UNIWERSYTET
MIKOŁAJA KOPERNIKA
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The use of SARS-CoV-2/COVID-19 convalescent plasma in context of activity of Regional Center of Blood Donation and Blood Treatment in Bydgoszcz

Dissertation for the degree of doctor of medical sciences

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Bydgoszcz 2022

SUMMARY

Treatment with plasma obtained from people cured of viral infection (CCP, convalescent plasma) is a well-known approach in the therapy of infectious diseases. Positive effects are obtained especially in those cases where no effective treatment or prevention of their spread (vaccination) is available. Convalescence plasma has been used, among others, during the Spanish influenza pandemic (1918). Patients with Spanish Influenza Pneumonia receiving human blood products after recovery had a clinically significant reduction in the risk of death. Plasma from convalescents was also used, among others in the treatment of measles, mumps, chicken pox, CMV infections or parvovirus B19. The World Health Organization (WHO) also recommended the use of convalescent plasma during the Ebola virus-induced hemorrhagic fever epidemic. The use of plasma from convalescents was also studied in the case of the SARS-CoV-1 outbreak in 2003, the 2009-2010 influenza H1N1 pandemic and the 2012 MERS-CoV epidemic. In 2009, during the AH1N1 influenza pandemic, a significant reduction in mortality was observed in the group treated with plasma of convalescents compared to the control group (20.0% vs. 54.8%). Also, in the case of the use of plasma in the treatment of MERS and SARS, better therapeutic effects were observed compared to the control group.

Plasma therapy for convalescents is effective and well tolerated in most cases. Serious adverse reactions are rarely reported. Especially in the case of the use of convalescent plasma in the treatment of various viral infections, it can be stated that such a procedure reduces mortality, lowers viremia, and consequently shortens the hospitalization time and accelerates the patients' convalescence. The use of convalescent plasma was an immediately available low-risk experimental therapy.

Due to the outbreak of the SARS-CoV-2 pandemic, on April 10th, 2020, the Ministry of Health, following the guidelines of the European Commission, informed the Blood Donation Centers in Poland about the possibility start-up a plasma collection program from COVID-19 convalescents.

Objectives of the study

Main objective: The main objective of the study was analysis of the use of SARS-CoV-2/COVID-19 convalescent plasma (CCP) in the first year of obtaining and using plasma of convalescents in Poland, i.e. from 01/05/2020 to 30/04/2021, in context of activity of Regional Center of Blood Donation and Blood Treatment in Bydgoszcz (RCKiK).

Specific objectives:

(1) Analysis of data from Poland, based on information of National Blood Center.
(2) Analysis of data of production of CCP in following stages: donor qualification, donation of blood by donors, production of plasma, dispensation of CCP to hospitals.
(3) Clinical data analysis of efficacy of CCP used in patients treated for COVID-19 in hospitals of the Kuyavian-Pomeranian region, based on the data obtained from these hospitals, including: the influence of time of CCP administration and its titer on time of discharge and overall survival with respect to other risk factors.

Methods:

The retrospective study based on RCKiK documentation covers the first year of obtaining and using plasma of convalescents, i.e. from 01/05/2020 to 30/04/2021.

Conducted:

1. Data analysis on the process of qualifying donors-convalescents, plasma collection and delivery to hospitals. These data will be analyzed against data from all over Poland, according to data from the National Blood Center.
2. Analysis of data on the use of plasma of convalescents in patients treated for COVID-19 in hospitals of the Kuyavian-Pomeranian region, based on data obtained from these hospitals.

Results:

Up to the end of April 2021 (30.04.2021) overall in 21 regional blood banks in Poland a total number of 121896,2 units of CCP were produced, including 14683 (12%) units in Bydgoszcz. 75858 units were issued for treatment, including 9330 units in the Kuyavian-Pomeranian region. This has classified Bydgoszcz (RBB, RCKiK) as a leading center in Poland.

Convalescents accounted for 11.9% of all donors who donated blood or its components to RCKiK in Bydgoszcz during the study period. The majority of donors were: men, among men -

multiple donors, and among women - first-time donors. A much larger group among convalescents (39,8%) than among other blood donors (23,4%) were people who came to donate blood for the first time (p <0.001) and those who donated blood more than 2 years after the last donation (19,8% vs 17,0%; p<0,001).

Most of donors donated once, while 28,8% at least twice. Majority of donations had place between December 2020 and March 2021 (peak od second wave and during third wave). Among the donors who made the first donation, the level of antibody titers remained at a comparable level for the period of 5 months after the onset of the disease. There was a slight increase in anti-SARS-CoV-2 antibody titer up to 150 days after onset, then the titer gradually decreased; the differences were statistically significant (p <0.001, Kruskal-Wallis test).
A vast majority of CCP were dispensed to 29 hospitals in kujawy-pomerania region, and 0,4% to other regions.

Clinical data were obtained from 3596 patients (50.1% of all patients treated with CCP in our region). Basic characteristics of the patients: males 59,5%; median age 68 years (range: 1,3-100 years); majority in moderate (56,8%) or severe (31,2%) clinical status; comorbidities in 78,4% patients. In 59% cases, CCP was administered in initial 24 hours of hospitalization (median: 1 day, range 1-49 days).
In cured patients, time of hospitalization correlated with day of administration of CCP (p<0,001), i.e., the sooner CCP was administered, the time of hospitalization was shorter.
The overall survival from COVID-19 was 78,3% in analyzed group of patients. The outcome was better:

- when CCP was administered during first day of hospitalization (79,9% vs 86,8%, p=0,057)
- in younger patients; for age <50 years 91,0% vs 76,2% for older ones (p<0,001)
- when respirator was not necessary: 78,7% vs 26,9% (p<0,001)
- good clinical status 92,5% vs moderate 81,0% vs severe 68,6% (p<0,001)
- without comorbidities 88,6% vs 75,9% (p<0,001)

Antibody level in CCP unit and blood group had no impact on survival from COVID-19.

In multivariate analysis, following risk factors contributed significantly to death from COVID-19: overall patient clinical status at admission (severe > modearte > good), comorbidities, necessity for use of respirator. Risk of death was decreased in: younger patients (no age threshold; continuous variable), while administration of CCP in first day of hospitalization had borderline significance (p=0,077).

The use of CCP was safe therapeutic approach. Mild reactions occurred only in 5/9356 (0,05%) after transfusion.

Conclusions

1. In the period from 01/05/2020 to 30/04/2021, RCKiK in Bydgoszcz was the most active center in Poland for obtaining, producing and distributing convalescent plasma to patients.
2. In the process of plasma donation, a very high commitment of donors was found, expressed in an increase in the number of donations:
    A. Relatively high percentage of donors were donors who donated blood for the first time and for multiple repeat donors.
    B. Most donors have made only one donation.
    C. Among the donors who donated the first donation, the antibody titer was comparable over the period of 5 months after the onset of the disease. There was a slight but statistically significant increase in the antibody titer up to 150 days after the onset of the disease, then the titer gradually decreased.
3. Early administration of convalescent plasma had beneficial effect for clinical course of patients with COVID-19.
    A. The time of plasma administration correlated with the reduction of hospitalization time in surviving patients.
    B. Administration of CCP during initial 24 hours after admission of patient to the hospital, tend to improve survival from COVID-19 (79,9% vs 76,8%, p=0,057).
    C. Antibody titer had no impact on time of discharge or overall survival of patients.
    D. The risk factors for COVID-19 therapy failure were: older age of patients (continuous variable), presence of comorbidities, severe or moderate general condition of the patient, and the need for a ventilator. The administration of plasma on the first day of hospitalization showed a borderline effect on the improvement of the cure rate (p=0,077).