PD solution (Baxter-Dianeal 137, Deerfield, IL) in a day. He had no prior history of peritonitis. The clinical picture was dominated by mild diffuse abdominal pain and tenderness. Analysis of the peritoneal effluent demonstrated a white blood cell (WBC) count of 480/μl with 90% neutrophils. Gram stain of the effluent revealed no bacteria. Culture of the specimen grew slow-growing, Gram-positive, pleomorphic, catalase-negative bacteria that were identified as Gemella morbillorum. The minimal inhibitory concentrations determined by E Test® for penicillin and vancomycin were 0.006 and 1 mg/L, respectively, which were interpreted as susceptible. Prior to identification of the bacteria, ampicillin–sulbactam (1.5 g bid) and ciprofloxacin (200 mg bid) were started intravenously as the regular therapy for CAPD peritonitis in our institution, and the same combination continued for 14 days. The WBC of the peritoneal effluent dropped to zero at the end of the first week of therapy. The patient was well when he was seen 1 month after his discharge.

Gemella morbillorum and Gemella hemolysa are Gram-positive coccobacilli of the mucus membranes of humans. Only a few cases of Gemella infection have been reported to date, and have been predominantly endovascular infections [2]. The first episode of peritonitis caused by Gemella morbillorum was successfully treated with cefazolin [3].

Gemella may be more involved in clinical disease than is presently recognized. They can be incorrectly identified as viridans streptococci, identified as Neisseria spp. because they are easily decolorized during Gram staining or left unidentified [2]. Our patient had no other underlying disease besides end-stage renal failure and no other infectious foci prior to this peritonitis episode. Translocation from the gastrointestinal tract may be responsible for this episode. We did not culture the stool of the patient before antimicrobial therapy to demonstrate Gemella. It is difficult to estimate how this microorganism caused this episode.

Gemella infections are seldom seen, and the identification in the laboratory has some limitations because of the characteristics of this bacteria. Therefore, the microbiological samples should be interpreted carefully and Gemella should be taken into consideration when slow-growing, catalase-negative, Gram-positive cocci are seen in samples. There are fatal Gemella infection reports in the literature [4,5]. Our case improved well with a β-lactum antibiotic as in the other patient mentioned above [3]. The response of two patients to therapy is not enough to reach a general conclusion about the prognosis, but the in vitro susceptibility results may be a useful guide in the management of these patients.

Conflict of interest statement. None declared.

Baskent University
Faculty of Medicine
Infectious Disease and Clinical Microbiology
Ankara
Turkey
Email: okurtazap@baskent-ank.edu.tr


doi:10.1093/ndt/gfh721

Measurement of cyclosporin exposure in renal transplant recipients during the early post-operative period: is C2 alone sufficient?

We note the association between achievement of target C2 [the 2 h post-dose blood cyclosporin (CsA) concentration] values and a lower incidence of acute renal transplant rejection reported by di Paolo et al. [1]. This is supported by other studies [2,3]. The authors also state that target C2 was not achieved during the early post-operative period in a significant proportion of patients, despite using high doses of Neoral®. The experience with C2 monitoring in our unit has been very similar, but our data also suggest that C2 is not a reliable measure of CsA exposure in the first week post-transplantation.

Having demonstrated an association between C2 and acute rejection (AR) in a retrospective study of patients in whom CsA dose adjustment was based solely on trough CsA levels (C0) [4], we introduced a target-driven protocol for CsA dose adjustment that was based primarily on C2 but also C0 and various clinical factors (see below). The protocol was applied to 60 consecutive renal transplant recipients (36 male, 55 Caucasian, age 45.9 ± 13.6 years, four with diabetes mellitus, time on renal replacement therapy 59.3 ± 49.4 months, 51 first grafts). The donor profile was as follows: 28 male, age 47.7 ± 16 years, 10 living/50 cadaveric. The mean number of human leukocyte antigen mismatches was A 0.79 ± 0.53, B 0.89 ± 0.54 and DR 0.19 ± 0.44. The standard immunosuppressive regimen comprised Neoral®, prednisolone and azathioprine (AZA), but 10 patients at high immunological risk received Neoral® and azathioprine (AZA), but 10 patients at high immunological risk received basiliximab and 11 were treated with mycophenolate mofetil in place of AZA. Neoral® was commenced at 10 mg/kg/day in divided doses and then adjusted according to C2 values (for doses 4/5 and then every fourth dose until hospital discharge, target range 1350–1650 ng/ml). Neoral® dose increases for patients with suboptimal C2 values were waived if paired C0 values exceeded 500 ng/ml or there was delayed graft function and/or clinical evidence of CsA nephrotoxicity.

The incidence of acute allograft rejection (biopsy-proven or suspected on clinical grounds with a good response to increased immunosuppression) within the first 20 days post-transplant was 10%. Delayed graft function occurred in 33.3% of cases. The incidence of adverse events was as follows: hepatitis [alanine aminotransferase >50 IU/l] 27%, hyperbilirubinaemia (serum bilirubin >30 μmol/l) 27%, haemolytic uraemic syndrome 3.3%, CsA nephrotoxicity (with improvement in serum creatinine following CsA dose reduction) 8.3%. Target range C2 values were achieved in 42, 67 and 67% of patients by days 3, 5 and 7, respectively. There was a non-significant trend towards a lower incidence
of AR in patients who achieved target range C2 values by days 3 (8 vs 11.4%), 5 (7.9 vs 13.6%) and 7 (7.5 vs 15%) post-transplant. The C2:C0 ratio changed considerably during the first week post-transplant: median values on days 3, 5 and 7 were 2.55, 2.82 and 3.46, respectively, with corresponding values of 2.45, 3.12 and 3.55 for patients who had data for all three time points (Figure 1, \( n = 40, P < 0.01 \)). The observed trend may be attributable to a progressive improvement in CsA absorption from the gastrointestinal tract (and therefore a more rapid attainment of peak CsA concentrations in the blood) and/or a progressive increase in CsA metabolism.

In summary, we have observed that although achievement of target C2 values is associated with a lower incidence of acute renal allograft rejection, changes in Neoral\textsuperscript{®} dose that are based solely on C2 data may be misguided because C2 is an unreliable measure of CsA exposure in the first week post-transplantation. It would seem prudent to take account of both C2 and C0 as well as clinical factors when making early adjustments to Neoral\textsuperscript{®} dose.

Conflict of interest statement. None declared.