CHAPTER 6

DISCUSSION

6.1 Base Line Characteristics

Between January 1993 to December 1998 , 102 CAPD patients were included in the analysis. Base line characteristics showed well balanced between middle age patients, and aging . The mean age was 57.3 years. 40 patients were diabetic. Peritonitis occurred 157 episodes in 72 cases (70.6%). The average rate of peritonitis was 1.54 episodes per year per person. The range varied from 0 to 9 episodes per case.

6.2 Factors affected the rate or risk of Peritonitis

The distribution of rate of peritonitis is not normal distribution by one-sample Kolmogorov-Smirnov Test (table 5.13), so the analysis by multiple regression is not appropriate . Logistic Regression Analysis is performed because, it is one type of the analysis which can serve the propose of the study to find the risk factors of peritonitis. By Logistic Regression Analysis (table 5.14), BUN level, duration, and education are found to be the risk of peritonitis ($P<0.05$).

Although , there is no report about the BUN level to the risk of peritonitis, but in this study, BUN level is the first factor that reduces the risk of peritonitis. Because the exponential is near to 1 (0.9645, 95% CI 0.933 - 0.997), so this effect is very small. The low BUN level has a risk only 1.036 times than the high BUN level (95%CI 1.003 - 1.071), which has no clinical significance .

However, it is surprising because BUN is the waste product and high BUN level should reflex the low immunity.

BUN (Blood urea nitrogen) is the waste product from protein metabolism. The high level of BUN represents the inadequacy of CAPD. The low level represents not only the adequacy, but also the malnutrition state. BUN level in this study can not reflect the nutrition or adequacy of the patients, because this study is a retrospective analysis. Some cases were assessed the adequacy of the dialysis. However , this finding can be explained by many hypothesis. The first, it is possible that the treatment between high BUN patients may different from the remainder. It is possible that the patients performed their dialysis more carefully, because they knew , from the physicians, that their blood chemistries were not good. In addition, because high BUN level represents the accumulation of waste product, so the patients might feel discomfort and visit the hospital more frequently, or they required some more treatment or some drugs that affected the peritonitis . The second , in high BUN patients , there may be some difference, from the low BUN group, in peritoneal dialysate. The BUN level , Ca level or other chemistries, in peritoneal dialysate in this group, may be higher or lower than the remainder, and affect the growth of bacteria or the peritoneal macrophages. Peritoneal macrophages (PM) perform first-line defense activity against peritonitis. Lin CY , 1990, studied the peritoneal macrophage function in CAPD, and found that this function correlated to the peritonitis (53) . PM function can assessed by many methods such as bactericidal activity , phagocytosis index, H202 production, interleukin-1, gamma interferon (INF-gamma),and tumor necrosis factor (TNF) production . The study of Suga H, 1990, showed that, low calcium level in the dialysate impaired the macrophage function (54). In the present , there is no study about the correlation of BUN level or other chemistries (except calcium level), in dialysate to macrophage function.

The adequacy of dialysis, the detail in treatment , and the chemistry of peritoneal dialysate, the function of macrophages, should be investigated in further cohort study.

Duration is the second factor that increases risk of peritonitis . This risk of high duration is only 1.0015 times than low duration (95%CI 1.002 - 1.0028), which is very small and has no clinical significance. Because the outcome of Logistic Regression is dichotomous (peritonitis or not) , so it should be true that the more duration of CAPD should give the more chance to develop peritonitis in one patient.

Education level is the third factor that is more strong to reduce the risk of peritonitis (Exp B. 0.2735, 95%CI 0.0950-0.786). In the analysis, education was divided into two groups, low education and high education. From the exponential value, the risk of peritonitis in low education is 4.21 times of high education (95%CI 1.27 - 10.52 times). The CAPD is the technique that the patients have to change the bags of the dialysate by themselves with aseptic technique. High educated patients may change the dialysate more carefully . They may also visit the physicians more earlier when there are the problems in dialysis such as catheter infection, fluid leakage. From the previous studies education was found to be the risk in the study of Korbet SM, in 1993 . He performed a retrospective assessment of risk factors for peritonitis among an urban CAPD population and reported that education level is one of the risk factors (11). The role of education may take part in the study of Chan-O, et al, 1993, in Thailand. In that study , they found , the right to get government medicare system, the failure to practice aseptic techniques, and the poor personal and accommodation hygiene were the risk of peritonitis. Low education may relate to the failure to practice aseptic techniques, and the poor personal and accommodation hygiene. However the well trained

procedure and the repeated training programs at the appropriate time should minimize this problem.

6.3 Factors Associated to Time to first peritonitis episode

In cases of peritonitis, by Pearson Correlation , duration , Hb, Alb, BUN, and bag system, are the factors that significant correlate to time to first episode of peritonitis. The other factors that have some correlation (correlation > 0.1) is the presence of catheter infection.

By Multiple Regression Analysis, three factors, are found associated with the time to first peritonitis episode. The first factor is duration that associates with the time to first episode of peritonitis (beta = 0.277, P = 0.000). By this correlation, if the time to first episode of peritonitis prolongs , it is the tendency of duration of CAPD to prolong too. However , the duration in this study is not the survival time. The duration is the time form insertion CAPD to the time at the end of the study, or the time which the patients develop uncontrolled peritonitis or receive kidney transplantation. So this correlation cannot be interpreted as the prognosis of CAPD.

BUN level is the second factor that associated with time to first episode of peritonitis (beta = 3.812, P = 0.017). By this correlation, if BUN level is high, the time to first episode of peritonitis prolongs. It means that, BUN reduces the risk of peritonitis. This result is the same as the result from the analysis by Logistic Regression . By Pearson Correlation Analysis, BUN correlates to time to first peritonitis episode (correlation = 0.341, P value = 0.003). The explanation of BUN in prolonging the time to first peritonitis episode is the same as mentioned in part of Logistic Regression Analysis.

The two evidences in both analysis confirm that the further study in high BUN patients about the chemistry of peritoneal dialysate and the function of macrophages, should be performed .

Hb level is the third factors that highest associate with time to first peritonitis episode (beta = 24.97, P = 0.027). Hemoglobin is the substance in red blood cells that can carry oxygen from lung to all tissues of the body. Low Hb level represents the anemic state of the patients . Patients with anemia will have many symptoms such as weakness, syncope. Anemia is the common problem in CAPD patients. Kidney is the organ that produce erythropoietin, which take part in genesis the red blood cell, so kidney failure affects the anemia. The high Hb level represents the ability of transferring the oxygen to the tissue that should improve the immunity . Recombinant erythropoietin (R-EPO) is the new drug that is effective in correcting anemia in patients on hemodialysis or CAPD. In the past, R-EPO was given to the patients by subcutaneous route. Now many physicians tried to study the administration of R-EPO in intraperitoneal route. Anemia can cause many symptoms. However anemia did not be reported to be the risk of peritonitis in the previous studies. From this knowledge, the correction of anemia can reduce the risk of peritonitis.

6.4 DM

DM is one of the controversial risk factors of peritonitis. Some researcher demonstrated DM as the risk factors such as Lye WC, in 1993 (23), Tielens E, in 1993 (16). Zent R, in 1994. In contrast, some authors found that the rate of peritonitis was not increase in diabetes, such as Viglino G, in 1994, (24), Domrongkitchaiporn S, in 1994 (1), and Bistrup C, in 1995 (7).

There are 40 diabetic patients (39.2%) in this study. The baseline characteristics show non statistically different between diabetic and non diabetic group, except age (table 7). By logistic regression analysis , DM is not the risk of peritonitis. The average rate of peritonitis in diabetic group is non statistically different from non diabetic . However, the mortality rate of diabetic patients is higher than non diabetic cases (40% Vs 17.7%, P value 0.02). There is no difference in technique survival in diabetic patients . Log Rank Test Analysis. The mean survival of diabetic patients is shorter than non diabetic group (970 days Vs 1509 days, P value .0056). The short survival can be explained by two factors. The first, DM associates with many diseases, such as ischemic heart disease, cerebrovascular disease. All of these, can affect the mortality. The second, the mean age in diabetic patients is higher than non diabetic patients (59.9 : 54.2 years , P value 0.02).

6.5 Aging

Age is the most interesting factor which is still controversy to be the risk of peritonitis. Most of the studies reported outcome of CAPD only in aging. Some investigators showed good outcome, such as Nichollis, 1984 (51), Suh H, 1993 (52). Some found worse outcome, such as Valente, 1990 (28), Sreide R, 1991 (26).

Chan-O and Sumethkul, from Ramathibodi Hospital, studied the risk factors in Thai CAPD patients and suggested that, limiting CAPD by age should be considered. They found that old patients tended to have the higher rate of peritonitis and shorter survival time (29). However, most of the patients in that study was middle age (age < 60 years) . In this study, there are 50 patients in the middle age group, and 52 cases in aging group. Both groups are well

balance in base line characteristics. By logistic regression analysis , age does not affect the risk of peritonitis and by multiple regression analysis , age does not associate to time to first peritonitis episode. The average rate of peritonitis in aging is non statistically different from the middle age. By survival analysis, aging does not affect both technique survival and mean survival. From this knowledge , the limitation of CAPD by age should not be performed.

Staphylococcus aureus infection

Staphylococcus infection is the risk factor which can be prevented in peritonitis. Exit site infection from S.aureus, and S.aureus nasal carriage were indicated to be the risk of peritonitis in many studies. Some studies reported S.epidermidis as the most common cause of peritonitis (29-30). Several studies found S.aureus to be the major cause of catheter infection (12, 30-37) and peritonitis (38, 39). Catheter infection from S.aureus was found associated with S.aureus peritonitis (12, 40, 41).

Chan-O and Sumethkul, from Ramathibodi Hospital, reported 81 episodes of peritonitis in seven-year study of CAPD patients. Only 16 episodes (19.75%) of peritonitis were cultured positive. In that group, S. aureus caused 2 episodes of peritonitis (12.5%) , and Coagulase negative staphylococci caused 4 episodes(25%). In this study, S.aureus caused only 2 episodes of peritonitis (1.3%) , and coagulase negative staphylococci caused 6 episodes(3.8%). From these two studies, Staphylococcus infection is not the common causes of peritonitis. However, it is more common in catheter infection. In this study, there were 47 episodes of catheter infection in 29 patients (28.4%). S. aureus caused twenty four episodes (51.1%) of catheter infection. Coagulase negative staphylococcus caused two episodes (4.3%).

All characteristics of the patients with S. aureus infection are not statistically different from the remainder except albumin level and duration. Albumin level in S.aureus infection cases is higher than non S.aureus group (3.5 vs. 3.1 gm/dl, P=0.01). Duration of S.aureus is longer than non S.aureus group (1038 days vs. 561 days, P=0.001). The average rate of peritonitis in S. aureus infection group is not statistically different from non infected patients. S.aureus infection is not statistically different in technique survival in comparison with no infected group and other infection. Survival rate of S.aureus infection is not different from the patients with no infection. In comparison between other infection, the survival rate of S. aureus infection is better than other infection by Log Rank Test . The better in survival rate may come from the easier in treatment this infection.