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Specific features of respiratory and intensive therapy for pulmonary infectious complications of acute and chronic kidney graft rejection

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The purpose of the study was *to determine the specific features of respiratory and intensive therapy of pulmonary infectious complications in acute and chronic kidney graft rejection.*

Material and methods. *The results of treatment of 7 patients with pulmonary infectious complications against an acute and chronic kidney graft rejection were retrospectively studied.*

Study results. *The total number of pulmonary infection cases made 7 among 54 cases of kidney transplantation from living related donors. In all cases, bilateral interstitial pneumonia was diagnosed. Six patients had positive dynamics on receiving a respiratory therapy and intensive care.*

Keywords: kidney transplantation, immunosuppression, chronic transplant rejection, infection, lung injury, intensive care

Nazyrov F.G., Ibadov R.A., Bakhritdinov F.Sh., et al. Specific features of respiratory and intensive therapy for pulmonary infectious complications of acute and chronic kidney graft rejection.

ARDS, acute respiratory distress syndrome

CMV, cytomegalovirus

CRP, *C*- reactive protein

IPLV, intrapulmonary percussive lung ventilation

KT, kidney transplantation

MLV, mechanical lung ventilation

NiCPAP, Noninvasive Constant Positive Airway Pressure

OD, optical density

PCR, polymerase chain reaction

PEEP, positive end-expiratory pressure

VAP, ventilator-associated pneumonia

Introduction

Among bacterial infectious complications in kidney transplant recipients, pulmonary infections account for 8 to 33% and play an important role in the structure of mortality of allogenous kidney recipients [1-3]. In this regard, patients after kidney transplantation (KT) should be included to a high risk group of fatal pulmonary infections [1].

One should remember that pneumonia in patients after KT can be caused by "atypical" pathogens (legionella, mycoplasma, chlamydia), viruses, pneumocysts, fungi, mycobacterium tuberculosis, and nontuberculosis mycobacteria. Nearly every 9th patient develops a polymicrobial infection, and in every 3rd-4th patient, pneumonia etiology remains unidentified despite a comprehensive examination [4].

In our opinion, one of the most difficult tasks in managing patients with pulmonary infectious complications after KT is the choice of optimal respiratory tactics and pathogenetic therapy in case of the acute respiratory distress syndrome (ARDS) development. On the one hand, the advent of premium-class ventilators with Open Lung technologies, electrical impedance tomography, etc. have produced significant effect on satisfactory outcomes in cases of ARDS of different etiologies, and on the other hand, a prolonged mechanical lung ventilation (MLV) per se can cause the development of ventilator-associated pneumonia (VAP), especially in patients with poor immune status.

In this regard, the use of NiCPAP (Noninvasive Constant Positive Airway Pressure) and intrapulmonary percussive lung ventilation (IPLV) is predetermined by the mode of mechanical ventilation, which, according to the resolution of the Congress of the European Respiratory Society (ERS-2013), has life-saving properties for patients who need respiratory support [6].

G. Riffard et M. Toussaint (2012) [5] note that IPLV allows the patient to breathe independently assisted with "percussive ventilation programming" providing the stage of lung assisted inflation (filling), followed by the percussive deflation of the lungs to a pre-specified baseline expiratory level (during a passive exhalation), thus ensuring:

- endobronchial percussive mixing;
- stepwise inflation: an increase in lung volume;
- automatic stabilizer of CPAP (level);
- the end-inspiratory time contributes to the passive expiratory clearance of secretion masses.

The purpose of the study was to determine the characteristics of respiratory and intensive care for patients with pulmonary infectious complications secondary to acute and chronic rejection of the kidney graft.

Material and methods

The study was based on the examination and treatment results in 54 patients after live-related orthotopic KT in the period 2010-2017, among whom 51 patients were operated on in our center. Pulmonary complications with the development of bilateral interstitial pneumonia were observed in 3 patients in the immediate postoperative period and in 4 patients in the long-term follow-up from 1 month to 4 years.

Other 3 patients were operated on in the clinics of India and Pakistan and later were hospitalized to our center with the clinical evidence of acute lung injury syndrome secondary to acute kidney graft rejection in 1 case, and chronic graft rejection in 2 cases.

The criteria for making the diagnosis were based on the regulatory documents of the American Thoracic Society/European Respiratory Society (ATS/ERS) International Multidisciplinary Classification of the idiopathic interstitial pneumonias (2013) [6].

Traditional methods of microorganism isolation and identification, assessing their sensitivity to antimicrobial agents, and dynamic control of *C*-reactive protein (CRP) content were used. The species of the isolated microorganisms were determined by conventional methods using identification media (manufactured by "HiMedia", India). In addition, the presence of antibodies against cytomegalovirus (CMV) in serum was assayed and CMV DNA was quantified by polymerase chain reaction (PCR).

At 6-12 hours after surgery, when oral drug administration became possible, the recipients received a 3-component maintenance immunosuppressive therapy, which was prescribed according to the clinical recommendations of the Russian Scientific Society and the Association of Nephrologists of Russia [7]. The recipients were given mean doses of prograf (tacrolimus) 0.12-0.13 mg/kg body weight per day and cellcept (mycophenolate mofetil) 2 g/day, followed by a dose decrease to 1 g/day. Low doses of corticosteroid hormones not exceeding 0.5 mg/kg of body weight were prescribed as the third component. In addition, all patients received antiviral, antibacterial, infusion, and symptomatic therapy.

Respiratory therapy consisted of non-invasive MLV using the ATS/ERS protocol (NiCPAP ASB, PEEP 8, Trigger 3 l/min, FiO_2 50%) interrupted to use the positive end-expiratory pressure (PEEP) mask and IPLV in the mode of low and medium percussion in combination with nebulizer therapy (the standard protocol + FarGALS solution diluted in a ratio of 1:4).

The NiCPAP mode was ensured using VELLA device (Viasys Healthcare Inc.). The procedures of mechanical percussive lung ventilation were performed using the IPV-HCBI-PHASICIMPULSATOR device (Percussionaire).

Thus, the use of NiCPAP and IPLV was based on the following:

- non-invasive MLV with permanent PEEP;

- mobilization of pulmonary airways whose patency was disrupted due to the retention of secretion masses, edema of mucosa and submucosa, and the bronchial spasm;

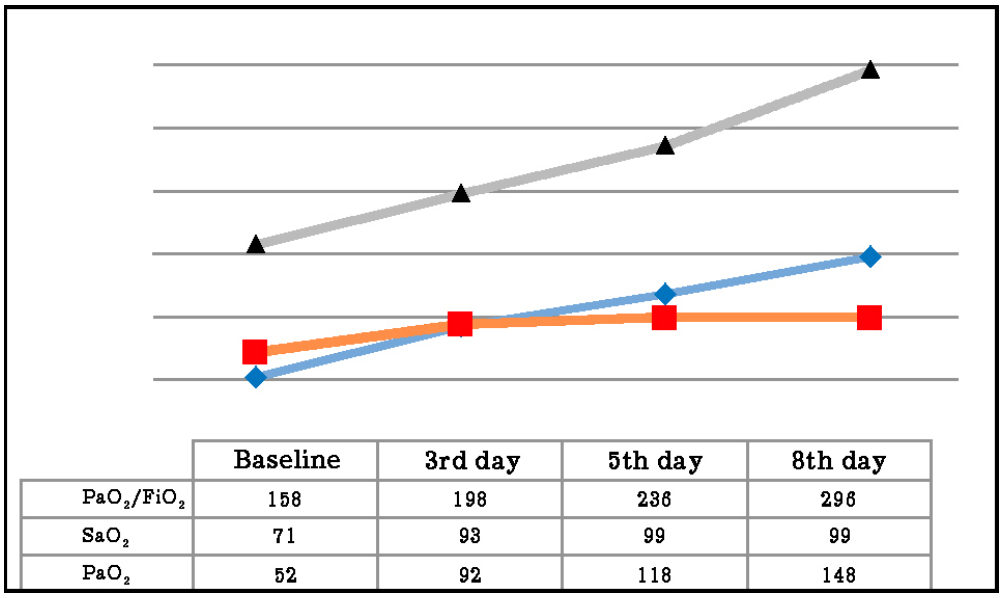
- creation of bilateral equal alveolar ventilation aimed at improving the oxygen supply and carbon dioxide removal;

- mechanical mixing of intrapulmonary gases by using diffuse intrapulmonary percussion to improve endobronchial oxygen diffusion and mobilization of carbon dioxide at the periphery (of the lungs);

- providing a significant intermittent "convection respiratory flow" for flushing CO_2 out.

Results and discussion

In markedly impaired immune status of patients and the respiratory status progression when using a standard treatment approach, the tracheal intubation and conversion to a traditional prolonged MLV with a high risk of VAP occurrence were predicted. In that connection, the whole complex of non-invasive respiratory therapy was used with a positive result.



	Baseline	3rd day	5th day	8th day
PaO_2/FiO_2	158	198	236	296
SaO_2	71	93	99	99
PaO_2	52	92	118	148

Fig. 1. Changes in arterial blood gas content over time

When assessing the changes in arterial blood gas content over time, there we noted a significant improvement in SaO_2, PaO_2, and PaO_2/FiO_2 compared to baseline values (Fig. 1). Positive trends were also seen in the

parameters of alveolar-arterial ($P_{(A-a)}O_2$) and arterial-alveolar ($P_{(a-A)}O_2$) oxygen gradients (Fig. 2), the degree of intrapulmonary shunt (Qs/Qt) (Fig. 3).

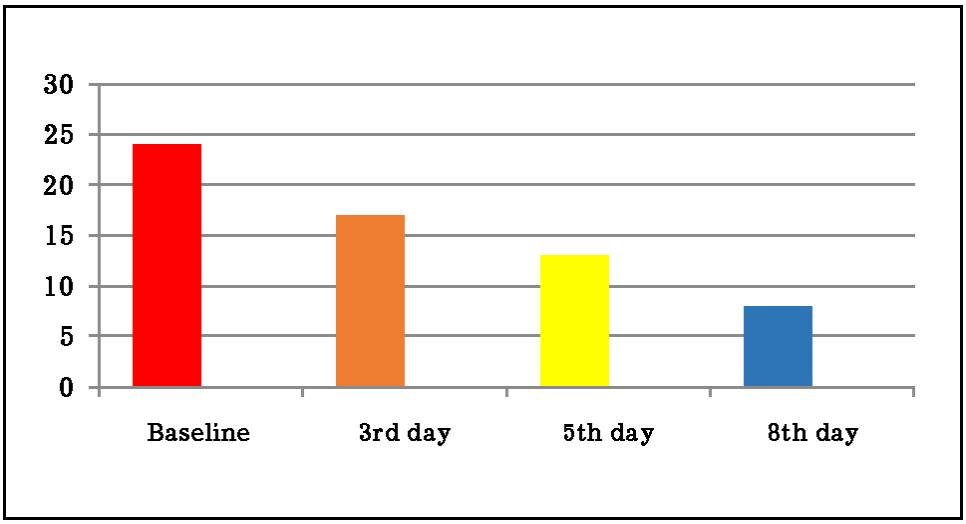


Fig. 2. Changes of alveolar-arterial oxygen gradient ($P_{(A-a)}O_2$) over time

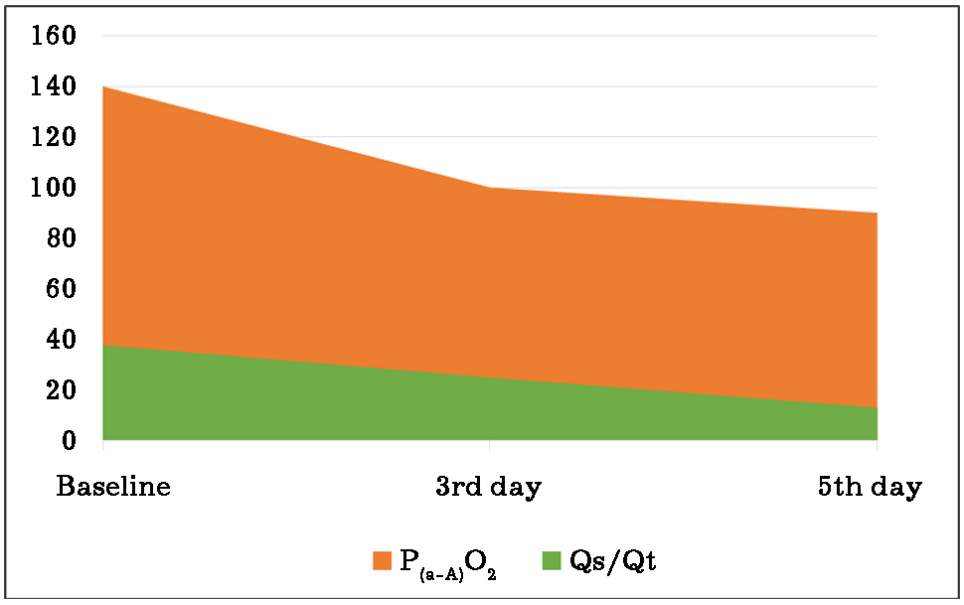
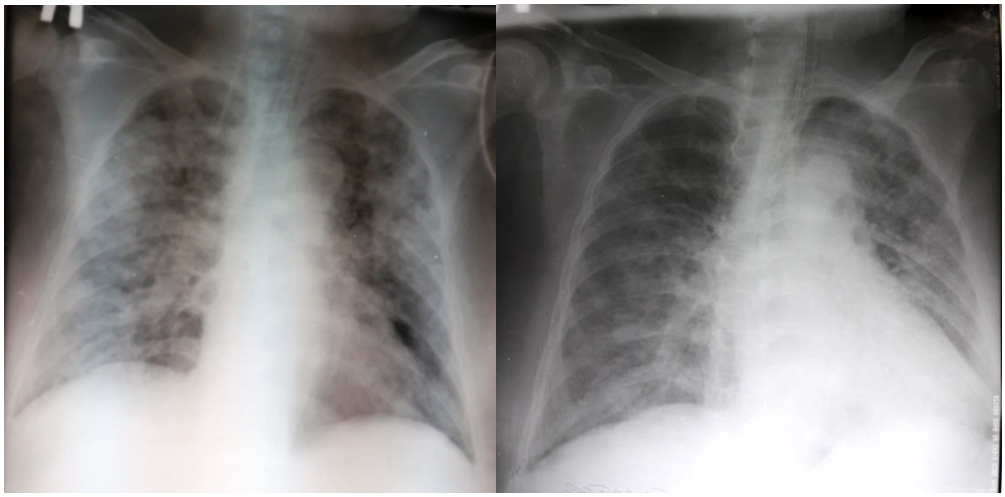


Fig. 3. Changes of arterial-alveolar oxygen gradient ($P_{(a-A)}O_2$) and pulmonary shunt (Qs/Qt) over time

The MLV duration was 9 ± 2.6 days.

We give an example of X-ray images of patient A., 36 years old, diagnosed with "bilateral interstitial pneumonia, moderately severe ARDS; a chronic graft rejection, the condition after live-related heterotopic kidney transplantation". As soon as on the 3rd day, the ARDS clinical and radiological manifestations regressed (Fig. 4).



Baseline 3rd day

Fig. 4. Changes in X-ray pattern at intensive care stages over time

The emerged edematous-ascitic syndrome and the increased blood urea and creatinine levels in 3 patients were the reasons for their connecting to intensive hemodialysis therapy that was performed daily for 3 hours with the ultrafiltrate removal at mean up to 1.5 liters. Simultaneously with hemodialysis initiation, tacrolimus doses were reduced from 6 mg to 3 mg per day, and mycophenolate mofetil dose was raised from 1000 mg to 2000 mg per day.

The isolated microflora was represented by gram-negative microorganisms (E. coli, K. pneumoniae) in all the cases. The results of antibiotic susceptibility testing showed that the most active drugs to them were piperacillin/tazobactam, imipenem, cefoperazone/sulbactam and

ofloxacin. In CRP values over 70 mg/L, a de-escalation antibacterial therapy was performed.

As far as anti-CMV IgG antibodies were identified with OD showing 3.0 nm (cut-off OD value = 0.273 nm), the antiviral therapy with ganciclovir was used, after which the control qualitative PCR assay was negative.

There was 1 death in a 47-year-old man in the early postoperative period. The cause of death included a rejection crisis, bilateral low-lobular pneumonia, severe ARDS, an acute cardiovascular failure.

Conclusions

1. Non-invasive respiratory techniques of intrapulmonary percussive lung ventilation and NiCPAP (Noninvasive Constant Positive Airway Pressure) with the hemodialysis inclusion are an alternative therapeutic tactics in patients with bilateral interstitial pneumonia and interstitial edema secondary to an acute or chronic kidney graft rejection.

2. The ventilation technology potential for intrapulmonary percussion ventilation in patients with pulmonary pathology allows the therapy optimization, respiratory tract protection, and the avoidance of mechanical ventilation-associated adverse events. Intrapulmonary percussive lung ventilation may be an independent type of respiratory therapy using an original technical respiratory mode with intermittent positive pressure and with the creation of extracorporeal percussion, and nebulizer therapy; it is the most effective in case of mucus hypersecretion into the bronchial tree lumen with the need for sputum drainage.

3. A complex prevention and treatment of pyoinflammatory lung diseases by using nebulizer therapy and fibrobronchoscopic bronchial lavage can reduce the incidence of early and late specific bronchopulmonary

complications, achieve a clinical improvement in patients as soon as on the 2nd-3rd day, and speed up their recovery.

Conflict of interests. The authors state that there is no conflict of interest.

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