Bacterial and Fungal Infections in the Early Post-transplantation Period After Simultaneous Pancreas-kidney Transplantation: Etiological Agents and Their Susceptibility

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ABSTRACT

Objective. This study aims to evaluate the frequency of microbial isolates and their susceptibility profiles cultured from clinical samples obtained from 26 simultaneous pancreas-kidney transplant (SPK) recipients suspected of infections during the early post-transplantation period.

Patients and Methods. Data on microbiologic culture of 26 adult patients undergoing SPK were collected prospectively from 2001 to the end of 2006. Isolation and identification of cultured micro-organisms were performed according to standard microbiological procedures and commercially available tests. Susceptibility of the strains to antibacterial agents was made by the Clinical and Laboratory Standards Institute guidelines.

Results. All the patients were followed prospectively for the first 4 weeks after surgery. In total, 263 samples from clinical materials obtained from 26 SPK recipients were cultured. Bacterial cultures were positive in 29.3% (n = 77) clinical samples. Of these, 219 microbial strains were cultured. Gram-positive bacteria were found in 64% (n = 140), Gram-negative bacteria in 22.8% (n = 50), and fungal strains were isolated in 13.2% (n = 29). Incidence rate values for subsequent isolation of micro-organisms in the sub-periods of time for decreasing the SPK were Gram-positive bacteria (102.3–18.7; I versus IV), growing the Gram-negative bacteria (14–46.1 I versus III) IV were 14, decreasing to fungi (22.1–1.6, I versus IV). Until now this early post-transplantation period was considered homogeneous time after transplantation. This study shows that this period is actually heterogenous, with statistically significant differences being observed between results obtained in consecutive 4 weeks after transplantation.

Conclusions. The results of this study show that the incidence rate was elevated with increasing age in the SPK group of patients. In the SPK group, our data showed the highest rate of isolation of micro-organisms compared with recipients of kidneys or liver.

THE TREATMENT of choice for a diabetic patient who has progressed to end-stage renal disease is a pancreas transplantation performed in conjunction with a kidney graft [1]. Pancreas recipients are at significant risk for infectious complications that can lead to significant morbidity and mortality [2]. Infections in simultaneous pancreas–kidney transplantation (SPK) recipients are a common cause of infectious complications in the early postoperative period [3]. According to the Poltransplant database, 293 SPKs were performed in Poland from 1998 to 2012 [4]. Despite improved management, it has been reported in many studies that one of the major factors influencing morbidity and mortality among transplantation patients is

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infection [5–6]. The development of the solid organ transplantation procedure in Poland over the last decade requires a better understanding of the issue of infections in transplant recipients in our country [7]. The aim of our study was to determine the etiologic agents associated with suspected bacterial and/or fungal infections and their susceptibility to antimicrobial agents among patients after SPK from 2001 to the end of 2006.

PATIENTS AND METHODS

The patient population included 26 SPK recipients in the first month post-transplantation (17 women and 9 men of ages between 24 and 54 years) who underwent transplantation between September 2001 and December 2006 and survived for >72 hours. All the pancreata and kidneys came from cadaveric donors and were preserved with Viaspan solution (Barr Laboratories, Reston, Virg). All recipients underwent SPK: the kidney was transplanted into the retroperitoneal space, the pancreas intraperitoneally with enteric drainage of the pancreatic juice. All patients were followed prospectively for urinary tract infections from the day of SPK and for the first 4 weeks after surgery.

Immunosuppression consisted of a calcineurin inhibitor, mycophenolic acid, steroids, and antibody induction according to the recommendations of the Polish Transplantation Society [8]. Basic antimicrobial prophylaxis was administered intravenously from the day of the operation until 7 to 10 days after transplantation: piperacillin/tazobactam (Tazocin, Wyeth, USA), fluconazole (Diflucan; Pfizer, New York, NY), and gancyclovir (Cymevene, Roche, Basel, Switzerland) [9].

Microbiological Investigation

The biochemical characteristics of cultured strains were investigated using API and/or ID tests (bioMérieux, France), according to the manufacturer's manuals. The susceptibility to antimicrobial agents of cultured strains was performed using the ATB system (bioMérieux) according to recommendations of the Clinical and Laboratory Standards Institute (CLSI, formerly known as the National Committee for Clinical Laboratory Standards or NCCLS). Additional tests were performed for investigation of extended spectrum beta-lactamase production by Gram-negative rods (ESBL – positive strains) by the double-disc synergy test of Jarlier. For identification of methicillin-resistant strains of *Staphylococcus aureus* (MRSA), methicillin-resistant strains of coagulase-negative staphylococci (MRCNS) strains, and high-level aminoglycoside-resistant strains of enterococci (HLAR), an automated ATB system (bioMérieux) was used. These strains are referred to in the article as multidrug-resistant (MDR) strains. Interpretation of the susceptibility tests of all strains was performed according to the CLSI/NCCLS recommendations.

Statistical Analysis. All data were recorded on standard forms and entered for computer analysis into MediStat software (Poland). The differences between isolated strains in the two periods were analyzed statistically using the χ^2 test with Yates' correction. The P value $< .05$ was considered statistically significant.

RESULTS

All the patients were followed prospectively from the SPK date and during the first 4 weeks after surgery. Of 26 recipients in the early post-transplantation period, 263 clinical samples were obtained. Cultures were positive in 29.3% (n = 77) clinical samples. Of these, 219 microbial strains were cultured. Gram-positive bacteria were found in 64% (n = 140), Gram-negative bacteria in 22.8% (n = 50), and fungal strains were isolated in 13.2% (n = 29).

All SPK patients were followed prospectively for the early period after transplantation yielding 168 microbial isolates from the surgical site. The most commonly isolated organisms were Gram-positive bacteria (65.5%) with domination of *staphylococci* (52.7%) as MRSA and MRCNS. The second most common were *enterococci* (33.6%) with the presence of HLAR strains (64.9%) and vancomycin-resistant enterococci (VRE) strains (2.7%). Gram-negative bacteria comprised 19% of positive cultures; among them were isolated extended spectrum beta-lactamase producers and carbapenem-resistant strains. Yeast-like fungi comprised 15.5% of positive cultures.

Urine

Urine specimens (n = 77) were examined in 26 recipients (100%) during the first month after transplantation. Bacterial strains were cultured from 15 (57.7%) SPK recipients. Among the 30 isolated strains, the most common were Gram-positive bacteria (53.3%) with domination of *Enterococci* (75%) and a presence of HLAR (58.3%) and VRE strains (25%). Gram-negative bacteria comprised 46.7% of positive cultures. Statistically nonsignificant differences were observed during the analysis of the changes in the occurrence of bacteria isolated from samples obtained from urine in the first month after SPK transplantation.

Blood

Among 66 clinical blood samples, there were 23 microbial isolates from blood samples of 17 recipients and catheter tips of 12 recipients. The most common isolates were Gram-positive bacteria (73.9%) with domination of *staphylococci* (64.7%) and MRCNS strains (81.8%). Gram-negative bacteria comprised 17.4% of positive cultures, whereas yeast-like fungi, 8.7% with a predominance of *Candida glabrata*.

Respiratory Tract

Four bacterial strains were cultured from the respiratory tract: Gram-positive bacteria *Enterococcus faecium*-HLAR, *Staphylococcus epidermidis*, and Gram-negative *Acinetobacter baumannii* and *Morganella morganii*.

The incidence rate (IR) values for subsequent isolation of micro-organisms in the sub-periods of time for decreasing the SPK were Gram-positive bacteria (102.3–18.7; I vs IV), growing the Gram-negative bacteria (14–46.1 I vs III) IV were 14, decreasing to fungi (22.1–1.6, I vs. IV). Until now, this early post-transplantation period was considered homogeneous time after transplantation. This study shows that this period is actually heterogenous with statistically significant differences being observed between results obtained in consecutive 4 weeks after transplantation. The results of this study also show that the IR was elevated with increasing age in SPK group of patients. The numbers of patients and