute, blood pressure less than 90/50 mm Hg, or need for mechanical ventilation) were recorded.

Prophylactic antibiotic therapy

Antibiotic prophylaxis in our center consisted of first-line antibiotic regimen for APD peritonitis was first- or second-generation cephalosporin plus an aminoglycoside, either tobramycin or netilmicin. Cefazolin combined with ceftazidime was also used as alternative.

Peritonitis therapy

Peritonitis episodes were treated with our center's standard antibiotic protocol, which has been changed systematically over time. The first-line antibiotic regimen for APD peritonitis was first- or second-generation cephalosporin plus gentamicin (loading dose 60 mg i.v. + 4-5 mg/L intraperitoneal). Cefazolin or cefoxitin (2 g i.v. + 50 mg/L intraperitoneal) combined with ceftazidime (2 g i.v + 1 g intraperitoneal) was also used in our PD unit since the year 2010 according to the ISPD peritonitis guidelines (17). Vancomycin was used as a second-line therapy for primary nonresponding patients. Antibiotic regimens for individual patients were modified when culture results became available. Treatment usually lasted for either 2 weeks or at least 7 more days after normalization of the effluent WBC count, whichever was longer. Requirement of cessation of peritoneal dialysis, temporarily or permanently, and death during peritonitis, were defined as treatment failure. Heparin administration (500-1000 IU/L of dialysis fluid) and exchange of tubing was performed routinely in all cases of peritonitis. The indications for catheter removal included peritonitis caused by *Pseudomonas species,* peritonitis caused by fungi, cases with prolonged course or multiple recurrences, and episodes with suspected bowel perforation.

Statistical methods

Continuous variables are expressed as mean + SD and categorical variables are expressed as percentage. Non- parametric Spearman Rank test was used for continuous variables correlation and Mann-Whitney test used for comparison of two groups. P values were not adjusted for multiple testing

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and therefore should be considered descriptive. Variables with significant univariate associations were candidates for multivariate analysis. Univariate and multivariate analysis was used to study the relationship of age, sex, diabetes mellitus, time on APD, hemoglobin and albumin levels and prophylactic antibiotic use with post-colonoscopy peritonitis. The statistical analyses were limited to data regarding only the first episode of peritonitis, unless otherwise noted. Statistical significance was accepted at $p < 0.05$. The statistical analysis was performed using SPSS for Windows version 20 *(IBM Inc. New York, USA)*.

Results

In a total of 163 APD patients included during the study period of 2 years and 6 months, 120 colonoscopies were performed in 120 APD patients. Mean age was 58.6 ± 10.1 years and duration of dialysis was 31.3 ± 8.6 months; 49 (40.8%) patients were diabetics. The 120 APD patients included in the study were randomized into two groups; group-1 (60 patients) who received IP ceftazidime prophylaxis prior to colonoscopy and group-2 (60 patients) who had colonoscopy without antibiotic prophylaxis. Randomization was 1:1. Demographic characteristics of patients are summarized in table-1. The two groups were age and sex matching. Diabetes mellitus was present in 43.3% and 38.3% and hypertension in 85.0% and 81.7% in the two groups respectively (p=0.3217 & 0.3340). Mean duration of diabetes mellitus and the duration on APD was 18.6 + 11.7 years and 19.5 + 9.3 years, 31.3 + 10.7 months and 30.6 + 12.2 months in groups 1 and 2 respectively (p = 0.3937 & 0.3821). The difference in overall fasting blood sugar (FBS) and hemoglobin A1-C (Hgb A1-C) was not statistically significant between the two groups. At the time of colonoscopy, the mean blood urea nitrogen (BUN), serum creatinine and renal creatinine clearance were 48.19 + 8.53 mg/dl and 46.32 + 9.84 mg/dl; 7.38 + 2.47 mg/dl and 8.13 + 2.87 mg/dl; 7.1 + 2.1 and 6.8 + 2.2 ml/min in groups 1 and 2 respectively with no statistical significance (table-1). Mean hemoglobin level, serum potassium (K+) and serum albumin were similar in both groups at the time of the procedure (table-1). Indications for and findings of colonoscopy are summarized in table-2 and figure-2. Of all colonoscopies 59.2% showed normal findings, 19.1% with colonic polyps at different sites, 10.8% with angiodysplastic-like lesions, 7.5% with colonic ulcer (s), 3.3% with diverticulae without diverticulitis and 1.7% had transverse colon stricture which was managed with stent insertion. Inflammatory bowel disease in the five patients was inactive for more than one year. Findings at colonoscopy are shown in figure-2. All Post-colonoscopy peritonitis occurred within 48 hours following the procedure. It was documented in 4 (6.7%) and 5 (8.3%) patients in groups 1 and 2 respectively (p =0.3243); the causative organisms were mainly gram-negative bacteria (5 out of 9 cases were gram negative bacteria, one with gram positive organisms, two negative culture and one with Candida albicans) (table-3). Peritonitis episodes were not documented in any patient with diverticulosis or biopsied colonic polyps. All peritonitis cases resolved with treatment and one patient from group 1 and 1 from group 2 required catheter removal because of fungal peritonitis in the former and refractory peritonitis in the later. Complications other than peritonitis were 0.0% in both groups. Different variables were analyzed to demonstrate its correlation with peritonitis episodes (Table-4). No significant difference in serum BUN or serum creatinine was observed between those who developed peritonitis and those who did not in the two groups. By multiple logistic regression analysis, the presence of diabetes mellitus was the only independent variable that entered into the best predictive equation over the development of enteric peritonitis (log likelihood ratio = -25.072, odds ratio = 17; 95% CI odds ratio: 2 - 151).

Table 1. Demographic characteristics of the study population

	Group 1(n = 60)	Group B (n = 60)	*p*
Age (years), mean + SD	59 + 10.5	57 + 12.3	0.2412
Female/Male (female %)	23/60 (38.3)	21/60 (35.0)	0.3210
Smokers (%)	23.3	26.7	0.3062
Hypertension, n (%)	51 (85.o)	49 (81.76)	0.2230
BMI at beginning, mean + SD	28.3 + 4.0	29.3 + 3.8	0.3020
Diabetes mellitus, n (%)	26 (43.3)	23 (38.3)	0.3868
Duration of diabetes, (years), mean + SD	18.6 + 11.7	19.5 + 9.3	0.2937
Duration on APD, months (mean + SD)	31.3 + 10.7	30.6 + 12.2	0.3891
Overall FBS in diabetics, mmol/L (mean + SD)	8.6 + 1.2	8.4 + 1.8	0.2001
Overall Hgb A1C % in diabetics (mean + SD)	7.1% + 0.7	6.9 + 0.8	0.3773
Hgb at colonoscopy, gm/dl (mean + SD)	10.12 ± 2.25	10.32 + 2.74	0.2434
BUN at colonoscopy, mg/dl (mean + SD)	48.19 + 8.53	46.32 + 9.84	0.2862
Serum Cr. at colonoscopy, mg/dl (mean + SD)	7.38 + 2.55	8.13 + 1.87	0.4051
Serum K+ (mEq/L)	3.8 + 1.9	3.9 + 2.1	0.5100
Serum albumin (gm/l)	3.8 + 2.0	3.7 + 1.8	0.4224
Renal Cr Cl. ml/m (mean + SD)	7.1 + 2.1	6.8 + 2.2	0.3482

BMI: Body mass index, APD: automated peritoneal dialysis, FBS: Fasting blood sugar, Hgb: hemoglobin, BUN: blood urea nitrogen, Cr: creatinine, K+: potassium, Cr Cl: creatinine clearance.

Table 2. Indications for and findings of colonoscopy

Number (%)	Indication	Findings (number)	Action (number)
22 (18.3)	Screening for colonic Cancer	Normal (15) Transverse and descending colon polyps (7)	None (15) Biopsies and removal (7)
18 (15.0)	Investigation for iron deficiency anemia	Normal (15) Angiodysplastic like lesions (3)	None (15) Biopsies & bleeding protocol (3)
16 (13.3)	Altered bowel habits (chronic diarrhea or chronic constipation)	Normal (9) Diverticulae (4) Transverse colon polyps (3)	None (9) None (4) Biopsies and removal (3)
15 (12.5)	Positive fecal occult blood testing without overt rectal bleeding	Normal (6) Angiodysplastic-like lesions (6) Descending colon polyp (3)	None (6) Biopsies & bleeding protocol (6) Biopsies and removal (3)
13 (10.8)	Overt rectal bleeding	Normal (3)	None (3)

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		Transverse or descending colon ulcers (5) Angiodysplastic-like lesions (3) Ascending & transverse colon polyp (4)	Biopsies & bleeding protocol (5) Biopsies & bleeding protocol (3) Biopsies and removal (4)
12 (10.0)	Finding of polyp (s) during sigmoidoscopy	Normal (7) Descending colon polyps (4) Angiodysplastic-like lesions (1)	None (7) Biopsies and removal (4) Biopsies & bleeding protocol (1)
10 (8.3)	Bloody effluent	Normal (9) Transverse colon polyp (1)	None (9) Biopsies and removal (1)
9 (7.5)	Family history of colon cancer or polyps	Normal (7) Ascending colon polyp (1) Descending colon ulcer (1)	None (7) Biopsies and removal (1) Biopsies (1)
5 (4.2)	Inflammatory bowel disease	Transverse and/or descending colon ulcers (3) Transverse colon stricture (2)	Biopsies (3) Stent (2)

Table 3. Microorganisms responsible for peritonitis

Patient's No#	Group 1 (4 cases) Microorganisms	Outcome	Patient's No#	Group 2 (5 cases) Microorganisms	Outcome
12	E. coli + Enterobacter	Treated	5	E. coli	Treated
18	Candida albicans	PD catheter removed	22	Klebsiella species	Treated
33	Klebsiella	Treated	29	Culture negative	Treated
35	S. aureus	Treated	40	Enterobacter	Treated
			59	Culture negative	Treated

Table 4. Comparison of characteristics of patients with and without peritonitis after colonoscopy

	Group 1 Peritonitis No peritonitis	*p*	Group 2 Peritonitis No peritonitis	*p*
Number (%)	4 (6.7) 56 (93.3)		5 (8.3) 55 (91.7)	0.3243
Age (year)	58.0 + 10.3 57.0 + 12.3	0.3012	58.1 + 11.1 58.2 + 10.7	0.4642
Diabetes, n (%)	4/4 (100) 22/56 (39.3)	0.0312	5/5 (100) 18/55 (32.7)	0.0336
Duration on APD, month, (mean)	31.1 + 9.5 30.7 + 10.4	0.3292	29.7 + 10.2 30.1 + 9.4	0.3844
BUN, mg/dl (mean)	47.6 + 9.7 48.3 + 11.2	0.4004	46.0 +7.8 45.8 + 10.1	0.4005
Creatinine, mg/dl (mean)	7.2 + 2.2 7.1 + 2.4	0.4137	7.8 + 2.7 8.0 + 2.2	0.3334
Hemoglobin, gm/dl (mean)	9.8 + 2.4 10.1 + 2.2	0.3146	10.1 + 2.7 10.3 + 1.9	0.4113
Serum K+, mEq/l (mean)	3.8 + 1.1 3.7 + 1.8	0.4480	3.7 + 2.0 3.7 + 2.1	0.5131
Serum albumin, gm/dl (mean)	3.7 + 2.2 3.8 + 1.2	0.3433	3.6 + 1.9 3.7 + 2.2	0.5010

APD: automated peritoneal dialysis, BUN: blood urea nitrogen, K+: potassium

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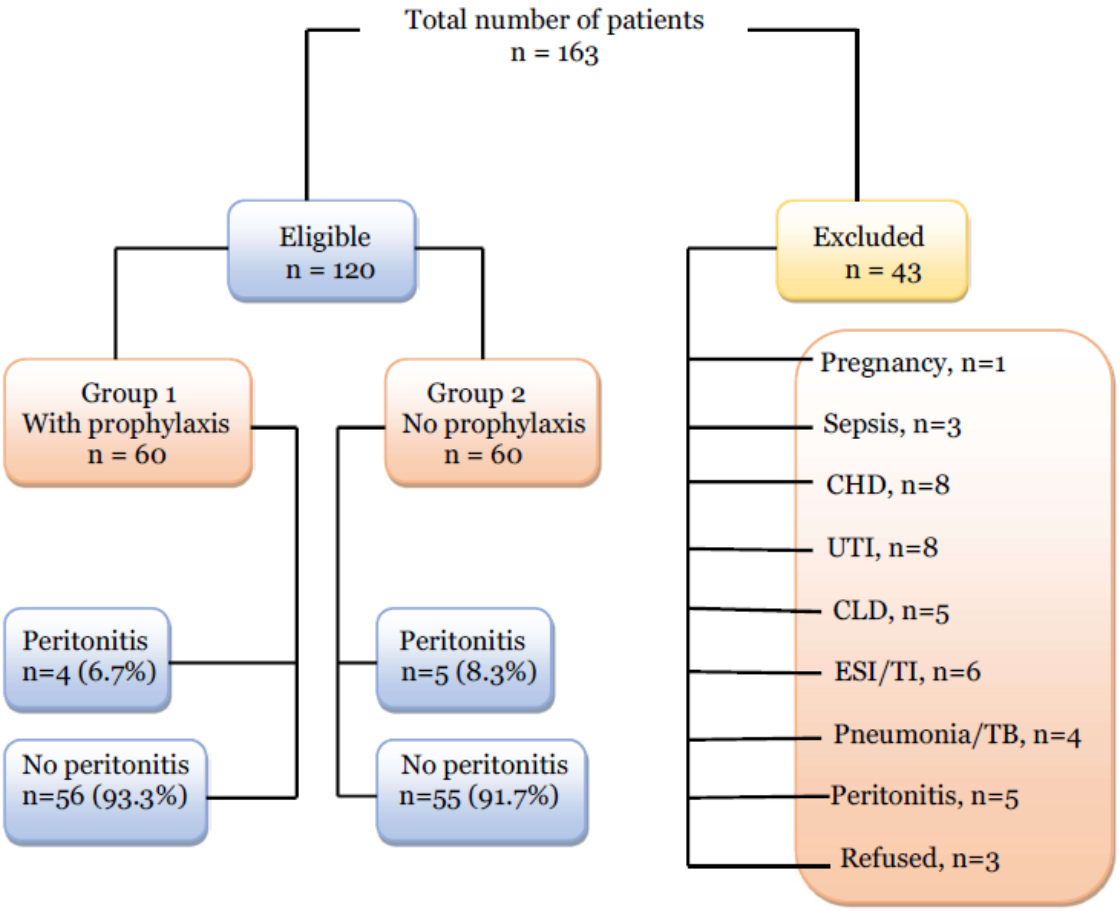

Figure 1. Consort diagram demonstrating study design and patients' progress

CHD: chronic or valvular heart disease, UTI: urinary tract infection, CLD: chronic liver disease, ESI: exit-site infection, TI: tunnel infection, peritonitis: ongoing or previous.

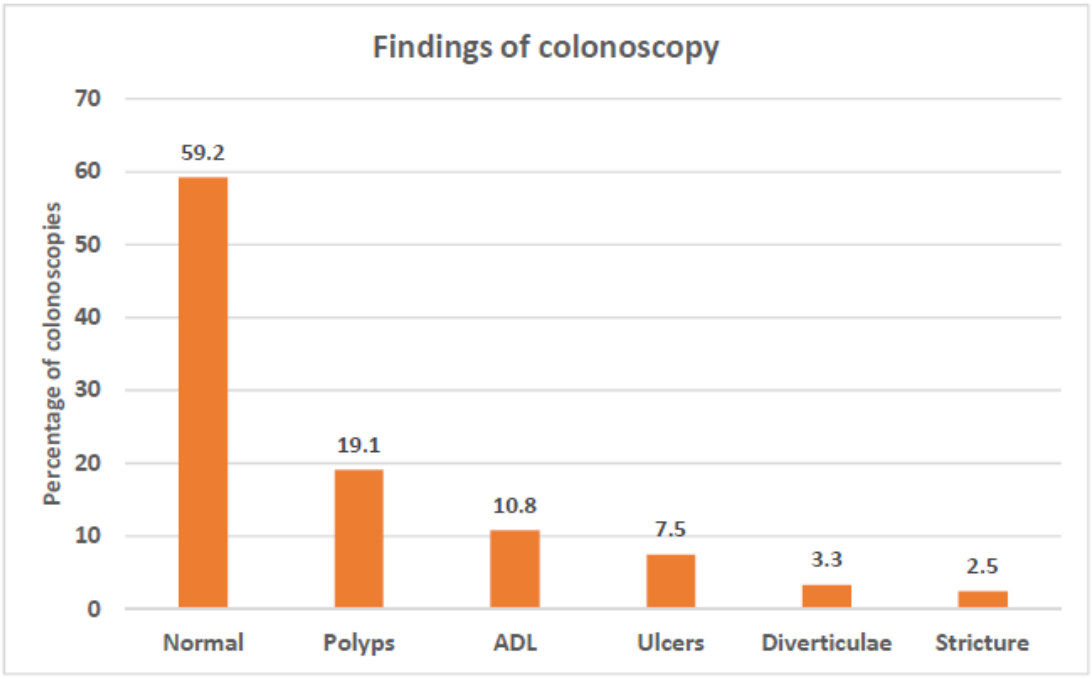

Figure-2. Colonoscopy findings in the study population

Discussion

Peritonitis in PD patients after colonoscopy is a known but infrequent complication. A retrospective study from Hong Kong revealed an average risk of peritonitis after colonoscopy of 6.3% in 77 CAPD patients after 97 endoscopic procedures. Colonic biopsy or other interventions such as polypectomies apparently did not increase the risk of peritonitis (19-21). The source of contamination in those cases not associated with catheter exit-site or tunnel infections is thought to be transmural (1, 19). Micro-organisms may gain access to the peritoneum from the intestinal lumen or through genital organs (22, 23). Diagnostic instrumental procedures, such as colonoscopy, have been implicated in the development of these peritonitis episodes (14, 15). Post colonoscopy peritonitis in patients undergoing PD is thought to result from translocation of microorganisms across the bowel wall (24) and it has been alleged that gastrointestinal endoscopic procedures in those patients can lead to peritonitis (25). However, in many cases there is no evidence that links peritonitis to colonoscopy as a risk factor (21, 22). The recommendations concerned with colonoscopy in PD patients are not based on randomized controlled trials because such studies in PD patients are limited. Where there is no definitive evidence; but the group feels there is sufficient experience to suggest a certain approach, this is indicated as "opinion" based. The recommendations are not meant to be implemented in every situation but are recommendations only. Each center should examine its own pattern of infection, causative organisms, and sensitivities and adapt the protocols as necessary for local conditions (20). Contrary to Yip et al (11) who, in a selected cohort, suggested that diverticulosis may be a risk factor for the development of enteric peritonitis, we did not encounter such complication in our patients. Moreover, colonic diverticulosis did not appear to affect the outcome of colonoscopy in our study. Supporting our findings was the report by Toda et al. (26) who studied 317 PD-candidate patients over approximately 4 years and concluded that asymptomatic diverticulosis identified by computed tomography was not a risk factor for enteric peritonitis in their study population. In addition, colon biopsy or polypectomy did not appear to further increase the risk of peritonitis in our cohort. A retrospective study by Yip et al. (27) found that the risk of peritonitis after colonoscopy without antibiotic prophylaxis was 6.3%. The authors however, indicated that it lacks statistical significance. Interestingly, the International Society for Peritoneal Dialysis recommended antibiotic prophylaxis before any procedure involving the abdomen or pelvis, including colonoscopy (16). Again, it is important to notice that these recommendations were based only on observational studies and case reports. The 2005 and the 2016 ISPD guidelines suggested empirical 1- gram ampicillin or aminoglycoside with or without metronidazole before colonoscopy (16, 28). These guidelines recommend antibiotic prophylaxis for CAPD patients undergoing colonoscopy with polypectomy; however, there has been little literature to support these recommendations. Studies on these guidelines are rare, and randomized controlled trials to support this recommendation are lacking. Moreover, these new guidelines clearly stated that the optimal antibiotic regimen has not been determined by clinical studies yet (16). Contrary to the suggestions above, the American Society for Gastrointestinal Endoscopy and the British Society of Gastroenterology do not suggest prophylactic antibiotics before colonoscopy (29, 30). There exists a lack of consensus on this issue. There have been few case reports in the literature on peritonitis following colonoscopy in peritoneal dialysis patients (6, 7, 14-16). These reports suggested that instrumental procedures such as colonoscopy may precipitate gram-negative peritonitis in PD patients. On the other hand, some literature reported bacterial peritonitis following endoscopic polypectomy in peritoneal dialysis patients despite antibiotics prophylaxis (10). So far there are no strong data demonstrating a causal association between endoscopic procedures and bacteremia or that antibiotic prophylaxis prior to endoscopic procedures protects against bacteremia. Much of the existing data reflects estimated risk associated with conventional endoscopic techniques. There are no results available that confidently quantify bacteremia rates with newer endoscopic procedures such as per oral endoscopic myotomy, endoscopic submucosal dissection, flexible colonoscopy or polypectomy (11). Use of a single IP antibiotic prophylaxis was encouraged by many authors based on pharmacokinetic (PK) evidences. In the study of the PK of IP cefazolin and ceftazidime, Elwell, et al. reported serum cefazolin and ceftazidime levels that exceeded the minimum inhibitory concentrations for susceptible organisms (8 mg/L) throughout the 20 hours study period. Predictive equations suggested that 1000 mg IP of cefazolin or ceftazidime every 24 hours would produce average steady-state trough serum cefazolin and ceftazidime concentrations of 70 +/- 52 mg/L

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and 17 +/- 7 mg/L, respectively. In another study, Tobudic, et al. (28) reported that the maximum serum concentrations after intravenous and IP administration of other antibiotics were comparable. Ratios of IP to systemic exposure indicated good systemic exposure after intraperitoneal application but limited penetration of the antibiotic into the peritoneal fluid after the intravenous dose. Similar results were reported by Weisholzer, et al. and Low, et al. (29). In 2006, A well designed prospective study of PK of cefepime by Elwell, et al. suggested that most APD and CAPD patients would achieve adequate serum cefepime concentrations if infused with a standard dose of 1000 mg given IP (9). It is becoming an accepted policy to use IP instead of IV antibiotics in PD patients when needed, as IP applications of antibiotics achieves a higher target-site concentration, less gastrointestinal side effects and improved compliance. We studied APD patients with and without IP antibiotic prophylaxis before flexible colonoscopy. The difference in peritonitis episodes in our study between the two groups was not statistically significant (6.7% vs. 8.3%, $p > 0.05$). Interestingly, transient bacteremia occurs frequently during routine daily activity, often at rates exceeding those associated with endoscopic procedures. Brushing and flossing of teeth has been associated with rates of bacteremia of 20% to 68%, use of toothpicks with rates of 20% to 40%, and even activity that might be considered entirely physiologic, such as chewing food, with rates ranging from 7% to 51%. By multiple logistic regression analysis, the use of prophylactic antibiotics prior to colonoscopy was not a predictive variable for developing post-colonoscopy peritonitis in our study population. One patient from those who received prophylactic antibiotics had Candida species in peritoneal fluid culture. Although we could not prove the relation between antibiotic prophylaxis and the development of this un-expected growth, it is not unreasonable to speculate that antibiotic administration may have favored intestinal non-bacterial overgrowth (Candida in our case) and use of more than one antibiotic may make it even worse. Given the notorious possibility of resistant strains' development and the relative rarity with which most PD patients undergo colonoscopy procedures, the frequency and risk of colonoscopy-related bacteremia, as we demonstrated in our study, is trivial compared with the frequency of bacteremia encountered with routine daily activity. This may provide a reasonable basis against routine administration of antibiotic prophylaxis prior to all endoscopic procedures. There are, however, some limitations in our study. First, this study was conducted in a single tertiary medical center, and endoscopy-associated complications may vary in different hospitals. Second, the study was conducted on a selected group of APD patients after applying strict exclusion criteria. Third, the study used a single antibiotic and may have underestimated the importance of combined antibiotic prophylaxis. Therefore, larger randomized trials are required to explore the necessity of antibiotic prophylaxis in the prevention of post-colonoscopy PD peritonitis. Nevertheless, our study has the strength of being the first prospective randomized study in this field.

Conclusion

There was no correlation between the risk of peritonitis and intraperitoneal prophylactic ceftazidime. Only old age, diabetes mellitus and low serum albumin appeared to be of significance. Neither polypectomy; partial or complete nor diverticulosis were associated with increased incidence of post-colonoscopy peritonitis. However, the study may have underestimated the importance of antibiotic prophylaxis. Therefore, larger prospective multicenter randomized trials are needed.

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