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Research Article

Mupirocin or Neomycin for Exit-Site Care in Children with Chronic Peritoneal Dialysis

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Abstract

Objectives: Exit-site care is important in prevention of Peritoneal Dialysis (PD) associated infections. But there was no clear recommendation for standard exit-site care. The aim of the study was compare local mupirocin and neomycin in exit-site care of chronic PD.

Methods: 32 children in chronic PD was included the study. The mean age was 11.3±4.8 years and mean follow-up period for dialysis before study was 15.9±10 months. The patients were randomized to mupirocin (n=16) or neomycin (n=16) groups and followed for 12 months. Mupirocin or neomycin was added to standard exit-site care with local dressing every alternate day.

Results: Total 313 patient follow-up months was recorded. Mean exit-site score at beginning and end of the study was not different in both groups. The increasing of the exit-site score between beginning and end of the study was significant in mupirocin group ($p<0.01$). Total 6 exit-site infection (3 culture negative, 1 MRSA, 1 *pseudomonas* and with 1 *corynebacterium*) was found in 4 patients. The incidence of exit-site infections was 24 treatment months in mupirocin group and no exit-site infection was found in neomycin group ($p=0.036$). Total 15 peritonitis (5 culture negative, 4 MRSA, 2 *streptococcus*, 2 staphylococcus, 1 *E.coli*, 1 *enterococus*) was recorded in 13 patients during study. The peritonitis incidence was not different between mupirocin and neomycin groups respectively (20.9 vs. 20.9 treatment months.

Conclusion: Neomycin is more effective then mupirocin for prevention of exit-site infection in children with chronic PD with relatively higher local adverse events.

Introduction

Peritoneal Dialysis (PD)-related infections are serious complications that can lead to hospital admission, catheter loss, PD failure and worsening of survival [1,2]. Exit-Site Infections (ESI) has been shown to have a significant impact on PD complications. ESI is the pathway to developing subsequent tunnel infection and peritonitis that leads to high rates complications [3,4]. Exit-site infections and catheter-related peritonitis are caused by especially gram-positive *Staphylococcus* aureus, and gram-negative *pseudomonas aeruginosa* [5,6]. Infection with *S. aureus* and *P.aeruginosa* is a major challenge in PD therapy [7]. As a result, efforts should be focused more on prevention rather than the treatment of ESI as a means of reducing the rate of PD-related infections.

Many different exit-site dressing protocols have been proposed as a preventive measure to decrease infections by these organisms [8-10]. But there was no clear recommendation for standard exit-site care. The International Society for Peritoneal Dialysis (ISPD) recommends implementing exit-site dressing immediately post-operatively and at least daily or on alternate days after completing training [10]. Different cleansing agents for exit-site care with either povidone-iodine or antibacterial soap have been studied [11,12]. Mupirocin calcium ointment 2% applied as prophylaxis to the exit site has been shown to be effective in reducing *S.aureus* exit-site infection but is not effective against *pseudomonas* or other gram-negative infections [9,13]. In contrast, aminoglycosides such as gentamicin cream applied daily to the exit site as prophylaxis reduces gram-negative exit-site infection and are as effective against *S.aureus* as mupirocin [14]. There are no studies showing any benefit in the use of aminoglycosides over mupirocin for care of exit-sites in long-term chronic PD patients.

The purpose of this study is to evaluate the potential effectiveness of the application of mupirocin or neomycin for catheter exit-site care in preventing ESI and peritonitis in children on chronic PD.

Material and Method

The study was conducted at the Department of Pediatric Nephrology and Dialysis, Dr. Behcet Uz Training and Research Hospital, Izmir, Turkey. Thirty-two children (17 female, 15 male) who were on chronic PD and practicing PD for more than 3 months were included in the study. Children with colostomy or vesicostomy or under 2 years old was excluded because known higher rates of PD-associated infection incidence. The patients were randomized to mupirocin (n=16) or neomycin

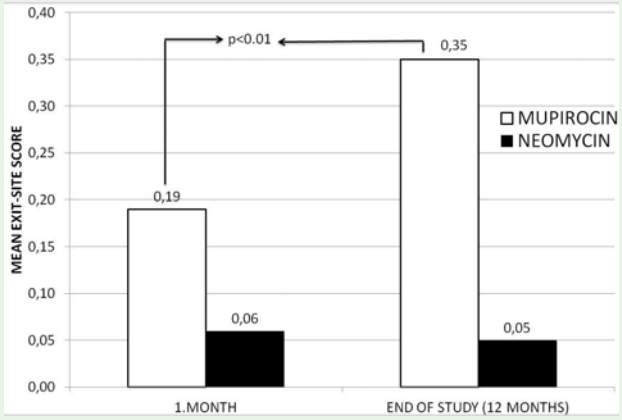

Figure 1: Mean exit-site score start and end of the study (12 months) between mupirocin and neomycin groups.

(n=16) groups and followed for 12 months. Mupirocin or neomycin was added to standard exit-site care with local dressing every alternate day. Exit-site infection was diagnosed according to standard scoring system [15]. Exit-site infection was defined as purulent discharge, with or without erythema of the skin at the catheter-epidermal interface [15]. A tunnel infection was defined as erythema, edema or tenderness over the subcutaneous pathway. Peritonitis was diagnosed with fever, abdominal pain, cloudy peritoneal dialysis effluent and increasing leukocyte (>100 cb/mm3, >50% neurophile).

All PD catheters were placed percutaneously by an experienced pediatric nephrologist in our unit. Tenckhoff swan-neck double-cuff curled catheters were used in all patients.

The catheter exit site care was made every other day catheter replacement by peritoneal dialysis nurse until the completion of the patient's relatives training. Patients were required to clean their exit site using povidone-iodine after drying, followed by topical mupirocin or neomycin antibiotic application to the exit site. The exit site was then covered with a sterile gauze dressing and the catheter immobilized with tape.

Infection-related complications, such as, ESI, tunnel infection and peritonitis were monitored. Exit-site swab cultures from the

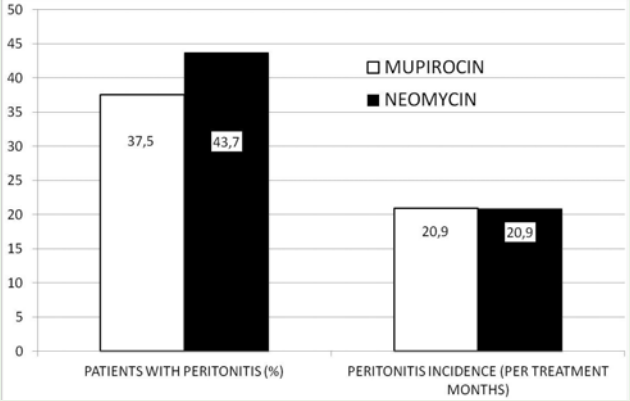

Figure 2: Percentage of patients with peritonitis and peritonitis incidence between mupirocin and neomycin groups.

catheter exit site were taken when infection was suspected. Samples of peritoneal effluent were also cultured when, clinically, peritonitis was suspected according to recommendations [15].

Local ethics committee approval was recorded before study.

Statistical Analysis

Non-parametric Mann-Whitney U test was used to compare variables within groups. The chi-square test and Fisher's exact test (when available) was used to compare groups. The data was expressed as the mean±Standard Deviation (SD) and a p value of less than 0.05 was considered to be statistically significant.

Results

The mean age was 11.3±4.8 years and mean follow-up period for dialysis before study was 15.9±10 months. Ten patients were excluded from the study for transplantation (3 patients), transfer to hemodialysis (3 patients), exitus (2 patients) or local significant adverse events of mupirocin or neomycin (each one patient). Total 313 patient follow-up months was recorded.

Mean exit-site score at the beginning and at the end of the study was not different in both groups. The increasing of the exit-site score between at the beginning and at the end of the study was significantly elevated in mupirocin group than neomycin group ($p<0.01$) (Figure 1).

Total 6 exit-site infection (3 culture negative, 1 MRSA, 1 *pseudomonas* and with 1 *corynebacterium*) was found in 4 patients. The incidence of exit-site infections was 24 treatment months in mupirocin group and no exit-site infection was found in neomycin group ($p=0.036$) (Table 1). No tunnel infection was determined during the study.

Total 15 peritonitis (5 culture negative, 4 MRSA, 2 streptococcus, 2 *staphylococcus*, 1 *E.coli*, 1 *enterococus*) was recorded in 13 patients during the study. We observed 2 MRSA, 1 streptococcus, 1 *enterococus*, 1 *staphylococcus* infections in the neomycin group and 2 MRSA, 1 streptococcus, 1 *staphylococcus*, and 1 *E.coli* infections in the mupirocin groups.

There were 2 cases in mupirocin group and 3 in Neomycin group with culture negative peritonitis. The peritonitis incidence was not different between mupirocin and neomycin groups respectively (20.9 vs. 20.9 treatment months) (Figure 2).

Local adverse events (redness, crusting or bullous skin lesions) was observed in 12.5% of mupirocin and 25% of neomycin group patients ($p>0.05$).

Table 1: Exit-site infections in mupirocin and neomycin groups.

Group	Culture negative	Culture positive*	Total
Mupirocin	3	3	6
Neomycin	0	0	0
Total	3	3	6

*1 methycilline resistant staphylococcus aureus, 1 pseudomonas and with 1 corynebacterium (p:0.023)

Discussion

The PD community has tried very hard to prevent catheter-related infections; however, there is no uniform policy. In recent years, the effectiveness of local application of mupirocin at the exit site has been observed in different parts of the world [9,11]. Very low rates of ESI, especially gram-positive ESI, have been demonstrated. Long-term use of mupirocin, however, is not without its problems. First, emergence of resistance after several years of routine use of mupirocin has been reported [9,10]. Second, mupirocin is not active against most gram-negative organisms. This is reflected by the very low incidences of gram-positive infection in most studies. After eradication of gram-positive infection, other organisms, gram negative organisms in particular, may take the lead. Last but not least, the high cost of routine mupirocin application is another major consideration. Neomycin, on the other hand, possesses activities against both gram positive and gram-negative organisms and the cost of neomycin cream is much lower than that of mupirocin ointment.

There are no studies showing any benefit in the use of neomycin over mupirocin for care of exit-sites in long-term chronic PD patients. To our knowledge, ours is the first study looking into the role of topical application of mupirocin or neomycin at the exit site on the rate of ESI and peritonitis in chronic PD children.

Bernardini and colleagues was compare gentamicin cream versus mupirocin ointment in the prevention of ESI [14]. Their study showed the superior effect of gentamicin against gram-negative organisms while at the same time maintaining gram-positive coverage.

In the study of Chu et al similar infection rates were observed: concerning ESI, the group on gentamicin cream had infection rates similar to mupirocin ointment [16].

We evaluated effectivity of mupirocin and neomycin on the ESI occurrence and found that neomycin was more effective in ESI prevention.

In the study of Chu et al the important observation was the virtual absence of gram-positive ESI in the mupirocin group. But in our study, ESI with gram positive microorganisms such as MRSA and *corynebacterium* in mupirocin group were seen. This case can be important for the aspect of mupirocin resistance.

On the other hand, peritonitis rates were similar in the two groups in Chu and colleagues' study. In contrast to the study by Bernardini and colleagues [14], gram-negative peritonitis occurred at the same rate in both groups and showed superior results for gentamicin in preventing gram-negative infections, with gram-positive coverage similar to that of mupirocin [14]. In our study, there were no significant differences between cases treated with neomycin or mupirocin for the development of peritonitis. There were both gram negative and positive growth seen in mupirocin group and only gram positive growth in the neomycin group.

Conclusion

In conclusion, neomycin cream is superior to mupirocin ointment in the prevention of ESI. In this study, peritonitis occurred at the same rates in both groups. At this moment, both drugs can be recommended for prophylaxis of PD-related peritonitis.

Centers should examine trends in infection rates and bacterial susceptibilities to determine the most appropriate agent for prevention of ESIs and peritonitis in PD patients.

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