

Vitamin C as an adjunct to COVID infections

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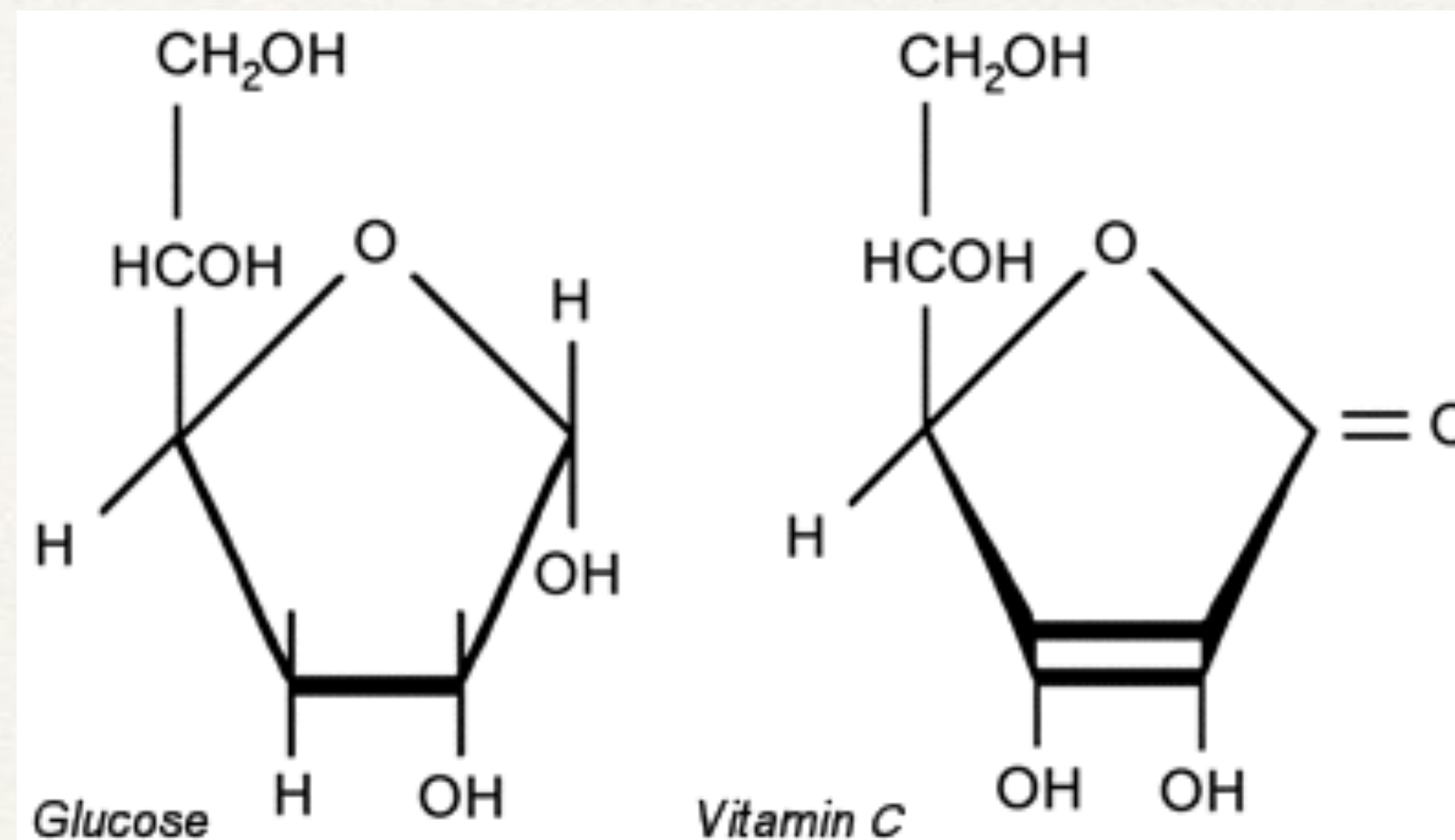
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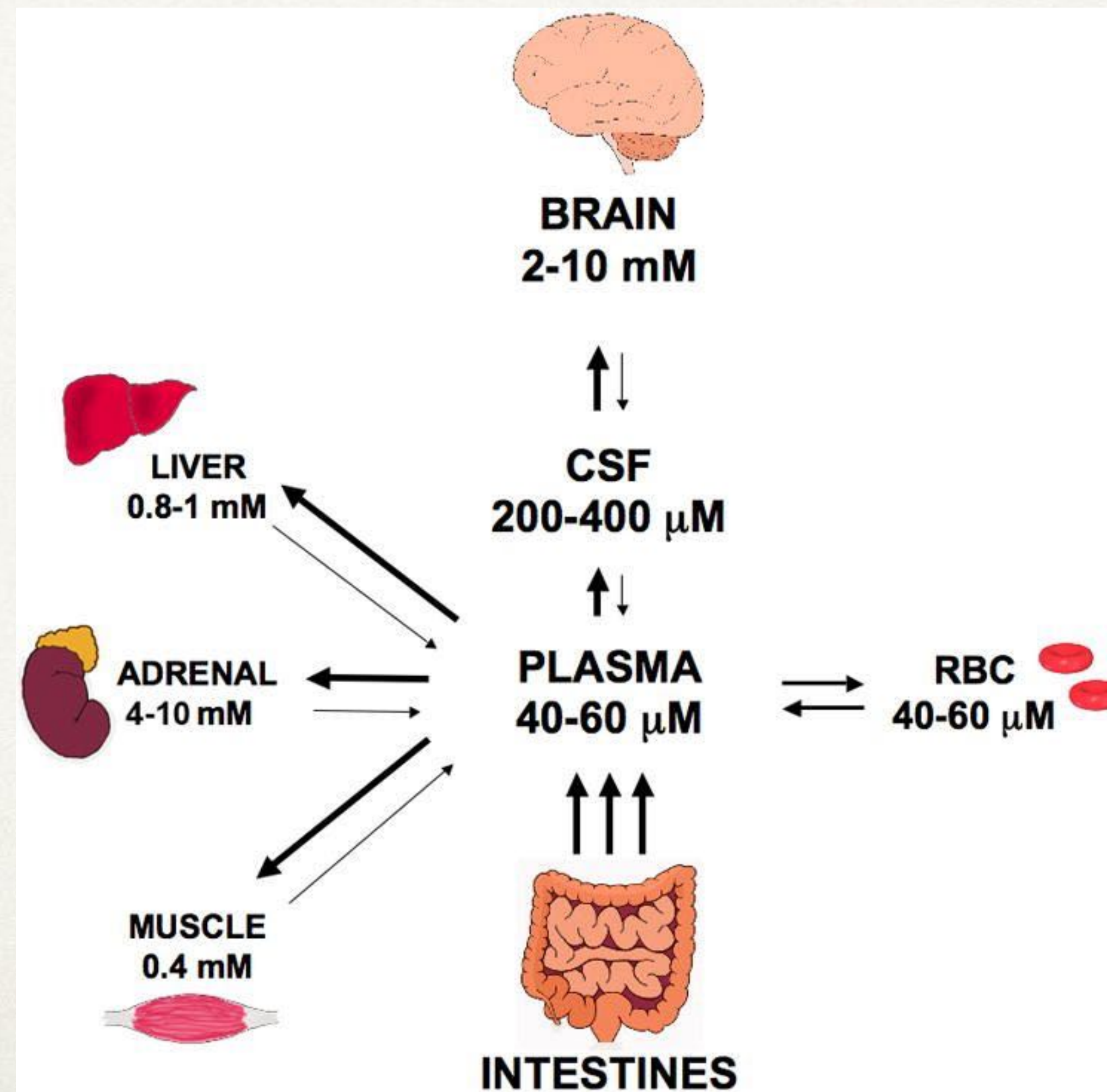
March 22, 2020 Manila Philippines

Ascorbate

- ❖ ANTI OXIDANT AT LOW DOSES
- ❖ physiologic concentration 50umol/L
- ❖ ascorbate and glucose are very similar in structure



Ascorbate in Tissues



Vitamin C in against infections

- ❖ actively destroys bacterial , viral^{1,2,3,4} and fungal infections via Fenton reaction.
- ❖ directly act as an antioxidant to act on free radical damage caused by bacterial , viral^{3,4} and fungal infections
- ❖ increased neutrophil, phagocyte and lymphocyte production, increase WBC motility, phagocytic activity^{5,6,7}
- ❖ lowers cortisol and inflammatory cytokines (CRP, TNF, IL-1, IL-8)⁸

VITAMIN C against Sepsis

Hydrocortisone, Vitamin C and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Study. by Paul E. Marik, MD, FCCM, FCCP, et al.

- ❖ 47 patients as control vs treatment group
- ❖ procalcitonin >2 ng/ml within 24 of ICU admission
- ❖ IVC 1.5g q6h for 4 days or until discharge (100ml NSS or D5W for 30-60mins)
- ❖ hydrocortisone 50mg q6h 7 days or until discharge
- ❖ Thiamine 200mg q12h for 4 days or until discharge (50ml NSS or D5W for 30 mins)
- ❖ Mortality Treatment group 4/47 (4.5%) vs control 19/47 (40.4%)
- ❖ None of the treatment group died of sepsis

Ascorbate in Sepsis and ARDS

- ❖ CITRIS- ALI trial by Fowler et al⁹.
- ❖ Multi-center, randomized, double blind, vitamin C in patients with ARDS secondary to sepsis
 - Acute onset hypoxemic respiratory failure.
 - Bilateral opacities not explained by ARDS *onset* must have occurred within <48 hours of study inclusion.

Absence of active kidney stones.

- ❖ Vitamin C 3.5g IV q6 for 4 days or placebo

QUESTION Can intravenous administration of high-dose vitamin C reduce organ failure scores and biomarkers of inflammation and vascular injury in patients with sepsis and acute respiratory distress syndrome (ARDS)?

CONCLUSION This randomized clinical trial found that in patients with sepsis and ARDS, high-dose vitamin C compared with placebo did not significantly reduce organ failure scores or improve biomarker levels.

POPULATION

90 Men
77 Women



Adults in the intensive care unit (ICU) with sepsis and ARDS for <24 hours

Mean age: 55 years

LOCATIONS

7 ICUs in the United States



INTERVENTION

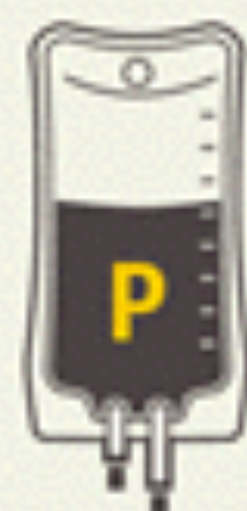


167 Patients analyzed

84

Vitamin C

Intravenous vitamin C infusion, 50 mg/kg every 6 hours for 96 hours total



83

Placebo

Dextrose infusion every 6 hours for 96 hours total

PRIMARY OUTCOME

Change in organ failure assessment (mSOFA), biomarkers of inflammation (C-reactive protein), and vascular injury (thrombomodulin)

FINDINGS

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Change in mSOFA score, points (range 0-20)

Vitamin C 3 points **Placebo** 3.5 points

C-reactive protein at 168 hours, µg/mL

Vitamin C 54.1 µg/mL **Placebo** 46.1 µg/mL

Thrombomodulin at 168 hours, ng/mL

Vitamin C 14.5 ng/mL **Placebo** 13.8 ng/mL

Between-group differences were not significant:

mSOFA, **-0.10** (95% CI, -1.23 to 1.03)

C-reactive protein, **7.94 µg/mL** (95% CI, -8.2 to 24.11)

Thrombomodulin, **0.69 ng/mL** (95% CI, -2.8 to 4.2)

Ascorbate in Sepsis and ARDS

Secondary outcomes	Vitamin C	Placebo	P value
Mortality at day 28	25 / 84 (29.8%)	38 / 82 (46.3%)	0.03
Ventilator Free days	13.1	10.6	0.15
ICU free days to day 28	10.7	7.7	0.03
Transfer out of ICU by 168hr	21 / 84 (25%)	10 / 83 (12.5%)	0.03
Hospital free days	22.6	15.5	0.04

Ascorbate prevention against Coronavirus

Vitamin C 12.5g cocktail

- NSS 125 mL
- Sodium Ascorbate Vitamin C 25 mL (12.5g)
- Magnesium sulfate 10 mL
- Add Vitamin B complex
- Drip for 30-40 min

Vitamin C 25g cocktail

- NSS 250 mL
- Sodium Ascorbate 50 mL (25g)
- Magnesium sulfate 20 mL
- Add Vitamin B complex
- Drip for 40-60 min

China Experience on Ascorbate on Coronavirus

❖ [ClinicalTrials.gov Identifier: NCT04264533](https://clinicaltrials.gov/ct2/show/study/NCT04264533)

❖ ZhiYong Peng, Zhongnan Hospital

Ventilation-free days [Time Frame: on the day 28 after enrollment] days without ventilation support during 28 days after patients' enrollment

- Drug: VC 12g Vitamin C will be infused in the experimental group twice a day for 7 days by the infusion pump with a speed of 12ml/h.
Other Name: Vitamin C
- Drug: Sterile Water for Injection 50ml sterile water for injection will be infused in the placebo comparator group twice a day for 7 days by the infusion pump with a speed of 12ml/h.

China Experience on Ascorbate on Coronavirus

Expert consensus on comprehensive treatment of coronavirus disease in Shanghai 2019

- The government of Shanghai, China has announced its official recommendation that COVID-19 should be treated with high amounts of intravenous vitamin C.
- (1) Dosage recommendations vary with severity of illness, from 50 to 200 milligrams per kilogram body weight per day to as much as 200 mg/kg/day.¹⁰

Pharmacokinetics

- ❖ IV vitamin C half-life 4.3 h (SD 2.6-7.5 h) for a 1.5gm IV initial dose and half-life 6.9 h (IQR, 5.7-8.5 h) for multiple doses¹²
- ❖ 1.87 hr (SD. \pm 0.40) for a 60gm infusion¹¹ in prostate cancer patients
- ❖ Oral doses have a half life of 30 minutes¹³

Vitamin C: Pharmacokinetics

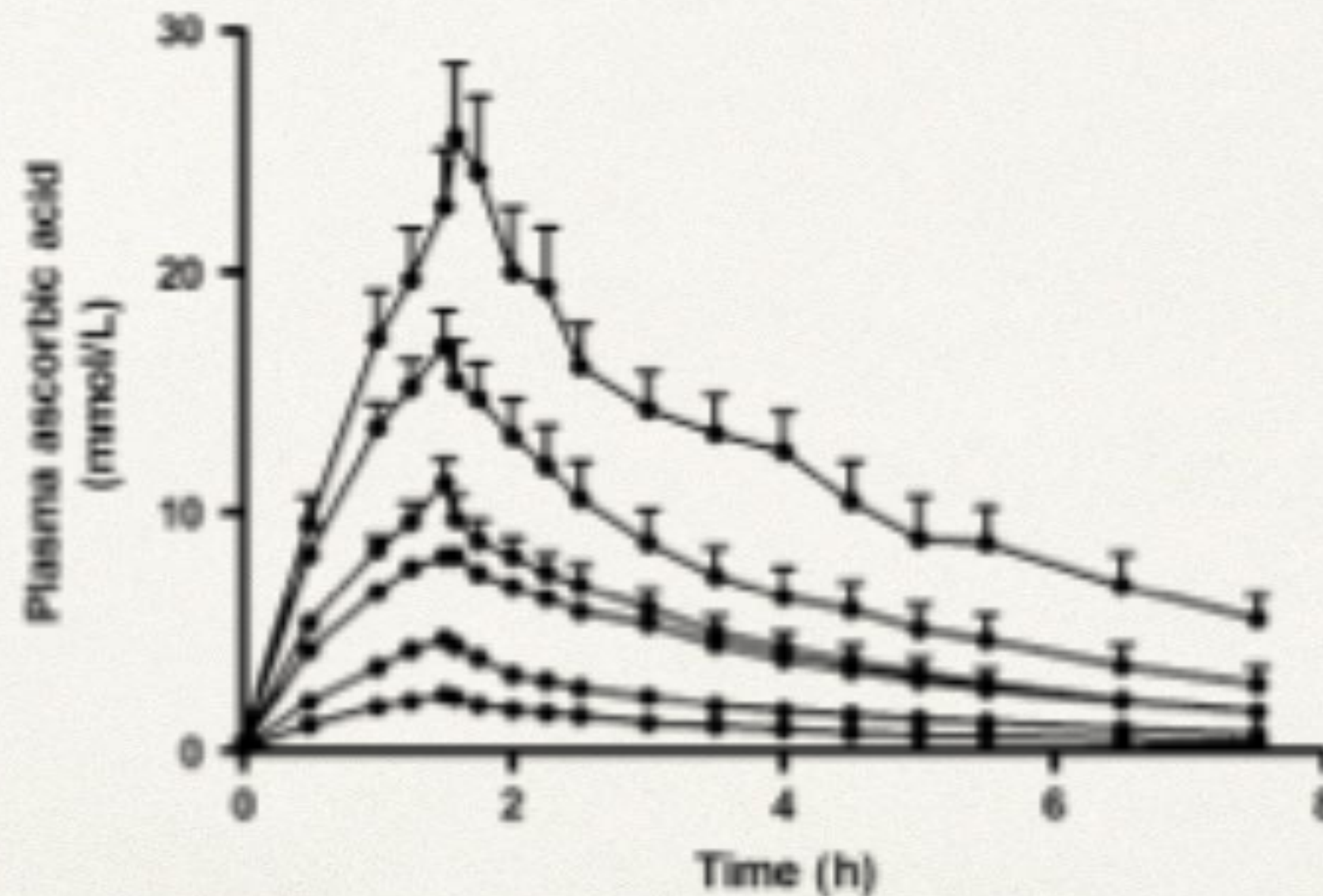


Figure 1. Mean plasma ascorbic acid concentrations \pm SEM during and following infusions of 0.1, 0.2, 0.4, 0.6, 0.9 and 1.5 g/kg ascorbic acid. Each point represents the mean value for either 5 or 6 patients.

Side Effects of Ascorbate

- ❖ pain on IV site (60-70%)
- ❖ lowers serum glucose, potassium, calcium (100%)
- ❖ Increases serum osmolality (thirst), dehydration (100%)
- ❖ increase uric acid, oxalate excretion (100%)
- ❖ Back pain and spasms (10%)
- ❖ Kidney toxicity due to high urates and oxalates (1 case report)
- ❖ Chills and cold sweats (hypothermia, hypoglycemia, hypocalcemia or hypokalemia?) (1-2%)
- ❖ Difficulty of breathing or chest tightness (<1%)
- ❖ Flushing of the skin (1%)

Precautions

- ❖ Glucose 6 Phosphate dehydrogenase deficiency
- ❖ Hypoglycaemia, hypokalemia, hypocalcemia
- ❖ Falsely elevates glucose levels as ascorbate is similar to glucose! Check sugar after 2 hrs from ascorbate infusion
- ❖ Check uric acid, creatinine every 2 days

Vitamin C protocols

	6 grams	12 gms	15 grams	30 grams	50 grams
Vitamin C (500mg/ml) ml	12	24	30	60	100
Magnesium 250mg/ ml	1	1	1	2	4
Calcium (10%)			1	1	1
IV fluid (NSS/ STERILE Water)	30	50	100	200	500

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Thank you and more power to you all!!