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Impact of Sodium Ascorbate High Dose on Quality of Life and Pain in Patients Diagnosed With and Treated for Terminal Cancer (Real-World Data Study)

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Abstract

Cancer pain is a complex issue of significant importance in daily clinical practice, requiring a multidimensional approach. Approximately 90% of cancer pain cases can be effectively managed through the appropriate and often combined use of pharmacological and non-pharmacological treatments. In addition to the analgesic drugs outlined in the WHO analgesic ladder, the concurrent use of adjuvant drugs may be considered, which are sometimes essential for effective cancer pain management. These treatments can be adjusted based on the presence of inflammatory processes and oxidative stress.

Methodology: This is an observational, descriptive, retrospective, real-world data study conducted in daily practice at the Country Medical Center in Bogotá, Colombia. It involved patients with any type of cancer diagnosis who were receiving chemotherapy, radiotherapy, oncological surgery, and/or hormonal therapy. From 2018 to 2023, protocols for intravenous high dose of sodium ascorbate were applied, resulting in a sample of 92 patients.

Results: The administration of sodium ascorbate at dose of 100 to 300 and 300 to 600 mg/kg/day showed statistically significant improvements in quality of life ($P = .000$). However, only the 300 to 600 mg/kg/day dose demonstrated a statistically significant reduction in pain ($P = .0061$).

Conclusions: It is possible that by controlling or reducing inflammation, pain sensation can be decreased, therefore high dose of an antioxidant such as sodium ascorbate may be an alternative to improve oxidative stress and inflammation as an adjuvant to analgesic prescription according to pain management guidelines for cancer patients.

Keywords

sodium ascorbate, high dose, cancer, oxidative stress, pain, quality of life

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Introduction

Pain is a common issue among cancer patients, with a prevalence of 90% in advanced stages of the disease. The International Association for the Study of Pain defines it as an unpleasant sensory and emotional experience, associated or not with tissue damage, or described in terms of such damage.[1] Thus, pain is not merely a sensation caused by nociceptor stimulation but also involves an emotional component. Cancer-related pain is a complex and significant issue in daily clinical practice, requiring a multidimensional approach. Approximately 90% of cases can be relieved through pharmacological and non-pharmacological treatments.[2]

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The main causes of cancer-related pain include tumor invasion of adjacent structures (70%), diagnostic and therapeutic procedures (20%), neoplasm-induced syndromes (<10%), and other non-oncological conditions such as osteoarthritis, osteoporosis, and ischemic heart disease.[1]

At the molecular level, cancer-related pain is characterized by the release of prostaglandins, cytokines, and growth factors by tumor cells, indicating that inflammatory processes play a crucial role in its development. This is also linked to oxidative stress and processes such as lipid peroxidation,[3] which are closely associated with the production of reactive oxygen species (ROS), such as superoxide radicals, thereby contributing significantly to pain progression. In addition, the release of various cytokines, including TNF-α, IL-1β, and IL-6, further aggravates symptoms due to their pro-inflammatory effects.[4]

The World Health Organization (WHO) primarily recommends prescribing analgesic medications based on their potency and the type of pain the patient experiences.[5] However, ~20% of patients do not experience adequate relief despite the use of high dose of opioids, along with adjuvant and non-opioid medications, or they suffer from a high incidence of undesirable side effects,[6] for this reason, the concomitant use of additional adjuvant drugs could be considered. If inflammation and oxidative stress are properly controlled, these agents may serve as complementary alternatives to enhance pain management in cancer patients.[7] Vitamin C (ascorbate form), is the primary non-enzymatic, water-soluble antioxidant present in plasma.[8] Most mammals synthesize ascorbic acid in the liver from glucose; however, humans, guinea pigs, primates, and certain bats lack this ability and must obtain it through their diet. Ascorbate has been reported to have anti-inflammatory effects, associated with reduced secretion of pro-inflammatory cytokines such as tumor necrosis factor, interleukin-23, and C-reactive protein.[9]

The relationship between vitamin C and cancer is highly complex. The role of oxidative stress in cancer initiation and progression is well-documented, and cancer patients often exhibit low plasma levels of vitamin C with a reduced response to supplementation. This hypovitaminosis may be a side effect of certain anticancer therapies or result from increased vitamin C uptake by tumor cells.[6]

Experimental and epidemiological evidence regarding vitamin C and cancer risk remains inconclusive. Studies have shown associations between vitamin C infusion and inflammatory biomarkers, suggesting potential improvements in symptoms and biomarker levels, with a possible benefit in quality of life (QoL).[10]

Multiple studies have described the beneficial effects of vitamin C in various types of cancer, reporting positive responses in terminally ill patients and evaluating general aspects such as quality of life. These findings have shown statistical significance, suggesting a potential protective association with vitamin C use,[11] in studies examining the relationship between vitamin C and cancer, Cameron and Campbell[12] found that a daily dose of 10 g, administered continuously during the first 10 days, was effective against cancer. However, this effect was not observed in double-blind, placebo-controlled trials conducted at the Mayo Clinic, where the same dose was administered exclusively via the oral route. This discrepancy suggests that the route of administration may influence the bioavailability of ascorbate, which in turn affects its potential anticancer properties.[13]

When administered orally, ascorbate concentration in the plasma of healthy humans is tightly regulated, resulting in only a slight increase that does not produce a significant effect in specific indications,[2] in contrast, after intravenous infusion, plasma ascorbate levels reach much higher concentrations.[14] Notably, intravenous administration can lead to plasma ascorbate levels 30 to 70 times higher than the highest tolerated oral dose,[15] however, these elevated concentrations are relatively transient due to rapid renal clearance, with a half-life of ~2 hours in circulation.[12]

Given these factors and the challenges that randomized clinical trials may face in evaluating the use of high-dose vitamin C as an adjuvant in cancer patients, this study was designed as a real-world data analysis. The proposed hypothesis is that high-dose intravenous vitamin C, when assessed under real-world clinical conditions, may demonstrate protective and adjuvant effects in cancer patients, including the reduction of pain and improvement in quality of life, which cannot be fully captured through randomized clinical trials due to population heterogeneity, ethical limitations, and variability in the response to sodium ascorbate.[16]

Moreover, there is significant variability in the effects of sodium ascorbate attributable to differences in individual metabolism, baseline nutritional status, tumor biology, and variations in dosing regimens. Under this premise, the hypothesis is reinforced by the notion that real-world studies allow for the evaluation of therapeutic effects in routine clinical practice, reflecting patient heterogeneity and providing valuable insights—including evidence on pain reduction and its physical and emotional dimensions—that randomized clinical trials may not always capture.[14-16]

Materials and Methods

According to the experience of our institution in the care of patients with different types of cancer, seeing that high doses of sodium ascorbate have had clinical results of improvement of side effects and pain, it was decided to conduct the present study, which aims to evaluate the impact of the high dose of sodium ascorbate according to different management protocols with different concentrations of intravenous dose in patients diagnosed with cancer of different etiologies, within the daily practice in a

medical institution in Bogota (Country Medical Center). A review of the medical records determined the patients of the cohort, identifying those who met the requirements established in the inclusion and exclusion criteria.

The study was approved by the Scientific Research Committee of the Colombian Society of Preventive and Orthomolecular Medicine, which reviewed this work in accordance with Colombian research regulations, specifically Resolution 8430 of 1993, Resolution 2378 of 2008, the Declaration of Helsinki, and Good Clinical Practice guidelines for research.

The oxidative stress biomarker was evaluated using the Free Radical Analytical System (FRAS) 5 assay, a methodology designed to quantify the antioxidant capacity of plasma. This analysis was considered in the study design and included in the data collection process. The results obtained did not show statistically significant differences between the comparison groups; therefore, the values are presented descriptively, without performing additional inferential analyses.

Type of Study

An observational, descriptive, retrospective real-world data study was conducted in the city of Bogotá, Colombia (Country Medical Center), involving patients diagnosed with cancer of any etiology who had undergone chemotherapy, radiotherapy, oncological surgery, and/or hormonal therapy.

Selection of Study Population

This study focused on patients who received high-dose intravenous sodium ascorbate between 2018 and 2023. A retrospective review of medical records was conducted in patients admitted with a diagnosis of cancer of any etiology during this 5-year period.

Inclusion Criteria

- Patients over 18 years old.
- Diagnosis of malignant cancer of any etiology.
- Patients under any cancer treatment.
- Patients treated with high dose of sodium ascorbate according to the institution's protocols.
- Patients who have completely finished their Sodium Ascorbate treatment.
- Application of EORTC QLQ-30 quality of life for cancer treatment.
- Patients who have all the information in the medical record.

Exclusion Criteria. The following exclusion criteria were defined as exclusion criteria:

- Patients under 18 years old.
- Patients with a previous allergy to sodium ascorbate or to any of its excipients/vehicles.
- Patients without a diagnosis of malignant cancer of any etiology.
- Severe liver failure.
- GFRe $\leq$30 mL/min/1.73 m^2 (defined by the formula CKD-EPI SCr).
- History of any organ transplantation requiring active immunosuppressive therapy that may interfere with renal function.
- Receiving dialysis (either acute or chronic) or need imminent dialysis at the time of application.
- Patients with known HIV infection.
- Patients with known or suspected history of oxalate nephropathy or hyperoxaluria, chronic iron overload, G-6PD-deficiency anemia.
- Patients with known hemochromatosis.
- Patients who have not completely finished their sodium ascorbate treatment.
- Patients whose medical records are incomplete or lack essential information.

Intervention. The sodium ascorbate therapy administered was the 11.2 g in 100 mL vial solution (equivalent to 10 g of ascorbic acid) from Biological Therapies Australia (sodium ascorbate solution 112.49 mg/mL, injection for intravenous infusion 100 mL; Biological Therapies). The administration protocol was as follows: day 1, 5 g of vitamin C in a 30-minute intravenous infusion; day 2, 15 g in a 40-minute infusion; day 3, 30 g in a 50-minute infusion; and day 4, 50 g in a 60-minute infusion. The interval between dose was 7 days. The vehicle used was SSN 0.9% 500 mL. The total duration of intravenous vitamin C treatment was 4 days at 7-day intervals, after which oral vitamin C was added at a dose of 1 g/day for 30 days.

Data Collection and Variables. Information was collected through a research form, which included data from patients' medical records, demographic and clinical-epidemiological factors, treatment details, clinical symptom assessments, laboratory test results, and the final clinical outcomes, specifically pain levels and quality of life.

The demographic factors were: age, sex, occupation, education level and socioeconomic stratum; clinical aspects: cancer etiology, laboratory tests (tumor markers, C-reactive protein, erythrocytes, hemoglobin and hematocrit, leukocytes, thrombocytes, creatinine, and oxidative stress). Important aspects for quality of life were assessed with the EORTC QLQ-30 tool, which was previously validated in a quality of life assessment study with sodium ascorbate.[17] EORTC QLQ-C30 scores were recorded before the vitamin C intervention and after the fourth treatment with sodium ascorbate. Pain intensity was evaluated using a visual analog scale consisting of a

numeric line from 0 (no pain) to 10 (worst imaginable pain), completed by the patient.[1]

Statistical Analysis

For the present analysis of this study, a database in Excel (Microsoft) was initially used, which was parameterized according to the variables to be studied, recoding for subsequent statistical analysis, with this tool the descriptive and analytical analysis was performed. During the recoding of variables, the dose of sodium ascorbate applied according to previous protocols and according to the patient's weight and the dose applied were converted into values of mg/kg/day, making it easier to standardize and thus be able to make the different associations; for the analytical statistics, the χ^2 test with Yates adjustment was used, with a statistical significance of 95%, to associate the variables of quality of life, pain and the dose of sodium ascorbate applied, this test was performed with the EPIDAT version 3 program.1; for the logistic regression tests, a linear regression test was performed using the IBM SPSS Statistics 27 program.

Results

After reviewing the medical records and completing the database, including the parameterization and recoding of data, the target population consisted of 92 patients, recruited in the daily consultation of the institution with the application of the previously described sodium ascorbate protocols; the characteristics of the study population are described below, as well as the results obtained.

Characterization of the Population

Table 1 shows the different demographic characteristics of the 92 patients, their distribution by gender, which is 37 (40.22%) male, 55 (59.78%) female, all patients over 18 years old, as evidenced in the age distribution, as well as their occupations, educational levels, and socioeconomic status.

Table 2 describes the specific clinical variables of the 92 patients, such as the type of cancer classified and recoded by systems and the types of treatments they have undergone.

Table 3 shows the different paraclinical tests that are relevant in the treatment of these patients, such as the blood count, platelets, and FRAS 5, a test, that is, useful to measure the oxidative stress in patients.[18] Table 3 also includes patients with alterations in the levels of these paraclinical tests, such as those with anemia, thrombocytopenia, elevated creatinine, and decreased creatinine, as well as the results of FRAS 5.

Table 4 summarizes the results of the EORTC QLQ-C30 quality-of-life instrument, broken down into physical and activities of daily living, psychosomatic aspects, pain, overall quality of life, and general health status. Scores from before the vitamin C intervention and after the fourth treatment with sodium ascorbate were used to classify each patient's evolution as worsened, unchanged, or improved.

As seen in Table 4, following the application of high dose sodium ascorbate, there was an improvement in patients when assessed using the EORTC QLQ-C30 tool, with statistically significant results in each domain. For physical activity, 67 patients improved ($\chi^2=11$; $P=.000$; CI=5.9-23.6); for daily activities, 82 patients improved ($\chi^2=200$; $P=.000$; CI=59.7-665); for psychosomatic aspects, 77 patients improved ($\chi^2=79$; $P=.000$; CI=29.2-215); for quality of life and general health status, 77 patients improved ($\chi^2=49.7$; $P=.000$; CI=20.5-119.8); and finally, for the pain variable, 35 patients improved ($\chi^2=1.4$; $P=.31$; CI=0.7-2.76), the latter not being statistically significant.

As shown in Table 5, all patients who received the high dose of sodium ascorbate were classified into 2 groups: those who received 100 to 300 mg/kg/day and those who received 300 to 600 mg/kg/day. It is important to clarify that the higher doses expressed in mg/kg/day corresponded mainly to patients with lower body weight, as the dosing was standardized according to individual weight; this explains why some patients received higher concentrations of intravenous vitamin C.

Regarding the pain variable, 11 patients improved in the 100 to 300 mg/kg/day group, while 24 patients improved in the 300 to 600 mg/kg/day group ($\chi^2=3.74$; $P=.0061$; 95% CI=1.5-9.0), indicating a statistically significant impact when administering a higher dose of sodium ascorbate.

For the variables of quality of life and general health status, improvement was observed in both dose groups, with 41 and 36 patients showing improvement, respectively ($\chi^2=0.58$; $P=.51$; 95% CI=0.19-1.74), with no statistically significant differences between them. Thus, similar improvement rates for this variable were observed at both doses, consistent with findings reported in previous vitamin C research.[17]

Finally, regarding oxidative stress measured using the FRAS 5 assay, 10 patients improved their score by more than 25% in the 100 to 300 mg/kg/day group, compared with 23 patients in the 300 to 600 mg/kg/day group ($\chi^2=4.6$; $P=.5$; 95% CI=0.52-38.7). This result was not statistically significant, likely because this test was performed in only 36 of the 92 patients included in the study.

Based on the above, it is evident that multiple variables can influence the final results we have evaluated regarding the outcome variables (pain and quality of life). For this reason, the decision was made to apply logistic regression to assess the contribution of each variable that might affect pain. When evaluated in a general manner, the result is not statistically significant ($P=.310$). However, when adjusting

Table 1. Demographic Description.

	Male	%	Female	%	Total	%
Gender distribution	37	40.22	55	59.78	92	100
Age group						
Under 30 y	2	2.17	3	3.26	5	5.43
30-45 y	8	8.70	6	6.52	14	15.22
45-60 y	24	26.09	14	15.22	38	41.30
60-80 y	20	21.74	9	9.78	29	31.52
80 or more	1	1.09	5	5.43	6	6.52
Mean	59.65		58.56		58.72	
Variance	354.96		171.99		243.48	
SD	18.84		13.11		15.62	
Minimum	20		20		20	
Max	90		90		90	
Range	70		70		70	
Weight						
Mean	68.63		64.63		66.30	
Variance	233.30		233.30		233.30	
SD	15.2		15.2		15.27	
Minimum	36		45		36	
Max	105		110		110	
Range	69		65		74	
Occupation						
Administrative—office	11	11.96	24	26.09	35	38.04
Farmer—field work	3	3.26	1	1.09	4	4.35
Merchant—trader	2	2.17	1	1.09	3	3.26
Teacher	1	1.09	5	5.43	6	6.52
Student—technician	3	3.26	5	5.43	8	8.70
Home—retired	5	5.43	14	15.22	19	20.65
Engineer—designers	5	5.43	1	1.09	6	6.52
Military	3	3.26		0.00	3	3.26
Health personnel	3	3.26	4	4.35	7	7.61
Religious	1	1.09		0.00	1	1.09
Level of education						
Primary		0.00	1	1.09	1	1.09
Secondary	9	9.78	21	22.83	30	32.61
Technician	3	3.26	3	3.26	6	6.52
Professional	24	26.09	29	31.52	53	57.61
Postgraduate	1	1.09	1	1.09	2	2.17
Socioeconomic status						
Low		0.00	1	1.09	1	1.09
Middle	18	19.57	41	44.57	59	64.13
High	19	20.65	13	14.13	32	34.78

for the sodium ascorbate dose variable of 300 to 600 mg/kg/day, the result becomes statistically significant ($P = .0061$), as shown in Table 6.

Discussion

Among the approaches available to reduce oxidative stress is the infusion of high dose vitamin C, which has been used for over 50 years in many countries worldwide. Vitamin C use was initially aimed at correcting severe vitamin C deficiency (scurvy) which was observed in several medical conditions and is associated with musculoskeletal pain. In this context, analgesic properties were observed in specific clinical settings. Other pathologies, such as complex regional pain syndrome, acute and postherpetic neuralgia, and cancer, have also shown specific benefits in pain management associated with the use of vitamin C. Among the proposed mechanisms, one suggests that vitamin C acts as a

Table 2. Clinical Description.

Types of Cancer classified by Systems	Male	%	Female	%	Total	%
Types of cancer classified by systems						
Breast and adnexal cancer		0.00	23	25.00	23	25.00
Digestive system cancer—mouth—anus	12	13.04	8	8.70	20	21.74
Prostate and male sexual organs cancer	11	11.96		0.00	11	11.96
Uterus—cervix and female sexual organs cancer		0.00	8	8.70	8	8.70
Central and peripheral nervous system cancer	4	4.35	3	3.26	7	7.61
Thyroid cancer	1	1.09	5	5.43	6	6.52
Leukemias and lymphomas	3	3.26	3	3.26	6	6.52
Respiratory system cancer	2	2.17	2	2.17	4	4.35
Skin and adnexal tumor	1	1.09	2	2.17	3	3.26
Kidney and urinary system cancer	2	2.17		0.00	2	2.17
Bone tumors	1	1.09	1	1.09	2	2.17
Types of treatments						
Chemotherapy	14	15.22	23	25.00	37	40.22
Surgical + chemotherapy	2	2.17	14	15.22	16	17.39
Chemotherapy + radiotherapy	3	3.26	7	7.61	10	10.87
Surgical + chemotherapy + radiation therapy	5	5.43	5	5.43	10	10.87
Radiotherapy	7	7.61	1	1.09	8	8.70
Surgical	3	3.26	3	3.26	6	6.52
Surgical + radiotherapy	3	3.26	2	2.17	5	5.43

Table 3. Paraclinical Results.[19,20]

Paraclinical	Male	%	Female	%	Total	%
Tumor markers	11	11.96	3	3.26	14	15.22
Patients with complete blood count	17	18.48	25	27.17	42	45.65
Patients with Hb and Hto values	19	20.65	29	31.52	48	52.17
Patients with anemia	9	9.78	10	10.87	19	20.65
Patients with platelet levels	15	16.30	24	26.09	39	42.39
Patients with thrombocytopenia	8	8.70	7	7.61	15	16.30
Patients with creatinine levels	16	17.39	28	30.43	44	47.83
Patients with elevated creatinine levels	4	4.35	4	4.35	8	8.70
Patients with decreased creatinine levels	0	0.00	2	2.17	2	2.17
FRAS* 4	16	17.39	20	21.74	36	39.13
FRAS 5 worsened	1	1.09		0.00	1	1.09
Improves FRAS 5 by 0%-25%		0.00	2	2.17	2	2.17
Improves FRAS 5 by 50%-75%	14	15.22	16	17.39	30	32.61
Improved 75% or more	1	1.09	2	2.17	3	3.26

Abbreviation: FRAS 5, Free Radical Analytical System.

cofactor in the biosynthesis of amidated opioid peptides, particularly through the enzyme peptidyl-glycine α-amidating monooxygenase. However, this represents only one of several potential mechanisms involved in its analgesic effects.[21]

Several studies have supported the therapeutic role of vitamin C in oncology, particularly as an adjuvant treatment aimed at improving quality of life, modulating oxidative stress, and reducing disease- or therapy-related symptoms. In breast cancer, Mansoor et al observed that weekly intravenous administration of 25 g of vitamin C for 4 weeks, in combination with standard treatment, reduced the intensity of common symptoms such as nausea, loss of appetite, fatigue, and insomnia. Similarly, Vollbracht et al reported that weekly intravenous applications of 7.5 g of vitamin C as adjunct therapy in stage IIa to IIIb breast cancer

Table 4. Quality of Life Results.

Quality of life	Worsening	%	Same	%	Improvement 0%-50%	%	Improvement 50%-100%	%	χ^2	*P*	CI
Physical activity	3	3.26	22	23.91	64	69.57	3	3.26	11	.000	5.9-23.6
Daily activity	1	1.09	9	9.78	76	82.61	6	6.52	200	.000	59.7-665
Psychosomatic aspects	4	4.35	11	11.96	37	40.22	40	43.48	79	.000	29.2-215
Pain	1	1.09	56	60.87	2	2.17	33	35.87	1.4	.310	0.7-2.76
Quality of life and general health	4	4.35	11	11.96	45	48.91	32	34.78	49.7	.000	20.5-119.8

significantly reduced disease- and treatment-induced symptoms including fatigue, depression, vertigo, and hemorrhagic diathesis, with no adverse events reported.[22,23]

In a prospective study of terminal cancer patients, Yeom et al demonstrated that combined intravenous (10 g twice daily) and oral (4 g daily) vitamin C administration significantly improved global health status, physical, emotional, cognitive, and social functioning, and reduced fatigue, nausea, vomiting, pain, and appetite loss. Similarly, Takahashi et al reported a significant improvement in quality of life, assessed by the EORTC QLQ-C30 questionnaire, after administering high-dose intravenous vitamin C (10 g twice at 3-day intervals) followed by daily oral supplementation (4 g), with notable reductions in fatigue and insomnia.[24,25]

In more advanced or treatment-resistant cancer populations, Günes-Bayir and Kiziltan found that intravenous vitamin C (2.5 g) in patients with bone metastases unresponsive to radiotherapy led to better functional outcomes, a 50% reduction in pain intensity, and a substantial increase in median survival (10 vs 2 months in controls), suggesting clinically meaningful palliative benefits. These results are consistent with the recommendations of Klimant et al, who proposed intravenous vitamin C infusions (5-25 g) as a safe complementary intervention to reduce inflammation, restore antioxidant capacity, and improve fatigue, pain, and sleep quality.[26,27]

At the molecular level, Polireddy et al and Ma et al demonstrated that pharmacological plasma concentrations of ascorbate induce selective cytotoxicity in pancreatic and ovarian cancer cell lines by depleting NAD^+ and ATP, causing DNA damage, activating the ATM/AMPK pathway, and inhibiting mTOR signaling. These mechanisms appear to enhance the efficacy and reduce the toxicity of chemotherapeutic agents such as gemcitabine, carboplatin, and paclitaxel. In the phase I PACMAN trial (Welsh et al), escalating intravenous ascorbic acid doses (15-125 g twice weekly) achieved plasma levels above 350 mg/dL and were well tolerated, with a mean survival of 13 ± 2 months in patients completing at least 2 treatment cycles. Likewise, Hoffer et al confirmed the safety and tolerability of intravenous ascorbate at 1.5 g/kg in combination with chemotherapy, with no clinically relevant metabolic alterations or increase in oxalate excretion.[28-31]

While Levine et al initially described vitamin C as primarily antioxidant, without significant pro-oxidant effects in humans, subsequent studies using pharmacologic intravenous doses revealed its capacity to decrease inflammatory mediators and exert beneficial pro-oxidant effects within the tumor microenvironment through the selective generation of cytotoxic hydrogen peroxide. Collectively, these findings suggest that vitamin C at high doses can modulate both redox balance and metabolic pathways linked to cellular proliferation and survival, translating into multidimensional clinical benefits.[32]

As we have seen, the use of vitamin C as an adjuvant treatment for cancer patients is not new; however, many variables still need to be identified and better understood, particularly considering that vitamin C is effective at high dose but its efficacy depends on numerous clinical and patient-specific factors that must be standardized to achieve tangible clinical outcomes. Another variable to consider is the formulation of vitamin C: there are different pharmaceutical presentations, such as ascorbic acid, calcium ascorbate, and sodium ascorbate, among others, which have shown favorable clinical results.[33] Nevertheless, based on our experience, not all of these formulations can be safely administered at high or very high dose without sometimes producing undesirable side effects, such as pain at the injection site, phlebitis, fever, and occasional headaches. From our clinical experience, sodium ascorbate is the safest formulation for administering high or very high dose, providing reliable safety in patient care with minimal adverse effects.[34]

This real-world study in cancer patients suggests that high-dose sodium ascorbate can improve quality of life and clinical parameters such as inflammation and oxidative stress, thereby contributing indirectly to pain relief. The identification of a reference dose above 300 mg/kg/day provides a practical framework for developing protocols and guiding clinicians in using this strategy as an adjuvant option. It is also important to consider that patients with higher body weight may present additional factors that could blunt the clinical response to intravenous vitamin C beyond receiving lower weight-adjusted doses. Individuals with higher body mass often exhibit chronic low-grade

Table 5. Results After Treatment With Sodium Ascorbate According to the Dose Administered.

Vitamin C dosage	Male	%	Female	%	Total	%
100-300 mg/kg/day						
Pain						
Worsening	1	1.09		0.00	1	1.09
Same	12	13.04	23	25.00	35	38.04
Improved	8	8.70	3	3.26	11	11.96
Quality of life and general health						
Worsening	1	1.09		0.00	1	1.09
Same	3	3.26	2	2.17	5	5.43
Improved	17	18.48	24	26.09	41	44.57
FRAS* 5						
Worsening	1	1.09		0.00	1	1.09
Improved by <25%		0.00	1	1.09	1	1.09
More than 25% improvement	8	8.70	2	2.17	10	10.87
300-600 mg/kg/day						
Pain						
Worsening		0.00		0.00	0	0.00
Same	9	9.78	12	13.04	21	22.83
Improved	7	7.61	17	18.48	24	26.09
Quality of life and general health						
Worsening		0.00	3	3.26	3	3.26
Same	1	1.09	5	5.43	6	6.52
Improved	15	16.30	21	22.83	36	39.13
FRAS 5						
Worsening		0.00		0.00	0	0.00
Improved by <25%		0.00	1	1.09	1	1.09
More than 25% improvement	7	7.61	16	17.39	23	25.00

Analysis of the Impact of the 300-600 mg/kg/day dose with respect to the 100-300 mg/kg/day dose.	χ^2	*P*	CI
Quality of life and general health	0.58	.51	0.19-1.74
Pain	3.74	.0061	1.5-9.0
Oxidative stress	4.6	.5	0.52-38.7

Abbreviation: FRAS, Free Radical Analytical System.

Table 6. Logistic Regression.

Independent variables	Wald	*P*	CI
Gender	0.000		
Age	0.000		
Cancer diagnosis	0.000		
Type of cancer treatment	0.000		
Sodium ascorbate treatment (mg/kg/d)	197.592	.000	2.089–494.356

Wald indicates whether a variable has a real effect on the model. CI showing the precision of the estimated effect.
Abbreviation: CI, confidence interval.

systemic inflammation and an increased oxidative stress burden, which may reduce the effective bioavailability or biological activity of vitamin C. Although these variables were not directly assessed in our cohort, this mechanism has been well documented and may partially explain the more modest improvements observed in heavier patients.[35] However, given the observational design of this study, limitations such as selection bias, confounding, and

information bias must be acknowledged, which restrict the ability to establish causality. Therefore, these findings should be interpreted as preliminary associations that support the need for larger, multicenter studies with greater methodological rigor.

Conclusions

Pain in cancer patients is multifactorial, with inflammation and oxidative stress playing central roles in its persistence and severity. Our real-world experience suggests that high-dose sodium ascorbate, particularly at doses above 300 mg/kg/day, may provide meaningful benefits by reducing inflammation, attenuating oxidative stress, and indirectly alleviating pain, while also contributing to improved quality of life. These findings highlight sodium ascorbate as a potentially safe and valuable adjuvant in supportive cancer care, complementing conventional analgesics and addressing treatment-related complications. However, further large, multicenter studies with rigorous methodology are needed to validate these observations, refine dosing strategies, and evaluate additional outcomes such as inflammatory biomarkers, pain relief, and functional improvement, with the ultimate goal of offering cancer patients safer and more comprehensive options for pain management.

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Ethical Considerations

The study was approved by the Scientific Research Committee of the Colombian Society of Preventive and Orthomolecular Medicine, which reviewed the protocol in accordance with Colombian research regulations, specifically Resolution 8430 of 1993, Resolution 2378 of 2008, the Declaration of Helsinki, and Good Clinical Practice guidelines for research involving human participants.

Consent to Participate

Written informed consent was obtained from all patients, requesting their authorization for the administration of sodium ascorbate infusions. The document explained the potential benefits and risks of the intervention, clearly stating that patients could withdraw their consent at any point during therapy. Additionally, participants were asked for permission to use their clinical data for statistical analysis and for publication in scientific journals, ensuring that confidentiality was strictly maintained at all times.

Author Contributions

Hugo Mario Galindo Salom was responsible for the collection of clinical data and patient follow-up, as well as the interpretation of clinical results and the final approval of the manuscript. Carlos Alberto Carrillo Bravo (corresponding author) contributed to the conception and design of the study, data analysis and interpretation, and the overall supervision of the project. Helber Armando Prieto Lozano drafted the initial version of the manuscript, conducted the literature search and organization, and provided support in the statistical analysis. Paulo Andrés López Posada performed the critical revision of the intellectual content, methodological adjustments, and contributed to the discussion of results. All authors approved the final version of the manuscript and take responsibility for the integrity and accuracy of its content.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data Availability Statement

Due to confidentiality and patient data protection, the datasets generated and analyzed during this study are not publicly available. However, additional information may be requested from the corresponding author (Carlos Alberto Carrillo Bravo; email: bravoscarlos04@gmail.com, under justified circumstances.

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