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Beetroot (*Beta vulgaris L.*) juice supplementation and hemoglobin response in head and neck cancer patients after chemotherapy

Suplementasi jus buah bit (Beta vulgaris L.) dan respon hemoglobin pada pasien kanker kepala dan leher pasca kemoterapi

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Abstract

Anemia frequently occurs in patients with cancer and can worsen due to chemotherapy. The literature on non-pharmacological interventions to increase hemoglobin levels in patients with head and neck cancer following chemotherapy remains limited. This study aimed to measure the effect of beetroot juice supplementation on changes in hemoglobin levels in patients with head and neck cancer who had undergone chemotherapy. Methods: An experimental study with a one-group pretest–posttest design was conducted at dr. Zainoel Abidin General Hospital, Banda Aceh (July–November 2024). The sample consisted of all head and neck cancer patients undergoing chemotherapy cycles I–VI (total sampling, n=40), divided into two treatment groups: 100 g beetroot juice (n=20) and 200 g beetroot juice (n = 20). Hemoglobin levels were measured before and 14 days after the intervention. The analysis was performed using paired t-tests and effect sizes (Cohen's d). Results: Administration of 100 g of beetroot juice did not significantly alter hemoglobin levels, with an average difference of −0.24 g/dL (p = 0.241). In contrast, the 200-gram dose resulted in a significant increase in hemoglobin levels, with an average difference of +0.44 g/dL (p = 0.016) after 14 days of intervention. Furthermore, the estimated Cohen's d (pooled SD) was 0.51, indicating a moderate effect. In conclusion, the administration of 200 g beetroot juice for 14 days was associated with a small but statistically significant increase in hemoglobin levels in patients with head and neck cancer who underwent chemotherapy. Further studies in the form of RCTs with larger sample sizes and stricter compliance monitoring are needed to confirm these findings and assess their clinical relevance.

Keywords: Anemia, functional beverage, beetroot juice, nutrition intervention, post chemotherapy

Abstrak

Anemia sering terjadi pada pasien keganasan dan dapat diperburuk oleh kemoterapi. Bukti literatur mengenai intervensi non-farmakologis untuk meningkatkan hemoglobin pada pasien kanker kepala-leher pasca kemoterapi masih terbatas. Penelitian bertujuan untuk mengukur pengaruh suplementasi jus buah bit terhadap perubahan kadar hemoglobin pada pasien kanker kepala-leher pasca kemoterapi. Metode, penelitian eksperimental dengan desain one-group pretest–posttest dilakukan di RSUD dr. Zainoel Abidin Banda Aceh (Juli–November 2024). Sampel adalah seluruh pasien keganasan kepala-leher yang menjalani kemoterapi siklus I–VI (total sampling, n=40), dibagi menjadi dua kelompok perlakuan yaitu jus buah bit 100 g (n=20) dan 200 g (n=20). Kadar hemoglobin diukur sebelum dan 14 hari setelah intervensi. Analisis menggunakan uji t berpasangan, serta ukuran efek (Cohen's d). Hasil, pemberian jus buah bit 100 gram tidak menunjukkan perbedaan

bermakna terhadap kadar hemoglobin dengan selisih rata-rata −0.24 g/dL (p = 0.241). Sebaliknya, pada dosis 200 gram, terjadi peningkatan kadar hemoglobin yang signifikan dengan selisih rata-rata +0.44 g/dL (p = 0.016) setelah 14 hari intervensi. Selanjutnya, estimasi Cohen's d (pooled SD) ditemukan sebesar 0.51 atau memiliki efek sedang. Kesimpulan, pemberian jus buah bit 200 g selama 14 hari berkaitan dengan peningkatan kecil namun signifikan secara statistik pada kadar hemoglobin pasien kanker kepala-leher pasca kemoterapi. Studi lebih lanjut berbentuk RCT dengan ukuran sampel lebih besar dan pemantauan kepatuhan lebih ketat diperlukan untuk memastikan temuan ini dan menilai relevansi klinisnya.

Kata Kunci: Anemia, minuman fungsional, jus buah bit, intervensi gizi, paska kemoterapi

Introduction

Anemia is a common clinical complication in patients with cancer and can be exacerbated by antineoplastic therapy, particularly chemotherapy. Anemia in oncology patients contributes to a reduced quality of life, increased fatigue, and potentially compromises adherence to therapy regimens, which can worsen the patient prognosis. Modern surveys and reviews have reported a high prevalence of anemia in patients receiving cancer therapy. Prevalence rates vary by population and type of therapy, but some studies have reported an increase in the prevalence of anemia of greater than 40–60% during the treatment phase (Bozzini et al., 2024; Weir, 2021; Wondm et al., 2024).

Conventional therapeutic approaches for cancer-related anemia include iron supplements, blood transfusions, and erythropoiesis-stimulating agents. Although effective, these options have clinical limitations and side effects, including gastrointestinal reactions, transfusion risks, and potential long-term side effects in the oncology population (Bozzini et al., 2024). Therefore, functional food-based nutritional interventions with a high safety profile are attractive alternatives to explore as adjuvant therapies or preventive strategies against hemoglobin decline during and after chemotherapy (Gui et al., 2023).

Beetroot (*Beta vulgaris L.*) contains bioactive components relevant to the physiology of hematopoiesis and tissue perfusion, including inorganic nitrate (a precursor of nitrite to nitric oxide), folate, and betalain pigments, which have antioxidant and anti-inflammatory properties (Milton-Laskibar et al., 2021).

Proposed biological mechanisms include increased nitric oxide bioavailability for improved tissue perfusion and oxygenation, as well as the support of micronutrient substrates necessary for erythrocyte synthesis. Preclinical reviews and studies, as well as some clinical trials in non-oncology populations, suggest that beetroot juice supplementation may lower blood pressure, improve muscle perfusion, and, in some studies, improve hematological parameters in populations with nutritional anemia. However, evidence in patients with cancer, particularly those with head and neck cancer undergoing chemotherapy, is limited (Chen et al., 2021; Tan & Hamid, 2021).

A recent literature review indicates that most intervention studies with beetroot juice focus on the general population, athletes, or groups with nutritional anemia (e.g., pregnant women and adolescents), while evidence assessing the hematological effects of beetroot juice in oncology patients is still limited and heterogeneous in terms of design, dose, and duration of intervention (Tan & Hamid, 2021; Wondm et al., 2024). This gap is important because patients with head and neck cancer are at particular risk for anemia due to a combination of tumorological factors, chronic inflammation, and the cytotoxic effects of chemotherapy, which may modulate the response to nutritional interventions (Wagner, 2020).

From a clinical translational perspective, the comparative efficacy of two practical doses of beetroot juice (e.g., 100 g vs. 200 g) has not been adequately evaluated in the post-chemotherapy head and neck cancer patient population. Assessing the hemoglobin response to these two doses is important to: (1) determine the dose size that provides hematologic benefit without increasing dietary burden or side effects, (2) provide relevant empirical evidence for adjuvant nutrition

recommendations in oncology care, and (3) understand whether the effects reported in non-oncology populations can be replicated in patients with complex metabolic and inflammatory conditions after chemotherapy. Recent reviews have emphasized the need for focused clinical studies in the oncology population with designs that report hematologic outcomes and adherence parameters in a standardized manner (Chen et al., 2021; Tan & Hamid, 2021).

Based on this lack of evidence and the potential for significant clinical benefit in a referral hospital setting in a middle-income country, this study was designed to address this knowledge gap by directly examining the effect of two doses of beetroot juice on hemoglobin levels in post-chemotherapy head and neck cancer patients. This study is expected to provide local evidence that can support recommendations for adjuvant nutrition practices in oncology patients and serve as a basis for further, larger-scale randomized controlled studies. Therefore, this study aimed to assess the effect of two doses of beetroot juice (100 g and 200 g) on hemoglobin levels in post-chemotherapy head-and-neck cancer patients at dr. Zainoel Abidin Regional General Hospital, Banda Aceh.

Methods

Research Design

This study used a quasi-experimental design with two treatment groups and no control group (two-group pretest–posttest design). This design was chosen because of ethical considerations and the clinical limitations of including a control group without intervention in active cancer patients undergoing chemotherapy. Although it lacked an external comparison group, this design allowed for the analysis of changes in hemoglobin levels before and after the intervention between the two doses of beetroot juice (100 g and 200 g). This design weakness the limitations of causal inference due to the lack of a randomized control is acknowledged as a limitation of this study and is considered in the interpretation of the results.

Research Location and Time

The study was conducted at the Ear, Nose, Throat, and Head and Neck Surgery (ENT-BKL) Polyclinic and Inpatient Ward, as well as the Clinical Pathology Laboratory of dr. Zainoel Abidin Regional Hospital, Banda Aceh, Aceh Province, Indonesia. The implementation period will be from July to November 2024 and will include recruitment, intervention, and laboratory analysis.

Research Population and Sample

The target population included all patients diagnosed with head and neck cancer who underwent platinum- and/or taxane-based chemotherapy at dr. Zainoel Abidin Regional Hospital during the study period.

The inclusion criteria were as follows:

1. Patients aged ≥ 16 years.
2. Undergoing active chemotherapy (cycles I–VI).
3. The baseline hemoglobin level was 9–12 g/dL (mild-to-moderate anemia).
4. Not currently receiving blood transfusions or parenteral hematinic therapy.
5. Informed consent was obtained.

Exclusion criteria:

1. History of hematologic diseases (leukemia, bone marrow disorders, or bleeding disorders).
2. Chronic kidney failure or other severe systemic diseases.
3. The patient had a history of beetroot allergy.
4. Hb <9 g/dL or required transfusion during the intervention period.

Sampling Size and Techniques

The sampling technique used was total sampling, covering the entire population that met the inclusion criteria during the study period. Of the 47 eligible patients, 40 were willing to participate and completed the entire series of interventions (response rate ≈ 85%). Subjects were then divided into two treatment groups using a systematic allocation method based on the recruitment order to maintain the balance of baseline characteristics: Group A (n = 20): received 100 g of beetroot juice/day. Group B (n = 20) received 200 g of beetroot juice/day.

Data Collection Procedures

Baseline data collected included age, gender, clinical diagnosis, chemotherapy cycle, and initial hemoglobin level. Blood samples were collected twice by experienced laboratory personnel: before the intervention (day 0) and 14 days after the intervention (day 14). All blood samples were collected in the morning (8:00–10:00 a.m. WIB) during a minimum of 8-hour

fast to minimize physiological variations in hemoglobin levels due to hydration or circadian rhythms. Blood samples were analyzed using an automated hematology analyzer (Sysmex XN-1000, Kobe, Japan) at the Clinical Pathology Laboratory of Dr. Zainoel Abidin Regional Hospital, with daily internal quality control procedures.

Research Intervention

Red beetroot (Beta vulgaris L.) was obtained from a local organic farming supplier in Central Aceh, which has been certified as pesticide-free. Fresh tubers were washed, peeled, and mashed using a juicer extractor without added sugar or preservatives. The resulting juice was packaged in sterile 200 mL glass bottles and stored at 4 °C; each bottle was consumed within ≤ 24 h. Nutrient content was analyzed in random samples, and the average nitrate, iron, and folate contents were ~ 250 mg/100 g, 0.8 mg/100 g, and 35 µg/100 g, respectively (based on spectrophotometric analysis at the Nutrition Laboratory of Universitas Syiah Kuala).

Participants were asked to consume beetroot juice every morning for 14 consecutive days at a dose appropriate for their group. Compliance was monitored through daily consumption records and inspection of the remaining bottles at each follow-up visit (days 7 and 14). Participants who missed more than two days of consumption were recorded as non-compliant and excluded from the per-protocol analysis but were included in the intention-to-treat (ITT) analysis.

Data Processing Techniques

The collected data were entered into an electronic spreadsheet, double-checked, and analyzed using IBM SPSS Statistics software (version 26). Data distribution was tested using the Shapiro–Wilk test to determine the normality. Numerical data are presented as mean ± standard deviation (SD) or median (interquartile range [IQR]) according to their distribution.

The analysis model and statistical test used was the paired t-test, which aimed to measure changes in hemoglobin levels in each test group. In addition to the p-value (< 0.05 is considered significant), the mean difference, 95% confidence interval (CI 95%), and effect size (Cohen's d) were also reported to strengthen clinical interpretation.

Ethical Considerations

This study was approved by the Health Research Ethics Committee of dr. Zainoel Abidin General Hospital, Banda Aceh (Number: 146/ETIK-RSUDZA/2024). All procedures were performed in accordance with the principles of the Declaration of Helsinki. Participants were given a complete explanation of the purpose, benefits, and risks of the study and signed an informed consent form before participation. The identity of the respondents was kept confidential, and the data were used solely for scientific purposes.

Result and Discussion

Characteristics of Research Subjects

A total of 40 patients with head and neck cancer who met the inclusion criteria participated in this study. The participants were evenly divided into two treatment groups: 100 g (n=20) and 200 g (n=20) of beetroot juice. Most participants were male (67.5%) and in the adult age group (65%). The most common diagnosis was nasopharyngeal carcinoma (65%), and most participants were in their first cycle of chemotherapy (37.5%). The distribution of baseline characteristics between the groups was relatively balanced (Levene's test, p=0.124).

Most patients had mild-to-moderate anemia (Hb 9–12 g/dL) before the intervention. There were no significant differences in the baseline characteristics between the groups (p>0.05).

Table 1. Baseline characteristics of patients (n=40)

Variable	Group100 g (n=20)	Group 200 g (n=20)	Total (n=40)
Gender, male n (%)	17 (85,0)	10 (50,0)	27 (67,5)
Age, mean ± SD (years)	44,45 ± 15,6	52,9 ± 13,0	48,7 ± 14,3
Nasopharyngeal carcinoma diagnosis, n (%)	15 (75,0)	11 (55,0)	26 (65,0)
Chemotherapy cycle I–II, n (%)	11 (55,0)	11 (55,0)	22 (55,0)
HB before (g/dL), mean ± SD	11,12 ± 1,27	10,35 ± 0,84	10,74 ± 1,09

Table 2. Changes in hemoglobin levels before and after intervention through beetroot juice supplementation

Group	Hb Before (Mean ± SD)	Hb After (Mean ± SD)	Δ Hb (Mean ± SD)	95% CI	p-value	Cohen's d
100g Supplement	11,12 ± 1,27	10,88 ± 1,02	0,24 ± 0,42	0,17 – 0,65	0,241	-
200g Supplement	10,35 ± 0,84	10,79 ± 0,87	0,44 ± 0,39	0,09 – 0,79	0,016	0,51

The majority of patients had mild to moderate anemia (Hb 9–12 g/dL) before the intervention. There were no significant differences in the baseline characteristics between the groups (p>0.05); therefore, both groups were considered homogeneous.

Changes in Hemoglobin Levels

After 14 days of intervention, the 100-gram group showed a small decrease in hemoglobin levels (Δ = –0.24 ± 0.42 g/dL; p = 0.241; 95% CI: –0.65 to 0.17). In contrast, the 200-gram group experienced a mean increase in hemoglobin levels of 0.44 ± 0.39 g/dL (p = 0.016; 95% CI: 0.09–0.79).

The effect size was calculated using the pooled SD between the two groups, resulting in Cohen's d = 0.51, which indicates a statistically moderate effect size, indicating that the increase in hemoglobin levels at the 200 g dose has moderate biological significance, although it has not yet reached full clinical relevance. Although the mean increase in hemoglobin of 0.44 g/dL did not exceed the clinically meaningful limit (≥1 g/dL according to Aapro et al. (2018)), these results show a statistically significant positive direction of change and a moderate effect (Cohen's d = 0.51), so they can be considered to have biologically relevant potential.

The results of this study indicate that consuming 200 g of beetroot juice per day for two weeks can significantly increase hemoglobin levels in post-chemotherapy head and neck cancer patients, although this increase did not reach clinical significance. The increase in hemoglobin levels, with a moderate effect size, indicates that this intervention provides a positive biological response to the red blood cell formation process. In contrast, no changes were observed in the group receiving the 100-gram dose, suggesting that the effect of beetroot juice may be dose-dependent.

These findings support the hypothesis that the bioactive compounds in beets, particularly nitrate, iron, folate, and betalain pigments, play crucial roles in supporting hematopoiesis after cytotoxic therapy. Nitrate in beets is enzymatically converted to nitrite and subsequently to nitric oxide (NO), which improves tissue perfusion and stimulates the secretion of the hormone erythropoietin in the kidneys (Lundberg, 2018). This hormone plays a role in stimulates the formation of new red blood cells in the bone marrow. Furthermore, the folate and iron content in beets supports the synthesis of erythroid DNA and hemoglobin (Al Rahmad, 2023; Mayasari et al., 2023). This mechanism is strengthened by the antioxidant activity of betalains, which helps reduce oxidative stress due to chemotherapy, thereby maintaining a longer red blood cell lifespan (Clifford et al., 2015).

The increase in hemoglobin found in this study is in line with the study by Sakar Emad Ali & AL-Qadhi (2025), who reported an increase in Hb levels after the consumption of beetroot juice in individuals with mild anemia. Similarly, Bryan et al. (2023) explained that natural nitrate supplementation from green leafy vegetables and tubers, such as beets, can increase erythropoietin levels and the efficiency of iron utilization. Tan and Hamid (2021) also showed that beetroot bioactive compounds can reduce oxidative stress and improve hematological status in patients with chronic inflammatory conditions, including cancer. These results provide preliminary evidence that high-dose beetroot juice consumption may act as an adjuvant nutritional intervention to support hemoglobin recovery after chemotherapy.

However, the increase in hemoglobin levels of 0.44 g/dL needs to be interpreted with caution. According to Bryer & Henry (2018), Changes in Hb levels of less than 1 g/dL typically do not have a significant clinical impact on anemia symptoms but can be interpreted as an early sign of hematopoietic recovery after therapy. This suggests that these results may reflect the physiological adaptation process after chemotherapy, facilitated by the intake of bioactive components from beets. Other factors, such as differences in nutritional status, type of

chemotherapy, and adherence to juice consumption, may also influence individual responses to this intervention.

Despite its positive effects, this study has several important limitations that need to be acknowledged. First, the study design without a control group limits the ability to draw causal conclusions between the intervention and the increased hemoglobin levels. Second, the small sample size (n=40) and relatively short intervention duration (14 days) limit the statistical power and generalizability of the results. Third, several confounding factors, such as iron intake, nutritional status, hydration, and inflammation levels, were not strictly controlled, which could have influenced the results. Fourth, the clinical effect was relatively small, although statistically significant. These limitations suggest that further research with a randomized controlled trial (RCT) design and a larger sample size is needed to confirm these findings more conclusively.

Nevertheless, the findings of this study have important practical implications. Consuming 200 g of beetroot juice per day can be considered a safe nutritional support approach for cancer patients to help maintain hemoglobin levels during the post-chemotherapy recovery phase. This intervention is relatively easy to implement, has a low risk of side effects, and can be combined with conventional therapies. However, it is important to note the potential for mild gastrointestinal side effects and the natural sugar content of beets, which may be inappropriate for patients with certain metabolic disorders. Therefore, standardization of juice formulations, clinical monitoring, and long-term safety evaluations are needed before this intervention can be widely recommended in oncology nutrition clinical practice.

The results of this study add to the scientific evidence regarding the role of beetroot-based functional foods in supporting hematological recovery in patients with cancer. The moderate increase in hemoglobin levels and modest statistical effect suggest that this intervention has promising physiological potential, although it is not yet fully clinically meaningful. With further robust studies and more rigorous designs, beetroot juice could be an evidence-based adjuvant nutritional therapy in the management of anemia in patients with cancer after chemotherapy.

Conclusion

This study shows that consuming 200 g of beetroot juice per day for 14 days resulted in a statistically significant increase in hemoglobin levels in head and neck cancer patients after chemotherapy compared to a 100-gram dose. Although the average increase in hemoglobin was relatively small (approximately 0.44 g/dL), these results demonstrate the physiological potential of beetroot's bioactive components particularly nitrate, iron, folate, and betalains in supporting red blood cell formation (hematopoiesis) after cytotoxic therapy.

Clinically, this intervention can be considered a safe and easy-to-implement adjuvant nutritional approach to help maintain hemoglobin levels during the post-chemotherapy recovery phase, especially in patients with mild-to-moderate anemia. However, because the improvement in hemoglobin levels is still limited in clinical practice, further studies with randomized controlled trials (RCTs), longer intervention durations, and measurement of additional hematological biomarkers such as ferritin, erythropoietin, and serum iron status are needed to further verify its effectiveness and mechanisms of action.

Practical advice: beet juice should be administered in moderate to high doses (approximately 200 g per day), accompanied by monitoring of consumption compliance and the patient's nutritional status. Healthcare professionals in the field of oncology nutrition may consider integrating beet juice into a diet program for anemia recovery, considering digestive tolerance and the natural sugar content of beets.

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