Effect of polymerized type I collagen in hyperinflammation of adult outpatients with symptomatic COVID-19: a double blind, randomised, placebo-controlled clinical trial

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Background

Currently, therapeutic options for outpatients with COVID-19 are limited, in Mexico Polymerized Collagen type I (PCTI) has been tested as a useful option.

Methods

Double-blind, randomised, placebo-controlled clinical trial of PTIC vs placebo. To evaluate the safety, efficacy and effect of the intramuscular administration of polymerized type I collagen (PTI C) on hyperinflammation, oxygen saturation and symptom improvement in adult outpatients with symptomatic COVID-19. Eighty-nine adult participants with a confirmed COVID-19 diagnosis and symptom onset within the 7 days preceding recruitment were included from August 31, 2020 to November 7, 2020 and followed for 12 weeks. Final date of follow-up was February 4, 2021. Patients were randomly assigned to receive either 1.5 ml of PTIC intramuscularly every 12 h for 3 days and then every 24 h for 4 days (n=45), or matching placebo (n=44).

Results

Of 89 patients who were randomised, 87 (97.8%) were included in an intention-to-treat analysis; 37 (41.6%) were male and mean age was 48.5±14.0 years. The IP-10 levels decreased 75% in the PTIC group and 40% in the placebo group vs baseline. The comparison between treatment vs placebo was also statistically significant (*P*=0.0047). The IL-8 (44%, *P*=0.045), M-CSF (25%, *P*=0.041) and IL-1Ra (36%, *P*=0.05) levels were also decreased in the PTIC group vs baseline. Mean oxygen saturation ≥92% was achieved by 40/44 (90%), 41/42 (98%) and 40/40 (100%) of participants that received PTIC at 8, 15 and 97 days of follow-up vs 29/43 (67%), 31/39 (80%) and 33/37 (89%) of patients treated with placebo (*P*=0.001). The unadjusted accelerated failure time model showed that patients treated with PTIC achieved the primary outcome 2.70-fold faster (*P*< 0.0001) than placebo. In terms of risk, the group of patients treated with PTIC had a 63% lower risk of having a mean oxygen saturation < 92% vs placebo (*P*< 0.0001). Symptom duration in patients treated with PTIC was reduced by 6.1±3.2 days vs placebo. No differences in adverse effects were observed between the groups at 8, 15 and 97 days of follow-up.

Conclusion

Treatment with PTIC down-regulated IP-10, IL-8, M-CSF and IL-Ra levels, which could explain the PTIC effect on the higher proportion of patients with mean SaO2 ≥92% and a shorter duration of symptoms as compared with placebo.

Characteristic	1 day post-treatment with			8 days post-treatment with			90 days post-treatment with		
	PTIC (*N* = 44)	Placebo (*N* = 43)	*p* Value	PTIC (*N* = 42)	Placebo (*N* = 39)	*p* Value	PTIC (*N* = 40)	Placebo (*N* = 37)	*p* Value
SpO2 ≥ 92%, *n* (%)	40 (90.1)	29 (67.4)	.007	41 (97.6)	31 (79.5)	.009	40 (100)	33 (89.2)	.033
pSO_2; mean ± SD	94 ± 2.4	93 ± 3.3	.085	95 ± 1.7	93 ± 2.2	.003	95 ± 2.1	95 ± 2.3	.429
Median	94	93		95	93		95	95	
IQR	92–95	91–95		93–96	92–95		93–97	93–97	
O2 supplementation, *n* (%)	2 (4.5)	4 (9.3)	.381	1 (2.3)	1 (2.6)	.958	0 (0.0)	0 (0.0)	-
Inpatient admissions	0 (0.0)	3 (7.0)	.075	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-