Improvement of functional constipation with kiwifruit intake in a Mediterranean patient population: An open, non-randomized pilot study

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ABSTRACT

Introduction: Kiwifruit consumption has shown to improve functional constipation in healthy elderly population, according to studies in New Zealand and China. The aim of this study was to evaluate the effect of kiwifruit intake on functional constipation in a Mediterranean patient population characterized by its distinctive nutritional habits.

Material and Methods: An open, non-controlled and non-randomized longitudinal study was conducted in 46 patients with constipation (Rome III criteria). Patients monitored for five weeks: weeks 1 and 2 no kiwifruit and weeks 3-5 three kiwifruit per day (Green kiwifruit, Actinidia deliciosa var Hayward). Bristol Scale, volume of stools, and ease of defecation was self-reported daily. The evolution of the categorical variables was tested using the Bhapkar test; functional data methodology was used for continuous variables, and Generalized Estimating Equation (GEE) models were adjusted.

Results: The percentage of patients with ≥3 stools per week increased from 82.61% (95% CI: 69–91.2) at week 1 to 97.78% (95% CI: 87.4–99.9) at week 2 of kiwifruit intake, with 76.09% (95% CI: 61.9–86.2) responding during the first week. The reporting of stable ideal stools increased from 17.39% (95% CI: 8.8–31) at week 2 to 33.33% (95% CI: 21.3–48) at week 5. According to GEE models, the number of depositions increased significantly (p-values<0.001) in 0.398 daily units at week 1 the first week of intake, up to 0.593 daily units at week 5; significant improvements on facility in evacuation and volume of evacuation were found from the first week of intake (all p-values<0.001).

Conclusions: The intake of three kiwifruits per day significantly improves the quality of evacuation (number of depositions, volume, consistency and ease) in a Mediterranean patient population suffering from functional constipation.
Mejora del estreñimiento funcional con la ingesta de kiwi en una población mediterránea: Estudio piloto abierto no randomizado

RESUMEN

Introducción: Consumir kiwi mejora el estreñimiento funcional en la población anciana sana de Nueva Zelanda y China. Nuestro objetivo es evaluar el efecto del kiwi en la población mediterránea con estreñimiento.

Material y métodos: Estudio prospectivo longitudinal no cegado no aleatorizado. 46 pacientes adultos con estreñimiento (criterios Roma-III) fueron seguidos durante cinco semanas: dos previas y tres durante la intervención (3 kiwi/día) (Green kiwifruit, Actinidia deliciosa var Hayward). Autoinforme diario del número de deposiciones, consistencia y volumen heces y facilidad de evacuación. La evolución de las variables categóricas se testó con el test Bhapkar, las variables continuas mediante metodología de análisis de datos funcionales ajustando modelos basados en las ecuaciones de estimación generalizadas (GEE).

Resultados: El porcentaje de pacientes con ≥3 deposiciones/semana aumentó de 82,61% (IC 95%: 69–91,2) en la primera semana hasta 97,78% (IC 95%: 87,4–99,9) al final de semana 2 de consumo, con una respuesta del 76,09% (IC 95%: 61,9–86,2) en la primera semana. El porcentaje de heces consideradas ideales pasó de 17,39% (IC 95%: 8,8–31) en la segunda semana a 33,33% (IC 95%: 21,3–48) en la semana 5. Según los modelos GEE, el número de deposiciones aumenta significativamente (valor p<0,001) en 0,398 unidades diarias en la primera semana de consumo, hasta 0,593 unidades diarias en la última semana. A partir de la primera semana se observa mejoras significativas en el volumen de las heces y en la facilidad de la defecación (valores p<0,001).

Conclusiones: Consumir tres kiwis al día mejora significativamente la calidad de la evacuación (número deposiciones, volumen, consistencia y facilidad evacuación), en una población mediterránea de pacientes con estreñimiento.

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INTRODUCTION

Constipation is a symptom suffered by a large number of people, due to multifactorial causes. Worldwide general population prevalence of this symptom ranges from 0.7% to 79% (median 16%)\(^1\). Some factors associated with constipation are sex, with higher prevalence in females (especially during pregnancy)\(^1\), and age; in general it becomes gradually more prevalent after the 70 years of age, in women the increase is considerable from a young age (18–23 years old) to middle age (45–50 years old)\(^1\).

Although constipation frequently manifests itself during a limited time period and with a moderate impact on health, it represents a major problem not only because of its high prevalence but also for its personal, social, occupational and economic effects\(^2\). Both physical and mental impacts interfere with quality of life and personal wellbeing\(^3\). The costs of constipation healthcare and treatment are highly significant, consuming a large volume of resources, both in relation to the use of laxatives and to medical visits\(^4\) (even considering the large proportion of population that take medication without prescription)\(^5\).

Constipation is characterized by difficult or infrequent deposition, often accompanied by excessive straining during bowel movement or sensation of incomplete evacuation. In most cases, there is no underlying organic cause, and constipation is labelled as chronic idiopathic constipation.
and as a functional digestive disorder. The Rome-III criteria is a useful tool for the diagnosis of constipation that highlights the chronic nature of the disorder and the importance of symptoms beyond the infrequency of bowel movements.

Understanding its causes, prevention, and treatment will help most people find constipation relief. An individual’s medical history is very important in determining a constipation diagnosis. Primary healthcare professionals should enquire about dietary habits and lifestyle, pharmacological and toxic habits, complementary and alternative medicine, physiological bowel habits, use of laxatives and past disease history.

There have been several small-randomized controlled trials (RCTs) studying the relationship between dietary fiber and constipation. A meta-analysis demonstrated that dietary fiber can increase stool frequency in patients with constipation but also showed that dietary fiber did not improve stool consistency, treatment success, laxative use and painful defecation. On the consumption of fruits there are very few studies. A crossover RCT (40 patients) showed that dried plums 50g taken twice a day for 6 weeks, improve the number of stools per week and the score on the Bristol scale and improves symptoms associated with constipation and straining.

A growing body of scientific evidence supports the consumption of green kiwifruit as a digestive aid, as it leads to more effective digestion of dietary protein, increased faecal bulking and softening and better lubrication that assists the propulsion of contents along the colon. Recent studies have demonstrated significant results in the treatment of constipation in healthy elderly in patients with irritable bowel syndrome. These studies consistently report an increase in the frequency and ease of defecation, stool volume and softness.

Although literature suggests that kiwifruit consumption improves constipation symptoms, no studies have been carried out in adults nor in a Mediterranean patient population, which are characterized by its distinctive nutritional habits. The aim of the present study was to test the effect of kiwifruit consumption on functional constipation in a Spanish adult population.

**MATERIAL AND METHODS**

**Design:** Open non-controlled and non-randomized longitudinal study, on the effect of kiwifruit consumption in adult patients with diagnosed constipation.

**Setting:** The study was conducted in five primary healthcare centres in Barcelona, Catalonia, Spain.

**Period Study:** Between April and August 2013.

**Population sample:** Fifteen participating family doctors selected patients from the electronic medical records (e-HCAP) following inclusion and exclusion criteria. Each investigator was allowed to include a maximum of 4 patients. Forty-six subjects were selected for the study.

**Sample calculation:** According to results from Chang, sample size was calculated to detect a change in the proportion of individuals with 3 or more defecation per week from 56% to 86% (evolution from an average of 3.2 to 4.4 –-stable Standard Deviation (SD) of 1.3– in a normal distribution). Assuming a bilateral contrast for paired data, with a significance level of 0.05 and power of 0.8, a sample of 44 individuals was required (covering a 10% of dropout rate).

**Inclusion criteria:** Adults (aged 18 to 65) with e-HCAP constipation diagnosis, following Rome-III criteria:

- Two or more of the following:
  - Straining during at least 25% of defecations
  - Lumpy or hard stools in at least 25% of defecations
  - Sensation of incomplete evacuation for at least 25% of defecations
  - Sensation of anorectal obstruction/blockage for at least 25% of defecations
  - Manual manoeuvres to facilitate at least 25% of defecations (e.g., digital evacuations and support of the pelvic floor)
  - Fewer than three defecations per week; and
  - Loose stools are rarely present without the use of laxatives;
  - Insufficient criteria for irritable bowel syndrome;
  - Criteria fulfilled for at least 3 months with symptom onset at least 6 months before diagnosis.

**Exclusion criteria:** Patients with allergy to kiwifruit or latex; who have undergone gastro-intestinal surgery in the last year; taking medication to treat constipation; with oncological disease; taking narcotic medication or with organic gastroenterological diseases (except non-complicated diverticulosis).
Improvement of functional constipation with kiwifruit intake in a Mediterranean patient population: An open, non-randomized pilot study

**Intervention:** The duration of the study was five weeks. During the first two weeks patients were asked to follow their regular diet and avoid kiwifruit consumption. The next three weeks they were asked to consume three green kiwifruits (Actinidia delicosa var Hayward) per day, one at each main meal (breakfast, lunch and dinner). Throughout the five-week study period the patient had to continue their normal eating habits and exercise regime.

**Outcomes and their measurement:** Primary endpoint: proportion of patients with three or more stools per week, frequency of stool per week and number of responders (increase of ≥1 stool per week). Secondary endpoints: Consistency of stool - Bristol Scale\(^1\): classified as Type 1 (Separate hard lumps, like nuts-hard to pass), Type 2 (Sausage-shaped, but lumpy), Type 3 (Like a sausage but with cracks on its surface), Type 4 (Like a sausage or snake, smooth and soft), Type 5 (Soft blobs with clear cut edges -passed easily-), Type 6 (Fluffy pieces with ragged edges, a mushy stool), or Type 7 (Watery, no solid pieces, entirely liquid). Types 1–2 indicate constipation, with 3 and 4 being the ideal stools (especially the latter), and 5-7 tending towards diarrhoea. The Bristol Scale is a scale translated, validated and adapted into Spanish\(^\text{14}\). Volume of stool: very little (1), little (2), medium (3), reasonably much (4), a lot (5). Ease of defecation: very easy (1), easy (2), normal (3), difficult (4), very difficult (5). Patients answered eight satisfactions questions related to the improvement of defecation habits and quality of life. Other variables collected: use of laxatives, type of laxative, nutrition habits and special diets if present. All the variables were recorded in a daily basis, except the satisfaction of the patient that was recorded on a weekly basis. Other variables collected were age, gender, weight and height.

**Tools and instructions:** The five-week study design and associated activities are shown in the flow chart (Figure 1). Primary Care Professionals asked patients to participate in the study and explained it to them. Patients who voluntarily agreed to participate signed the informed consent, accepting all study procedures. Each participant in the study attended three consultations: the first one before starting the study, the second one after two weeks and the third one after five weeks. There was no follow-up period.

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**Figure 1.** Flow chart.

* Ticket collection and payment of the amount could be agreed with the patient in different ways (every other day, weekly, etc...)

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**Selected adults (age 18 to 65) with e-HCAP diagnose of constipation, following Roma III criteria n = 46**

- Two patients discontinued the commitment to participate in the study prior to the kiwi intervention
- Replacement participant following the same criteria n = 2

- To recruit the patient by phone or in consultation
- Week 1: 1) Normal diet 2) Fill dairy
- Week 2: 1) Normal diet 2) Fill dairy
- Week 3: 1) 3 kiwis/day (breakfast, lunch, dinner) 2) Fill dairy 3) Save all receipts for kiwis
- Week 4: 1) Fill dairy
- Week 5: 1) Collect the diary - Pay kiwis to the patients* - Enter data (google docs)

**VISIT 1**
- Study presentation
  - Acceptance study
  - Informed consent
- Including patient in the online database (google docs)

**VISIT 2**
- - Check the diary - Clarify doubts

**VISIT 3**
- - Check the diary - Collect the diary - Pay kiwis to the patients* - Enter data (google docs)
Improvement of functional constipation with kiwifruit intake in a Mediterranean patient population: An open, non-randomized pilot study

RESULTS

46 subjects participated in the study. 42 were women, with median age of 49.5 (IQR: [37.5, 56.7]), weight of 67kg (IQR: [59, 73]) and height of 160.0cm (IQR: [157.2, 165.0]). One participant abandoned the study due to bloating and abdominal pain.

The percentage of patients with ≥3 stools per week increased from 82.61% (95% CI: 69–91.2) at week 1 to a maximum of 97.78% (95% CI: 87.4–99.9) at week 4 (second week of kiwifruit consumption; Table 1). The maximum number of responders (increase of ≥1 stool per week) was detected at the first week of kiwifruit consumption [76.09% 95% CI: 61.9–86.2]]. The average increase of number of stools from first week to the fifth week was of 4.47 (IQR: [2.7]).

Mean daily evolution in the Number of depositions, Facility in evacuation and Volume of evacuation (treated as continuous functional data) is shown in Figure 2. Daily Bristol Scale, Facility in evacuation and Volume of evacuation distributions are plotted categorically in Figure 3. The percentage of individuals with any Bristol evaluation below Type 3 (constipation) decreased from 67.39% at week 2 to 35.56% at week 5; the variation in percentage of individuals with any Bristol evaluation beyond Type 4 (diarrhoea) increased from 26.09% to 44.44%. The percentage of individuals with ideal stools (Types 3 and 4) during all week increased from 17.39% (95% CI: 8.8–31) at week 2 to 33.33% (95% CI: 21.3–48) at week 5.

GEE models (Table 2) found statistically significant differences from week 2 for the three outcomes, concomitant with the beginning of the kiwifruit consumption. The daily Number of depositions increased from the 0.671 mean depositions at week 2 to an average of 0.398 per week at the first week.

To collect the information patients used a questionnaire designed ad hoc for a similar study conducted in Belgium (see Annex 1). The French original version of the diary was translated into Spanish and Catalan. The family doctors provided instructions on the recording of faecal characteristics. Patients chose their own language to respond. Investigators collected data from diaries in a Google Docs form.

Patients were supplied with kiwifruit by different ways. Some patients in the study bought the prescribed product. In other cases it was the investigator who provided kiwifruits. In one of the Primary Care Centres, the neighbourhood shopkeeper was the responsible for delivering kiwifruits to the patients. Patients who bought their own kiwifruit (Zespri) were refunded.

Statistical analysis: Demographics for patients were summarized calculating medians [Interquartile Range (IQR)] for continuous variables and proportions for categorical variables. Categorical variables were compared from baseline (second week) to last week using the Bhapkar test. For some analyses, Facility and Volume categorical variables were treated as continuous in order to provide results easy to interpret and taking into account individuals’ correlations; in these cases, one unit of gain should be interpreted as an improvement in one response category. Functional data methodology was used for some graphical representations. Stacked bar plots over time will be presented for categorical variables. To analyse week changes in daily variables Generalized Estimating Equation (GEE) models were adjusted15,16 (treating variables as continuous).

Ethics committee: The study protocol was submitted to the ethics committee of the IDIAP Jordi Gol i Gurina Foundation (http://www.idiapjgol.org/).

<table>
<thead>
<tr>
<th>Week</th>
<th>Number of Stools≥3</th>
<th>Increase of ≥1 Stool per week</th>
<th>Number of Stools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre Interv</td>
<td>1</td>
<td>82.61%</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>80.43%</td>
<td>54.35%</td>
</tr>
<tr>
<td>Interv</td>
<td>3</td>
<td>95.65%</td>
<td>76.09%</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>97.78%</td>
<td>57.78%</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>95.56%</td>
<td>44.44%</td>
</tr>
</tbody>
</table>
of kiwifruit consumption, and in 0.593 daily units at week 5 (both p-values<0.001). Evaluation of Facility in evacuation improved in 0.674 levels in average at the last week of follow-up in relation to the mean 2.702 score (p<0.001) at week 2 (p-value<0.001). The Volume of evacuation evaluation improved in 0.29 levels in average at the third week of kiwifruit consumption (p-value<0.001).

**Figure 2.** Evolution of daily outcomes (with 95% confidence intervals).

![Graphs showing daily outcomes](image)

**Table 2.** Generalized Estimating Equation (GEE) estimations on the week effect on number of depositions, facility in evacuation, and volume in evacuation (treated as a continuous), adjusting for individual’s correlation.

<table>
<thead>
<tr>
<th>Number of depositions</th>
<th>Facility in evacuation</th>
<th>Volume of evacuation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>marginal effect</strong></td>
<td><strong>Estimate (S.E.)</strong></td>
<td><strong>p-value</strong></td>
</tr>
<tr>
<td>week 1</td>
<td>-0.082</td>
<td>0.051</td>
</tr>
<tr>
<td>week 2</td>
<td>0.671</td>
<td>0.090</td>
</tr>
<tr>
<td>week 3</td>
<td>0.398</td>
<td>0.071</td>
</tr>
<tr>
<td>week 4</td>
<td>0.532</td>
<td>0.073</td>
</tr>
<tr>
<td>week 5</td>
<td>0.593</td>
<td>0.080</td>
</tr>
</tbody>
</table>

Second week was taken as the reference; the other coefficients are differences in relation to second week. GEE model for the number of depositions used the poisson link function; marginal effect was obtained as $\beta \exp (X\beta)$. 
Figure 3. Daily distribution of Bristol Scale, Facility in evacuation, and Volume of evacuation.

Bristol Scale presents type 1 as the lowest category and type 7 as the highest (both in red). Facility in evacuation categories are “Very difficult” (red), “Difficult”, “Normal”, “Easy”, and “Very easy” (green at top). Volume of evacuation categories are “Very little” (lower orange), “Little”, “Neither a little nor a lot”, “A lot”, “Abundant”, “Very abundant” (upper orange).

(1,1 - 1,3): (First digit: week, second digit: day)
Differences in the satisfaction evaluations between the second week and the fifth week were found statistically significant—according to Bhapkar tests—for bloating and swelling ($p<0.001$), urgent need to defecate ($p=0.007$), irritable mood ($p<0.001$), stool number ($p<0.001$), stool consistency ($p<0.001$), and enough stools ($p=0.031$). Changes in giving up activities ($p=0.243$) were not significant; while changes in stomach ache ($p=0.052$) did not reach the 0.05 threshold.

**DISCUSSION**

In this study, the global weekly evolution of the primary endpoints (Number of depositions per week, percentage of the patients with no constipation and number of responders) after kiwifruit consumption in Mediterranean patients suffering from constipation provided positive results. The evolution of daily outcomes (Number of depositions, Facility in evacuation, Volume of evacuation, and Bristol Scale) also had positive results. Most people in the study were women, which reflects the higher prevalence of constipation amongst them. These results allow us to conclude that increasing dietary fibre consumption in terms of kiwifruit improves constipation symptoms in a Mediterranean patient population. Furthermore, these results allow us to think that if kiwifruit consumption were maintained over time, possibly many people with a constipation diagnosis would not meet the diagnostic criteria of Rome-III constipation.

Our results are aligned to those of previous studies. Although New Zealand and Chinese studies present major differences in design (number of kiwis –1kw/30kg weight–, or twice a day) and population (elderly, volunteers), results also showed a significant improvement of symptoms$^{10,11}$. Results must be interpreted in light of the following limitations. Firstly, and most important a pre-post design without parallel controls is subject to bias, e.g. as regression to the mean. Likewise the fact that patients and physicians were not blinded and the short follow-up study period.

In addition, two patients abandoned the study prior to the kiwifruit intervention and one participant had to abandon the study due to bloating and abdominal pain; two new patients replaced the latter two patients, while the third patient was not replaced. Although respondents found questionnaires easy to complete, some limitations were detected; specifically, only one faecal evaluation was allowed per day, thereby not allowing coding cases where the number of stools per day was greater than one and the fact that responses to the self-perception of bowel movements could influence the outcomes.

The study controlled for baseline use of laxatives. Categorical longitudinal data should suitably be fit using multinomial logit models with random effects; however, the implementation of such models in statistical software is still not solidly established. In our study, ordinal categories were treated as continuous variables using GEE models, as multinomial logit models with random effects did not converge in our data (using MCMC methods). Results of our GEE models for these ordinal variables should be carefully interpreted taking into account the underlying nature of these variables.

The benefits of this intervention could go beyond the consumption of kiwifruit itself. It is noticeable that in the second week (still before intervention) patients started reporting a slight non-significant improvement of the results. Although not being statistically significant, this could suggest a change in other related habits and lifestyles just because of being part of the study, which could have slightly influenced study outcomes.

Despite these limitations, the study has its strengths. A huge effort was done in order to ensure adherence and compliance. Given the low-income profile of some participants, centres facilitated the process offering different alternatives: daily distribution of kiwifruit in the Primary Care Centre, distribution of kiwifruit by the neighbourhood store, etc. Participants once included in the study had two follow-up visits and were followed about taking laxatives, taken food and exercise. No significant changes were detected in these three aspects, although a lower consumption of laxatives was observed during the five weeks of follow up.

Data recording by family doctors using Google Docs form provided a good quality database for analysis. Moreover, given the small number of patients per investigator, in case of doubts on the completion of the diary, data was confirmed during the upcoming medical follow-up visits.

It would be interesting to assess whether similar results can also be achieved by taking one or two kiwifruit per day. On the other hand, the notable psychological impact of constipation is a major issue for many patients; therefore, the impact of consuming kiwifruit on other aspects (i.e. healthy habits, quality of life) would provide a holistic view of the real impact of kiwifruit consumption on health. Further research is needed to improve our knowledge on the benefits of kiwifruit on constipation and other health parameters through a RCT.

Although the laxative effect of fruit has been attributed to its relatively high content of fibre (about 3.4g per 100g of edible pulp), other kiwi phytonutrients are important not only to maintain a healthy intestinal regularity but also to
promote digestion\textsuperscript{17}. Some evidence suggests that kiwifruit can help protein digestion in the stomach, facilitating the process, especially after meals with high protein content\textsuperscript{18}. The kiwifruit can act as a prebiotic in selectively enhancing the growth of intestinal lactic acid bacteria\textsuperscript{19}.

Actinidin is the predominant enzyme of kiwifruit (specifically in the green variety) and is part of the soluble protein fraction. It plays a major role by enhancing protein digestion. There is also a wide range of enzymes involved in kiwifruit ripening, particularly enzymes involved in the metabolism of poly and oligosaccharides, and in the development of taste and flavour compounds\textsuperscript{20}.

Recent nutritional research shows that kiwifruit has nutritional characteristics that are different from those of most fruits\textsuperscript{21}. In fact, in many instances, the nutritional value of kiwifruit exceeds that found in other similar fruit products. Kiwifruit provides nutrients but it also offers many extraordinary benefits above and beyond what is normally found in most fruit. Understanding how the fibre in kiwifruit behaves during digestion is an important focus of our research.

**CONCLUSIONS**

In conclusion, the present study shows that consumption of three kiwifruits per day significantly improves the quality of evacuation in Mediterranean patients suffering from constipation, in terms of number of depositions, volume, consistency and ease, noticeable since the first week of consumption. Further research is needed to improve our knowledge on the effect of such intervention.

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**COMPETING INTERESTS**

OC was specifically subcontracted by Zespri to perform the statistical data handling and analyses and substantially contribute to the redaction of results and manuscripts. Participant physicians and patients were compensated for their collaboration, although no direct contact was established with Zespri (the Spanish Society of Family and Community Medicine carried out economic management with physicians and participants). The authors declare that they have no proprietary, financial, professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in this paper.

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**AUTHORS’ CONTRIBUTIONS**

All authors were involved in the study. JJM proposed the study. MM and JB performed research. MM and JA contributed to the conceptualizing the paper and literature review and were involved in acquiring and interpreting the data. OC analyzed the data. MM gave the final approval of this version of the manuscript. All authors read and approved the final manuscript.

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