Hospital Protection Correlates in Outpatient COVID-19 Convalescent Plasma Recipients

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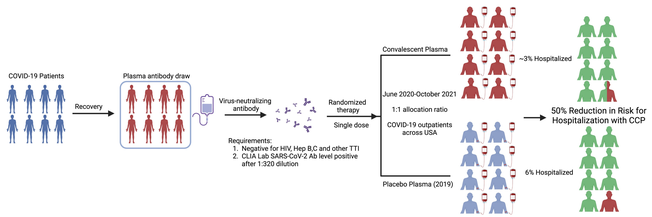
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BACKGROUND

High titer COVID-19 convalescent plasma (CCP) reduces hospitalizations among immunocompetent outpatients. This study evaluated recipient post-transfusion S receptor binding domain (S-RBD) IgG antibody levels and the association of progressing to hospitalization among unvaccinated outpatients with COVID-19 treated with CCP or control plasma.

METHODS

This analysis focused on participants from a multicenter double-blind, randomized, controlled trial comparing treatment of outpatients with COVID-19 convalescent plasma (CCP) or control plasma without SARS-CoV-2 antibodies. Participants with confirmed SARS-CoV-2 infection were transfused within 9-days of symptom onset between June 2020 and October 2021 (n=110 vaccinated control; n=105 vaccinated CCP; n=464 unvaccinated control; n=472 unvaccinated CCP; total n=589 control and n=592 CCP recipients). All subjects had specimens collected the day prior to transfusion (D-1), within 30 minutes after transfusion (D0), 14 (D14), 28 (D28), and 90 (D90) days post-transfusion. Ancestral SARS-CoV-2 S-RBD was measured by an in-house validated ELISA. All 54 COVID-19-related hospitalizations occurred within 2 weeks of transfusion.

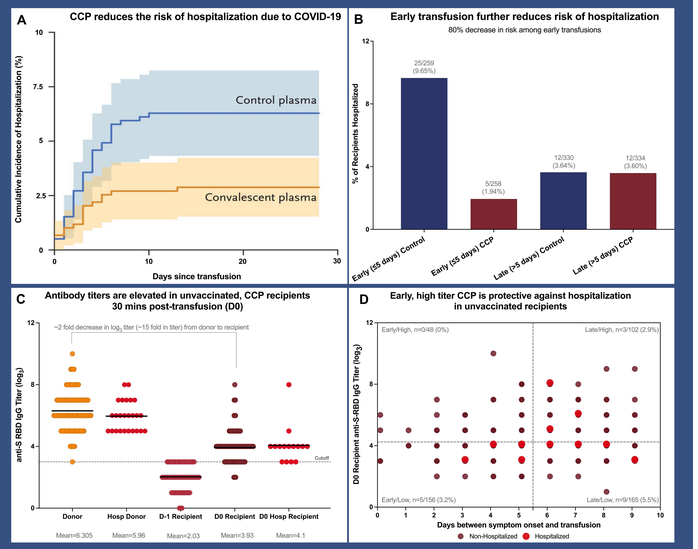


Recipient Characteristics			
	Control n=589	CCP n=592	Total n=1181
Age, mean (SD)	44.2 (13.9)	42.9 (14.3)	43.5 (14.13)
Sex, n (%)			
Male	237 (40.24%)	269 (45.44%)	506 (42.9%)
Female	352 (59.76%)	323 (54.56%)	675 (57.1%)
BMI, mean (SD)	29.68 (7.28)	29.11 (7.4)	29.39 (7.3)
Hypertensive, n (%)	136 (23.09%)	140 (23.65%)	276 (23.37%)
Asthmatic, n (%)	73 (12.39%)	59 (9.97%)	132 (11.2%)
Hospitalization, n (%)	37 (6.28%)	17 (2.87%)	54 (4.57%)
Days to Hospitalization, mean (SD) *	3.38 (2.43)	3.05 (3.19)	3.28 (2.67)
Immunosuppressed, n (%)	15 (2.55%)	15 (2.53%)	30 (2.54%)
Vaccination Status, n (%) **			
Unvaccinated	479 (81.3%)	485 (81.9%)	964 (81.6%)
Partially	31 (5.3%)	27 (4.6%)	58 (4.9%)
Fully	79 (13.4%)	80 (13.5%)	159 (13.5%)

*Days from transfusion to hospitalization
**Partially and fully vaccinated were grouped together for analyses

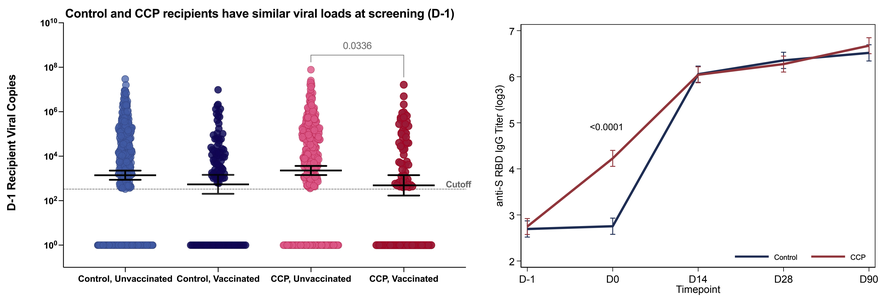
Early outpatient COVID-19 antibodies reduce hospitalizations

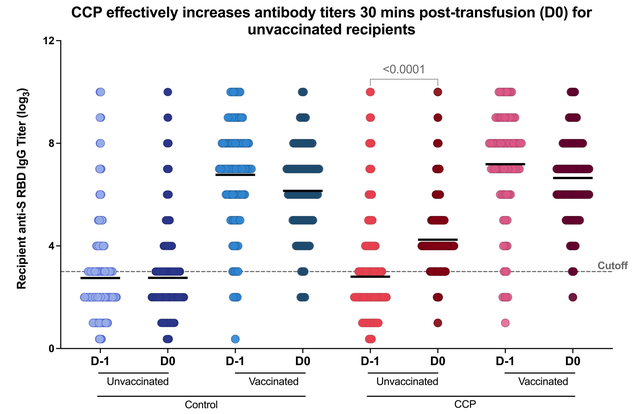
Treatment of COVID-19 in outpatients with convalescent plasma was previously reported an overall relative risk reduction of hospitalization by 54% (**A**). Early (≤5 days within symptom onset) transfusion of CCP is more protective against hospitalization. CCP recipients had an 80% reduction in risk for hospitalization compared to control recipients (**B**). CCP treatment effectively increases anti-S-RBD IgG titers within 30 minutes of transfusion for unvaccinated recipients (**C**). Among the unvaccinated CCP recipients, those who received early transfusion and had high antibody titers over 540 within 30 minutes of transfusion had the lowest proportion of hospitalizations (Fishers exact test p =0.009; **D**).



RESULTS

Post-transfusion anti-S-RBD IgG levels on D0 were significantly greater for CCP (median=4 titer, $\log_3$) compared to control (median=2 titer, $\log_3$; p <0.001) recipients. Neither sex nor age impacted antibody levels following CCP treatment at D14, D28, and D90. Vaccinated recipients had greater titers than unvaccinated recipients prior to transfusion with little change in titers post-transfusion. Unvaccinated recipients had low antibody titers on D-1 with CCP recipients exhibiting a significant increase in titer from D-1 to D0 compared to controls (mean fold change=1.89; p <0.001). Among unvaccinated recipients, those who received CCP transfusion late (>5 days after symptom onset) and had low D0 antibody levels (<540) had the greatest proportion of hospitalizations (5.5%). In contrast, those who received CCP transfusion early (≤5 days after symptom onset) with high D0 antibody levels (>540) had no hospitalizations. Unvaccinated CCP recipient anti-S-RBD IgG antibody levels on D0 correlated with donor anti-S-RBD IgG antibody levels (r=0.30, p <0.001).





CONCLUSIONS

- Among unvaccinated outpatients with COVID-19, CCP recipient antibody dilutional titers after transfusion over 540 titer correlated with protection against hospitalization when transfusion occurred within 5 days of symptom onset.
- Because there is a ~15-fold decrease in S-RBD IgG titers from donor to recipient, the optimum donor inverse titers may be over 7,000.

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