Intravenous Vitamin C

A Practitioner Guidebook

510-13SEP23

Contents

INTRODUCTION

What We Cover

Welcome to this practitioner guidebook about intravenous vitamin C (IVC).

- The Practitioner Guidebook provides what you need to know about prescribing and **managing** care, including protocols for the two main types of treatment programme.
- Later sections cover **delivering** treatment, including preparing solutions and managing any problems during administration.

Responsibility

IVC treatment should be carried out by registered clinical practitioners.

This guidebook explains how the doctors and nurses at Integrated Health Options (“The Clinic”) in Auckland, New Zealand, conducted IVC treatment for their patients based on scientific evidence and many years of clinical experience.

It is the responsibility of all healthcare practitioners referring to these guidelines to adapt them for safe use within their practice and for the individual needs of their patients.

MANAGING CARE

Prescribing Overview

Medicine Safety

Sodium Ascorbate Solution by Biological Therapies and Ascor L 500 ® by McGuff Pharmaceuticals are manufactured and distributed to pharmaceutical standards. Please refer to the product safety datasheets.

Intravenous Vitamin C Treatment Programmes

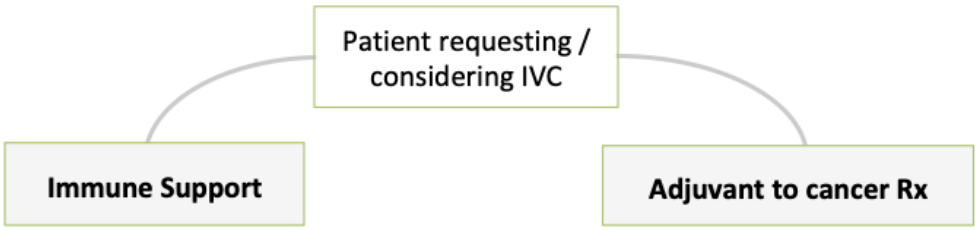
There are two broad programmes of intravenous vitamin C (IVC) treatment you might prescribe and manage:

- Immune support.
- Support for people with cancer.

See the IVC Treatment Protocols section below for details.

Indications, Contra-Indications, Precautions

This section is a summary. For more detail, refer to the rest of this guideline document.



Indications

- Scurvy or vitamin C deficiency
- Acute or recurrent viral or bacterial illness
- End of Life care – Quality of Life
- Before or after cycles of chemotherapy
- Before or after cycles of radiotherapy
- Pre and post surgical intervention
- General fatigue

- Refractory to standard Rx
- Refusing standard Rx *
- Completed standard Rx

* manage ethical implications carefully

Absolute Contra-Indications

For both treatment programmes:

- Acute renal failure
- Previous allergic reaction to vitamin C administration.

Precautions

For both treatment programmes:

- G6PD Deficiency
- Impaired renal function
- Pre-existing renal stones
- Congestive Heart Failure
- Severe thrombocytopenia
- PET, CT/MRI with contrast *
- Pregnancy or breastfeeding (no safety data)
- Unable to provide informed consent

* refer to Stand-Down Times section

Interactions with Other Treatments and Investigations

IVC can interact with some other treatments and investigations.
Refer to the Stand-down Times section below.

Assessing Risk

When assessing the risk level of IVC treatment for a patient, consider both clinical and ethical factors, including but not limited to:

Low Risk	Riskier	
	CLINICAL	ETHICAL
• Physically fit and active • Normal RFT • Clear diagnosis • Satisfactory and stable state • No Contraindications	• Abnormal & deteriorating RFT • Recurrent/active renal stones • Congestive heart failure • G6PD Deficiency • Established bleeding disorder • Very low platelets	• Unable to consent • Refusing recommended standard Rx • Family pressure • Unrealistic expectations • Financial hardship

Managing Intravenous Vitamin C Therapy

Indications

Vitamin C infusions are indicated for:

- Scurvy.
- Vitamin C insufficiency.

(Biological Therapies and McGuff Pharmaceuticals product datasheets)

Vitamin C infusions are also given for:

- Viral/Bacterial infections (Ströhle et al., 2011; Hemilä, 2017; Holford et al., 2020).
- Cancer (Fritz et al., 2014; National Institutes of Health, 2021; Mussa et al., 2022).
- Post-operative wellbeing (Baker et al., 2016; Ayatollahi et al., 2017; Hung et al., 2020).

Contra-Indications

- Acute renal failure.
- Previous allergic reaction to vitamin C administration.

Treatment Precautions

- Some people have a genetic deficiency that means higher doses of vitamin C may cause haemolysis (Juneja et al., 2022). Testing all patients' G6PD levels is strongly recommended before giving any more than 30g of Sodium Ascorbate or 25g of Ascorbic Acid.
- Patients at risk of fluid or sodium overload – such as with congestive heart failure, pedal and/or sacral oedema, acute and/or chronic renal failure, or dehydration – should be carefully managed (Mikirova et al., 2013).
- Use of IVC in patients who are undergoing chemotherapy or radiotherapy should be discussed with the patient and their oncologist. Pre- and post- chemotherapy or radiotherapy may be advantageous (Ma et al., 2014; Carr et al., 2014; Zhao et al., 2018; Furqan et al., 2022). See the Stand-down Times section below for general guidance.
- Patients can become mildly dehydrated so ensure patients are well hydrated before and during the infusion.
- If the urine becomes deep orange/black – dipstick the urine to check for haemolysis. Ensure G6PD is normal.
- If blood test indicates hypercalcaemia, avoid supplemental calcium in the infusion or orally. Do not prescribe vitamin D.
- Although excessive oral vitamin C is not recommended in people with haemochromatosis, the effect of intravenous vitamin C has not been studied in this population. Clinical experience has not raised any concerns relating to IVC increasing iron stores in people with haemochromatosis. However, if IVC is administered to individuals with iron storage diseases, regular monitoring of iron status is recommended.
- Pregnancy or breastfeeding (no safety data).
- IVC can interact with some other treatments. Refer to Stand-down Times below.

Renal Stones

- Oxalic acid is an end-product of metabolic oxidation of vitamin C. Oxalate nephropathy has been reported after administration of IVC in subjects with renal dysfunction (McAllister et al., 1984; Wong et al, 1994; Malhotra et al., 2020; Shen et al., 2023). However, in people with normal renal function the risk of oxalate crystallization in the kidney was not increased (Robitaille et al., 2009).
- Clinical experience is that patients do not experience an increased incidence of renal stones compared to the general population (Prier M et al., 2018). In patients with a history of renal stones the risk should be discussed before administering IVC.

Testing Precautions

- Leave at least 24 hours between IVC infusions and renal function testing to avoid false creatinine readings.
- For insulin-dependent patients who rely on test-strip readings for their insulin dose, there is a risk of overdose causing hypoglycaemia due to false elevation of blood glucose readings after high-dose vitamin C infusion (Sartor et al., 2015; Zhang et al., 2020; He et al., 2021). Diabetic patients should not rely on finger-prick (capillary) glucose tests until 8-10 hours after IVC treatment – possibly even 12 hours after treatment.

> * **NOTE**: A laboratory serum glucose test is **not** affected (Jackson et al., 2006).

- IVC can interact with some investigations. Refer to Stand-down Times below.

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IVC Treatment Protocols

There are slightly different protocols for **Immune Support** and **Cancer Support** programmes, described below. They share recommendations for consultation, testing, treatment review, and injectable preparations.

Consultation

- Take a comprehensive history and examination focusing on presenting health concerns, family history, past history including any history of renal stones, medications, supplements, allergies and focused physical examination as appropriate.
- Record patient's current oral vitamin C dosage.
- Develop a treatment plan for the appropriate treatment programme below.
- Relevant to the patient's condition and needs, discuss how vitamin C may act, its safety, side effects, and potential benefits. Patient must sign a Consent for Treatment.

Testing

- It is strongly recommended that blood tests be ordered prior to commencing doses greater than 30g of Sodium Ascorbate or 25g of Ascorbic Acid. This should include a G6PD, Renal Function (Creatinine, eGFR, Electrolytes), Calcium, CRP, and FBC. See the Managing G6PD Deficiency section below.
- It is usually safe to give up to 30g of Sodium Ascorbate / 25g of ascorbic acid before G6PD test results are back.
- It is advised that renal function is monitored throughout treatment. Testing is usually conducted at commencement of treatment, at four weeks, twelve weeks, then every three months. Patients with lower baseline renal function may be tested more frequently. See the Managing Renal Function section below.
- Additional tests may be patient-specific and ordered at the discretion of the consulting doctor.

Treatment Review

Treatment review is recommended at 2 weeks, 6 weeks, 3 months, 6 months or as indicated by patient needs.

Injectable Preparations

Standard clinical practices apply around prescribing for intravenous administration, including taking osmolarity into account. The following is for guidance only, based on clinical experience.

Carrier

The carrier solution for administration can be 0.9% saline, sterile water for injection, or glucose 5%. The dosage of Sodium Ascorbate/Ascorbic Acid may affect which carrier is prescribed.

- Patients managing a cancer diagnosis may prefer to avoid glucose.
- For doses above 50g of Sodium Ascorbate or Ascorbic Acid, saline is not recommended as a carrier due to impact on osmolarity.
- See the Preparing Intravenous Solutions section below for guidance on bag volumes and draining.

Ascorbic Acid dose	Sodium Ascorbate dose	Carrier Bag size	Saline 0.9%	Glucose 5%	Water For Injection
< **50** g	< **50** g	250 mL	☑	☑	☑
50-100 g	**50-90** g	500 mL	☒	☒	☑
> **100** g	> **90** g	1000 mL	☒	☒	☑

Additives

- Ascorbic Acid, 500 mg/mL *or* Sodium Ascorbate 300 mg/mL
  - Ascorbic Acid 25g in 50mL.
  - Sodium Ascorbate equivalent Ascorbic Acid, 26.5g in 100mL.
- (Optional) Calcium Gluconate 10% – 1 g in 10 mL.

Immune Support

Treatments are generally recommended 1 – 2 times per week but can be administered more frequently at the doctor's discretion and as indicated by patient needs.

1st Treatment

- Generally, 15 - 30 g Sodium Ascorbate / 15 - 25 g Ascorbic Acid.
- Saline 0.9%, sterile water for injection, or glucose 5%: 250 mL.

> * **NOTE**: Check G6PD prior to 2nd treatment if plan includes doses above 30 g Sodium Ascorbate / 25 g Ascorbic Acid.

2nd and Subsequent Treatments

- 15 - 60 g Sodium Ascorbate / 15 - 50 g Ascorbic Acid.
- Saline 0.9%, sterile water for injection, or glucose 5%: 250 mL.

Optional

- If previous symptomatic hypocalcaemia during infusion, consider 10 mL Calcium Gluconate for a patient receiving 60 g Sodium Ascorbate / 50 g Ascorbic Acid or greater (1g/10mL), unless hypercalcaemic.

Support for People with Cancer

- The usual treatment plan is two treatments per week for 6 - 8 weeks initially.
- If there is indication of benefit at review - including quality of life improvements, monitoring blood tests and any available scans - patient may continue with 1-2 treatments per week for another 6 weeks. If there is ongoing benefit, patient may continue treatment every 1 to 3 weeks longer-term. The administration of a standard EORTC QLQ-C30 questionnaire to monitor each patient's quality of life throughout treatment is recommended.
- If available, plasma vitamin C levels are tested once IVC dose is up to 1 - 1.1 g/kg of Ascorbic Acid or 1.1 - 1.2 g/kg of Sodium Ascorbate, until tolerance level is achieved. Plasma vitamin C levels are used to guide tolerance dosing. Aim for 350 - 400 mg/dL (Mikirova et al., 2013; Chen et al., 2015).
- Monitoring plasma vitamin C tests are conducted every 8-10 treatments to check tolerance levels are being maintained. Adjust IVC dose as required.

1st Treatment

- Generally, 15 - 30 g Sodium Ascorbate / 15 - 25 g Ascorbic Acid.
- Saline 0.9% or sterile water for injection: 250 mL.

> * **NOTE**: Check G6PD prior to 2nd Treatment.

2nd Treatment

- 30 - 60 g Sodium Ascorbate / 25 - 50 g Ascorbic Acid.
- Saline 0.9% or sterile water for injection: 250 mL.

3rd and Subsequent Treatments

- Ascorbic Acid can be increased up to 1.1 gram/kg for males, and 1 gram/kg for females, as tolerated.
- Sodium Ascorbate can be increased up to 1.2 gram/kg for males, and 1.1 gram/kg for females, as tolerated.
- See the Preparing Intravenous Solutions section below for guidance on bag volumes.

Optional

- If previous symptomatic hypocalcaemia during infusion, consider 10 mL Calcium Gluconate for a patient receiving 60 g Sodium Ascorbate / 50 g Ascorbic Acid or greater (1g/10mL), unless hypercalcaemic.

Consent for Intravenous Treatment

It is expected that each clinic will have its own approach to gaining the patient's written informed consent before beginning IVC treatment, reflecting its own professional obligations and advice. For your interest, this section presents one possible approach used at The Clinic.

How Do We Understand Consent?

An Interactive Process Between Health Practitioner and Patient

- Explain options.
- Expected risks, side effects, benefits and costs of proposed treatment.
- Convey information in form, language, manner suitable for patient.
- Requires:
  - Trust.
  - Non-pressured environment.
  - Support people if wanted.
  - Opportunity to ask questions/clarify/consider.
  - Can take away information if want.

A Patient Right

Right to make an informed choice and to give informed consent.

"right to information that a reasonable consumer, in that consumer's circumstances, would expect to receive"
(Information, choice of treatment and informed consent. Medical Council of NZ, March 2011).

Consent Discussion – Topics to Cover

- Understanding IVC treatment for patient's condition.
- Discuss safety – any known concerns/issues.
- Discuss side effects.
- Discuss available evidence.
- Advise can withdraw consent at any time.
- Discuss cost.
- Check consent to communicate with other health providers.
- Advise that this treatment is not supported by the majority of doctors.

Consent Discussion – Example Content

Refer also to other sections of these guidelines and references, and to other material relevant for the patient's condition and proposed treatment plan.

Safety

IVC has a very good safety record worldwide. There are a small number of case reports of possible links with renal failure and renal stones but all of these cases had other factors and medications involved so it is difficult to confirm if vitamin C was in any way a causal factor. At the Clinic, baseline renal function was monitored

regularly and no negative impact on renal function or incidence of renal stones was observed in patients having IVC. (See the Treatment Precautions section above)

In the Clinic's history since 1981, there were no deaths as a result of treatments provided. The Clinic did a blood test to exclude a rare genetic condition called G6PD deficiency. Patients with G6PD deficiency were not administered more than 30 grams of Sodium Ascorbate or 25 grams of Ascorbic Acid intravenously, as there is an increased risk of haemolysis (bleeding).

Side-Effects

IVC is normally well-tolerated. Some people notice side effects which are usually minor and transient, resolving within 1-2 hours. See Possible Effects of IVC for details.

> * **NOTE**: Always discuss effect of IVC on blood fingerprick glucose readings in diabetics. See Testing Precautions for details.

Potential Benefits

There are a growing number of clinical studies on IVC. The clinical studies available show benefits in burns patients, sepsis, improved recovery from a range of infections and pre- and post-surgery, and improved quality of life (QOL) in cancer patients. More clinical studies are required. Clinical experience supports potential benefits in all these areas. Benefits in chronic fatigue, some auto-immune conditions, and to support amalgam removal and wound healing have also been observed.

Consent Form Example

An example of a consent form, to be countersigned by a registered medical practitioner, is provided here:

> "I have been diagnosed with the following condition(s):
>
> .....
>
> Through my own research I have become aware of establishments in New Zealand and overseas that provide intravenous infusions of vitamin C or a combination with other nutrients.
>
> I understand that while the safety of these treatments is now supported by double-blind placebo randomised controlled trials, only a limited number of case studies and phase I or II clinical trials have shown efficacy. I am also aware that these treatments may cause complications ranging from non- drug effects to more serious side effects. I have been informed that in this clinic's history since 1981 there have been no deaths as a result of the treatments provided by this clinic (including in-home care, public hospital, hospices, private hospitals and rest homes).
>
> I have had ample time to consider all of the above and after seeking counsel from my next-of-kin and/or independent physician(s), I have decided to undergo such treatments.
>
> I understand and accept that I can withdraw from or the Doctor and staff of The Clinic can cease providing treatment at any time either party deems it to be appropriate.
>
> Before signing this consent form I have been made aware of the charges for treatment, testing and other services provided by The Clinic.
>
> I hereby provide consent for The Clinic to communicate with my primary healthcare provider and/or other health providers who are involved in my healthcare.
>
> I sign this consent being of sound mind."

Patients can strike out the clause about consent to communicate if they wish.

Managing G6PD Deficiency

Some people have a genetic deficiency which may cause haemolysis with high dose intravenous vitamin C (Campbell et al., 1975; Rees et al., 1993; Quinn et al., 2017; Lo & Mok, 2020; Juneja et al., 2022). Testing the patient's G6PD level before giving any more than 30g of Sodium Ascorbate or 25g of Ascorbic Acid is strongly recommended.

This section describes:

- Testing for potential G6PD genetic deficiency.
- Managing the situation appropriately if the test result is below normal range.

Testing for G6PD Deficiency

(Clinical Experience; Labtests reference range)

- Testing for G6PD deficiency is required for all patients considering having more than 30g of Sodium Ascorbate or 25g of Ascorbic Acid intravenously.
- Administering up to 30g of Sodium Ascorbate or 25g of Ascorbic Acid intravenously is considered safe in patients with G6PD deficiency.
- Normal range for G6PD is > 6.9 U/g Hb.

If Results are Below 6.9 U/g Hb

(Clinical Experience; advice from Labtests pathologist)

- Repeat G6PD test.
- Notify the patient's regular GP (if not yourself) that they have G6PD deficiency.
- Avoid administering > 30g of Sodium Ascorbate or 25g of Ascorbic Acid intravenously.
- Refer patients to www.patient.co.uk or a similar source for further information on G6PD deficiency.
- If you have any concern of low-grade haemolysis, order a haemolytic screen shortly after IVC administration: CBC, serum bilirubin, serum LDH, reticulocyte count.

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Managing Renal Function

Poor initial or unnoticed subsequent deterioration in patient renal function may affect ability to handle intravenous vitamin C (IVC) treatment (McAllister et al., 1984; Wong et al., 1994; Alkhunaizi et al., 1996; Malhotra et al., 2020; Maike et al., 2022; Shen et al., 2023). It is advised that the renal function of patients is monitored throughout a course of treatment and that any changes are managed.

Renal Function Testing

(BPAC, 2022; Clinical Experience)

- Obtain a baseline renal function test (RFT) on all new patients.
- For those having IVC, repeat RFT at 4 weeks, 12 weeks and then every 12 weeks.

Managing Changes in Renal Function

(Kidney Health New Zealand, 2017; BPAC, 2022; Clinical Experience)

- If the eGFR reduces 15-20%, repeat the RFT in 1-2 weeks. If there is further reduction, stop IVC and review patient as below.
- If the drop is within normal range (eGFR > 60) and is stable at recheck, review patient for obvious cause. If examination and investigation are normal, use clinical judgement to decide whether to either:
  - continue IVC with precaution of frequent RFT checks, or
  - stop IVC until cause is found.
- If the eGFR reduces more than 20%, stop IVC, review the patient, address any possible causes (eg: dehydration, high meat intake before the test, test done within 24 hours of infusion, new medications, etc).
- Repeat RFT 1-2 weeks later. If normalised or improving, restart IVC and monitor more closely until stabilised. If level continues to reduce, do not restart IVC until cause found. Refer back to GP.

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Stand-Down Times

This section specifies desirable intervals between intravenous vitamin C (IVC) treatment and other forms of medical treatment or investigation. There are some effects which may cause confusion to clinicians particularly if they have not been informed that the patient is having IVC infusions.

IVC Excretion

Vitamin C is promptly excreted by the kidneys with a half-life of around 2 hours (Stephenson et al., 2013; Nielsen et al., 2015). After an intravenous infusion blood levels of vitamin C return to normal after 8 - 10 hours.

Summary of Stand-Down Periods

Because of potential interactions, a clear period is recommended between IVC and other treatments.

For example, if a patient is scheduled for Chemotherapy on a Wednesday, their previous IVC treatment is recommended to be no later than Monday.

Clear period after IVC, before Procedure	Procedure	Clear period after Procedure, before IVC
24 hours	Blood tests	Nil
8-10 hours	Capillary glucose	Nil
24 hours	MRI – with contrast	24 hours
Nil	MRI – no contrast	Nil
24 hours	CT scan – with contrast	24 hours
Nil	CT scan – no contrast	Nil
24 hours	PET scan	24 hours
Nil	X-Ray	Nil
Nil	Ultrasound	Nil
1 whole day	Chemotherapy	2 days
Ask Dr	Daily oral chemotherapy	Ask Dr
2 whole days	Radiotherapy	5 days
24 hours	Surgery	Nil
24 hours	Iron infusion	24 hours

Blood Tests

High dose IVC may sometimes cause artefactual lab test results by interference in assays: decreased readings of direct bilirubin, lipase, UIBC, total cholesterol, HDL/LDL cholesterol, triglycerides, and uric acid; increased readings of sodium, potassium, calcium, and creatinine (Meng et al., 2005; Martinello et al., 2006; Yesildal & Isman, 2020).

Blood glucose test strips will show false elevation of readings with raised serum Vitamin C because vitamin C can interfere with the chemical reaction on the glucose strip (Al-Obaidi et al., 2021).

Leave at least 24 hours between IVC infusions and blood tests including renal function or creatinine tests to avoid false readings.

Diabetics

For insulin-dependent patients who rely on test-strip readings for their insulin dose, there is a risk of overdose causing hypoglycaemia (Sartor et al., 2015; Zhang et al., 2020; He et al., 2021).

Diabetic patients should **not** rely on finger-prick (capillary) glucose tests until **8 - 10 hours after** IVC treatment due to false elevation of readings when using test strips – possibly even 12 hours after treatment.

> * NOTE: A laboratory serum glucose test is **not** affected (Jackson et al., 2006).

Scans and imaging

PET scan

Blood glucose levels have a significant influence on PET scans as increased glucose levels can decrease 18F-FDG uptake in the brain and in tumours because of direct competition between binding sites and enzymes, which may lead to a false negative scan (Bahr & Wilson, 2014; Surasi et al., 2014; Sarikaya et al., 2019).

As IVC will cause a falsely elevated reading on point-of-care glucometers therefore, it should be avoided for 24 hours prior to PET scan.

MRI/CT with Contrast

Studies showed the contrast materials currently used – e.g. gadolinium for MRI, iodine-based compounds for CT – are generally safe in patients with normal kidney function whereas the incidence of contrast-induced nephropathy (CIN) is as low as 2% (Goldfarb et al., 2009). In these patients, the contrast medium injected is almost entirely passed out of the body within 24 hours.

In rare cases, the contrast can cause nephropathy, mostly in patients with impaired renal function and/or in those with diabetes (Li & Ren, 2020). Kidney dysfunction in CIN is usually reversible, with an acute decline in renal function generally occur within 24 - 72 h after contrast administration and return to baseline within 10 - 14 days (Andreucci et al., 2014; Cho & Ko, 2022).

One study has shown a protective effect on the kidneys of oral Vit C administered before and after contrast (Spargias et al., 2004) but conflicting results were reported in another study whereas combination of vitamin C and Pentoxifylline was administered to patients undergoing angioplasty (Shakeryan et al., 2013).

There were no reported nephropathy issues with IVC at the Clinic, and the Doctors' consensus was that stand down should be 24 hours before and after CT or MRI with contrast, but oral vitamin C could be continued.

Surgery

Before Surgery

Some researchers have shown positive effects of IV vitamin C administered just before and during surgery, such as less pain relief needed after surgery, less incidence of myocardial injury and less postoperative pulmonary complications after cardiac surgery, but only at lower doses, such as a few grams (Wang et al., 2014; Ayatollahi et al., 2017; Wang et al., 2020).

As IVC can affect blood test results, it is best to avoid IVC for 24 hours before surgery.

Anaesthesia

One study has shown reduced dosage of anaesthetics in patients undergoing total knee replacement surgery who received preoperative vitamin C infusion (Li et al., 2021). Animal studies suggest that vitamin C (given intramuscularly) before anaesthetic potentiates or enhances the effects of some anaesthetic agents (Elsa et al., 2005, Najafpour et al., 2007).

Recommendations regarding IVC and anaesthetic are the same as those for surgery.

After Surgery

No stand down time is needed if the patient is able to attend.

Chemotherapy and Radiotherapy

The results of recent clinical trials showed that combining IVC with chemotherapy and/or radiotherapy appeared to be safe, well tolerated and could effectively decrease standard therapy associated side effects (Bael et al., 2008; Monti et al., 2012; Welsh et al., 2013; Kawada et al., 2014; Ma et al., 2014; Hoffer et al., 2015; Schoenfeld et al., 2017; Zhao et al., 2018; Carr et al., 2018; Mansoor et al., 2021).

However, due to their small sample sizes and limited studies, it is recommended patients avoid IVC one day before and two days after chemotherapy; avoid IVC two days before and five days after radiotherapy.

If oral chemotherapy is given every day, normal stand-down times do not apply. Some of the clinical trials used IVC in conjunction with oral chemotherapy which seems to be safe, well tolerated and may synergistically increase survival time in some tumours (Bael et al., 2008; Schoenfeld et al., 2017; Allen et al., 2019). IVC may be given on a case by case basis after discussion with the patient.

Iron Infusion

Ferinject or other iron infusion. Mean plasma clearance range from 2.6 – 4.4 mL/min and terminal half-life from 7 – 12 h (Medsafe Ferinject Datasheet, 2021).

There are theoretical concerns that some of the circulating iron may be chelated by the vitamin C or that vitamin C and high concentrations of infused iron may enhance free radical generation via the Fenton reaction, which results in tissue damage (Kontoghiorghes et al, 2020; Pal & Jana, 2020).

In the absence of published evidence of the safety of combining these treatments, it is advisable to leave 24 hours before and after iron infusion.

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Possible Effects of IVC – Patient Guidance

The following is material the Clinic provided to patients:

Common Effects

During and after an infusion of vitamin C, you may experience some common effects. Most are mild and may last up to a few hours.

- **Dehydration** – You may feel thirsty during and after a vitamin C infusion. Please drink plenty of fluids, unless you are on a restricted fluids regime. If so, please discuss with our doctors.
- **Reduced blood sugar** – A vitamin C infusion can reduce your blood glucose level. Having a meal before your treatment and snacking during treatment reduces your risk of this. Please tell the nurses if you notice yourself sweating or feeling dizzy, shaky, or nauseous. We may need to give you a glucose drink to help you feel better.
- **Cramps, headaches, tingling, numbness** – You may experience cramps, headaches, tingling or numbness during the infusion. Tell a nurse if you feel shaky. We may need to give you a calcium and magnesium drink to help you with this.
- **Irritation or pain** – If you notice any irritation or pain during your infusion, please tell a nurse immediately. Sometimes if you move around, the needle gets dislodged and the infusion fluid will cause pain. Do your best to keep your arm still throughout the infusion. Occasionally people will notice increased pain at the site of a recent injury or trauma during an IVC infusion.
- **Tiredness** – You may feel tired after your treatment. Rest and drink plenty of fluids. This effect usually goes away after the first few infusions.
- **Blood tests** – A vitamin C infusion can make some blood test results artificially high (eg: creatinine level). Do your blood test before treatment or more than 24 hours after the infusion.
- **Finger-prick glucose testing** – For people with diabetes, do not rely on finger-prick (capillary) glucose test results for 8-10 hours after your treatment because a Vitamin C infusion can make the results artificially high. A blood serum glucose test is not affected, however.

Uncommon Effects

There are also several possible effects which are not common, and require medical attention:

- **Redness, pain, or swelling** – If you develop any redness, pain, or swelling after treatment please contact the Clinic staff urgently. If it is outside business hours, see a doctor at A&E or your GP's after-hours service.
- **Sore kidneys or blood in urine** – The Clinic monitors your kidney function while you have IVC treatment because there is a reported rare risk of increased kidney stones. The Clinic has not seen this in its patients. If you do notice pain in your kidney region (flanks) or any blood in your urine, please contact the Clinic staff.
- **Darkened urine or jaundice** – Some people have a genetic deficiency that means higher doses of vitamin C are inadvisable. The Clinic always test your G6PD enzyme level before giving more than 25g/30g of vitamin C. If you notice darkened urine or jaundice of your skin or eyes, please contact the Clinic urgently. If it is outside of business hours, see a doctor at A&E or your GP's after-hours service.

DELIVERING TREATMENT

Equipment Needed

Prepared IV bag with additives and primed IV giving set, tourniquet, selected butterfly or cannula needle, alcohol swabs, gauze square, prepared tape and/or opsite, felt tip pen.

Storing Supplies

Store and dispose of injectables and other supplies as directed on their packaging and datasheets. Sodium Ascorbate or Ascorbic Acid for injection should be kept refrigerated.

Preparing Intravenous Solutions

Each clinic has its own way of managing the preparation of IV bags. These are some helpful tips the Clinic picked up during its practice:

- Follow the specified storage temperatures and disposal periods for injectables to preserve their efficacy. After Sodium Ascorbate or ascorbic acid is mixed with water, it should be used within **6 hours** or disposed of.
- Keep the preparation environment clean, and also use alcohol swabs for the injection ports on IV bags and the tops of any opened vials. Use aseptic technique throughout.
- Preparing bags requires focus so discourage others from interrupting.

Vitamin C Options

The two forms of injectable vitamin C used are Sodium Ascorbate or Ascorbic Acid.

Sodium Ascorbate

Ascorbic Acid

Concentration	30 g / 100 mL	25 g / 50 mL
Vial volume	100 mL	50 mL

Carrier Solutions

The carrier solution for administration can be 0.9% saline, sterile water for injection, or glucose 5%.

The dosage of Sodium Ascorbate/Ascorbic Acid may affect which carrier is prescribed. For more details, see the Injectable Preparations section above.

Bag Volumes

The following are the Clinic's recommendations for preparing solutions. Bag draining may be required.

Sodium Ascorbate (100 mL vial)

Sodium Ascorbate dose	Bag preparation
< 35 g	Use a standard 250 mL bag of carrier solution.
35 - 49 g	Drain 50 mL from a standard 250 mL bag.
50 - 90 g	Drain 100 mL from a 500 mL bag of sterile water for injection.
> 90 g	Drain 200 mL or more from a 1000 mL bag of sterile water for injection.

Ascorbic Acid (50 mL vial)

Ascorbic Acid dose	Bag preparation
< 50 g	Use a standard 250 mL bag of carrier solution.
50 - 100 g	Use a 500 mL bag of sterile water for injection..
> 100 g	Drain 200 mL or more from a 1000 mL bag of sterile water for injection.

Calculate Drip Rate

Infusion rate for intravenous vitamin C must be *no faster than* **1 gram** per minute.

- Volume = **total** volume of fluid in the IV bag, including all additives.
- Drip **factor** is stipulated on the IV giving set.
- It is recommended that the calculated drip rate is written on the bag directly.

Calculate: **minimum*** time (minutes) = IVC dose (grams),

$$\frac{\textbf{volume}\ (\text{mL}) \times \textbf{drip factor}\ (\text{drops/mL})}{\textbf{time}\ (\text{minutes})} = \text{drips per minute.}$$

* Adjust upwards depending on the patient. Use a lower rate for first treatment/s and monitor tolerance.

Administering Infusions

Pre-Treatment Patient Check

As part of our standard clinical care, the Clinic's nurses administered a brief check before each treatment session. If there are any concerns about a patient's readiness for treatment, then an urgent doctor consultation is arranged. Questions, along the lines of the following can be asked:

Q1 – How were you after your last IV treatment?

Q2 – Since your last visit here, have you had any change in your condition or treatment schedule?

(prompt further if needed)…

- seen a doctor or specialist,
- been to hospital,
- had or planning any scans or other treatment like chemo or radiotherapy,
- changed the medication or supplements you take,
- had any abnormal events (like vomiting or fever)?

Q3 – Have you eaten?

Infusing

These are The Clinic's guidelines for administering an infusion:

- Check patient name, date of birth and vitamin C dose on IV bag with patient and against treatment sheet.
- Mark bag with start time, halfway, and expected finish time.
- Do not connect the IV if you feel there is a problem. If you are concerned about the patient showing unusual pallor, breathlessness, pulse, BP, or agitation, please alert doctor.
- Wash hands and insert cannula or 23-gauge butterfly needle, secure and connect IV.
- Set IV drip rate as calculated. Monitor every 5 minutes or so, as drip rate can alter very easily.
- Keep an eye on patient's IV site for any signs of tissuing (infiltration/extravasation). Instruct patient to inform nurse when they have pain at site or feel unwell in any way.
- Provide oral fluids (water, tea, juice) as required throughout the IV process, as IVC can cause mild dehydration and thirst. At doses above 30 grams observe for signs of hypoglycaemia.
- When an IV is removed, instruct patient to press firmly on the site for three minutes (or longer if the patient is taking anticoagulants since bleeding time will be prolonged).

Managing Infusion Problems

Emergencies

If a patient's condition requires urgent medical attention during their visit, follow your emergency procedures. Examples are: anaphylaxis, choking, collapse, hypocalcaemia, hypoglycaemia.

Symptoms and Problems

SYMPTOMS	EXPLANATION
Pain **Discomfort**	If patient complains of pain, act immediately. The patient may also feel faint because of the pain. *ACTION* • Assess site for swelling, redness and pain. • If no concerns and butterfly/cannula blood flashback is confirmed then proceed with IV. • A slight reposition of the needle may resolve discomfort. • Apply heat pack to the affected area either above or below the site (aching in the arm may be due to the infusion rate being too fast or the solution being too cold). • If it does not resolve, re-site IV with patient consent.
Swelling **Discomfort** **Burning** **Pain** **Tightness**	**Extravasation** IV fluid may leak into the surrounding tissue. It is commonly caused by needle dislodgement, patient movement or improper placement of the needle. The risk increases in older patients as their veins are thin and fragile. *ACTION* • Stop the infusion immediately and assess for swelling at the site. • If extravasation has occurred, stop the IV infusion. • Remove the IV needle immediately. Protect the exposed end of the IV giving set with a luer lock (see 'Avoiding Contamination' section below). • Apply pressure and an ice pack for pain and swelling. • Explain to patient what has happened and prepare patient for insertion of another IV line. • Once patient is ready to proceed, re-site the IV needle adhering to proper technique, either above the site or on the other arm. * **NOTE**: it is possible for an IV to continue to run into the tissue and for the patient to feel no pain.

SYMPTOMS	EXPLANATION
Nausea **Trembling/Shakiness** **Blurry vision** **Headache** **Decreased coordination** **Impaired judgement**	This may be due to **hypoglycaemic** effect of IVC. Once resolved, remind patient to eat before IV treatment, and to have a snack during the IV treatment. *ACTION* • Stop the infusion. • If symptoms are **Moderate** to **Severe**, give 2 tsp glucose dissolved in water or in fruit juice. • If symptoms are **Mild**, give drink of fruit juice. • If symptoms still persist, give 1 tsp of cal/mag citrate powder dissolved in either water or fruit juice. • Monitor patient, restart infusion as tolerated when symptoms resolve.
Tingling mouth or extremities **Numbness** **Muscle spasm/cramp** **Diplopia** **Stridor** **Tetany** **Convulsions** **+ve Trousseaux & Chvostek signs**	This may be due to **hypocalcaemic** effect of IVC. *ACTION* • Stop the infusion. • Give 1 tsp of glucose and 1 tsp of cal-mag citrate powder dissolved in either water or juice. • Monitor patient and restart infusion once symptoms have resolved. • If symptoms persist after 15 minutes, give another 1 tsp of glucose and 1 tsp of cal-mag citrate powder dissolved in either water or juice. • If symptoms persist, treat as a medical emergency. • Consider testing serum calcium at time of event and renal function 24 hours later.
Lightheaded **Faint**	*ACTION* • Stop infusion, tilt the chair and place pillows to raise feet. • Assess peripheral perfusion, pallor and breathing. • Talk quietly to give reassurance. • Assess blood pressure, heart rate, oxygen saturation. • Place cool flannel on forehead. • When possible, provide a glucose drink (two tsp dissolved in fruit juice). Report to doctor.

SYMPTOMS	EXPLANATION
Arm numbness	May be caused by arm position. *ACTION* • Reposition pillows and advise to move fingers to increase circulation • If this does not resolve, stop the infusion, inform the doctor and if appropriate re-site the IV needle to the other arm.

Preventing Contamination

If the IV needle has to be re-sited, protect the IV giving set from contamination. Once the needle is removed, disconnect it from the giving set and attach a blue luer lock to the exposed end of the giving set.

Discard the IV needle, following your clinic's Infection Control procedure.

Preventing Haematoma

After removal of IV needle, ensure the patient knows to apply pressure to the site for a minimum of three minutes.

If patient is on blood thinning medication encourage them to hold the site for longer; up to 5 minutes. Consider using an IV pressure pad for these patients.

Documentation

Any problems that have occurred during the patient's IV treatment should be recorded in your patient management system.