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A LIVING WHO GUIDELINE ON DRUGS FOR COVID-19

WHO covid-19 drugs guideline: reconsider using convalescent plasma

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On 6 December the World Health Organization recommended against using covid-19 convalescent plasma (CCP) to treat covid-19 based on a statistical summary of selected randomised controlled trials (RCTs). Unfortunately, the WHO summary avoided digging below the surface to ask critical questions about treatment timing, study populations, and antibody titre of the administered CCP in the reviewed RCTs.

Had WHO dug deeper, it would have noted that:

- Nearly all RCTs considered were conducted in patients admitted to hospital with covid-19 who had progressed through the viral replication phase to the inflammatory phase, when CCP is unlikely to work[1]
- In nearly all RCTs considered, signals of CCP efficacy were found in subgroups of patients treated early or in less severe stages of illness[2]
- Some RCTs used CCP with an insufficient amount of SARS-CoV-2-specific antibody[3]
- An RCT of CCP from Argentina, conducted in elderly outpatients shortly after diagnosis, reduced covid-19 progression by half.[4] A new RCT from the US has found that treating outpatients with CCP reduces hospital admissions by half.[5]

Had WHO consulted other sources of information, it would have noted that:

- Observational studies with careful propensity matching, some much larger than any published RCT, showed better outcomes with CCP[6]
- Several studies indicate the particular value of CCP therapy in immunosuppressed patients[7 8]
- A clear relationship between antibody titre in CCP and improved survival has been shown, if the patient is treated early enough[9]

An unfortunate consequence of the WHO recommendation is that it discourages CCP use in low and middle income countries, where this safe, inexpensive intervention may be the only antiviral available.

We urge WHO to revisit its recommendation by reviewing the totality and consistency of the evidence supporting benefit, taking into account the pandemic conditions and RCT design features that affected the findings from most large RCTs.

Competing interests: All authors have participated in published research on the use of convalescent plasma in covid-19.

Full response at: www.bmj.com/content/370/bmj.m3379/rr-15.

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