

Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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Does vitamin c prevent the occurrence of complex regional pain syndrome in patients with extremity trauma requiring surgery?

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Abstract

The complex regional pain syndrome is a neuroinflammatory pathology that affects the central and peripheral nervous system, characterized by disproportional pain in relation to the trauma experimented by the patient. It has been proposed that vitamin C could prevent the development of this syndrome in patients with limb trauma and surgery. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified two systematic reviews that indentified four primary studies, including one randomized controlled trial. We generated a summary of findings table following the GRADE approach. We concluded it is uncertain whether vitamin C prevents complex regional pain syndrome because the certainty of the evidence is very low.

Problem

Complex regional pain syndrome is a condition that may occur following a traumatism or extremity surgery. It contributes to a longer hospital stay and a slower rehabilitation process. Vitamin C is a safe and low cost medication, whose antioxidant properties might stabilize free radicals that normally damage the lipid membranes and the microcirculation, therefore it has been proposed it could prevent the onset of the complex regional pain syndrome in patients with extremity trauma, especially those that require surgery.

Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies in case more than one pertinent study is identified, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages

- It is uncertain whether vitamin C prevents complex regional pain syndrome in patients with extremity trauma undergoing surgery because the certainty of the evidence is very low.

About the body of evidence for this question

<p>What is the evidence. See evidence matrix in Epistemonikos later</p>	<p>We found two systematic reviews [1],[2] including four primary studies reported in six references [3],[4],[5],[6],[7],[8], of which only one correspond to a randomized controlled trial (reported in two references)[6],[7]. This table and the summary in general are based on the latter.</p>
<p>What types of patients were included</p>	<p>Adults (18 years or more), with a fracture of one or both wrists, under conservative treatment or surgery. All types of wrist fractures were included. The included surgical treatments were closed reduction external fixation (bridging technique), closed reduction and internal fixation (Kapandji) and open reduction and internal fixation.</p>
<p>What types of interventions were included</p>	<p>The study compared daily doses of 200, 500 and 1500 mg for 50 days starting the day of the injury. The comparison was against placebo.</p>
<p>What types of outcomes were measured</p>	<p>Incidence of complex regional pain syndrome clinically diagnosed using Veldman criteria, having to fulfill 4 of the 5 following criteria: Unexplained diffuse pain, disproportionate to the stage of fracture treatment. Difference in skin color relative to the other hand and wrist. Diffuse edema Difference in skin temperature relative to the other hand and wrist Limited active range of motion of the wrist and fingers, disproportionate to the stage of fracture treatment.</p>

Summary of findings

The information on the effects of vitamin C for the prevention of complex regional pain syndrome type I is based on one randomised controlled trial including 416 patients with 427 wrist fracture, of which 48 required surgical treatment (only the latter were considered in our analysis).

- It is uncertain whether vitamin C prevents complex regional pain syndrome in patients with extremity trauma that require surgery because the certainty of the evidence is very low.

Vitamin C for preventing complex regional pain syndrome in extremity trauma surgery				
Patients	Extremity trauma requiring surgery			
Intervention	Vitamin C			
Comparison	Placebo			
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITHOUT vitamin C	WITH vitamin C		
	Difference: patients per 1000			
Complex regional pain syndrome type I	91 per 1000	10 per 1000	RR 0.11 (0.005 to 2.412)	⊕○○○ ^{1 2} Very low
	Difference: 81 patients less per 1000 (Margin of error: 90 less to 128 more)			
RR: Risk ratio Margin of error = 95% confidence interval (CI). GRADE: evidence grades of the GRADE Working Group (see later in this article). * The risk WITHOUT VITAMIN C is based on the risk in the control group of the trials. The risk WITH VITAMIN C (and its margin of error) is calculated from relative effect (and its margin of error). ¹ We downgraded the certainty in two levels because of imprecision. The margin of error includes both clinically important benefits and harms. ² We downgraded the certainty of the evidence in one level because the study only considers a population of patients with wrist fracture, so it represents indirect evidence for other types of extremity trauma, which constitute most cases of interest.				

About the certainty of the evidence (GRADE)*

⊕⊕⊕⊕

High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision.

Other considerations for decision-making

To whom this evidence does and does not apply

- This evidence applies to patients 18 years or older with history of wrist fracture that require surgical treatment for its resolution.
 - Taking into account physiopathological reasons, it is reasonable to think the intervention effect would be similar in other traumatic events involving the limbs, such as foot and ankle fractures surgically treated. The identified observational studies include some of these populations but the very low certainty of the evidence that comes from them does not modify our conclusions substantially.
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About the outcomes included in this summary

- This summary only considers the incidence of complex regional pain syndrome as an outcome.
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Balance between benefits and risks, and certainty of the evidence

- Even though there are no adverse effects reported in healthy patients with the use of vitamin C with the doses recommended by the analyzed study, it is not possible to conduct an adequate risk/benefit balance due to the very low certainty of the evidence about the benefits.
-

Resource considerations

- Although it is a low cost intervention, it is not possible to conduct an adequate cost/benefit balance due to the very low certainty of the existing evidence.
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Differences between this summary and other sources

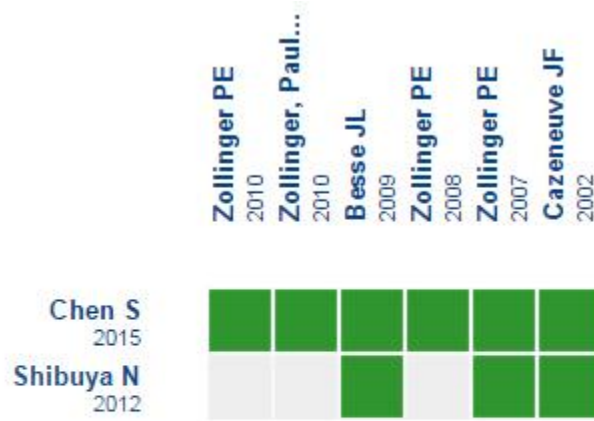
- The key messages of our summary are partially discordant with the conclusions of the individual systematic reviews identified [\[1\]](#),[\[2\]](#), which provide a more optimistic conclusion. This is partially explained because they give more weight to the observational studies. However, the inclusion of these studies in our summary does not change our conclusions substantially.
 - The main conclusion of this summary is partially discordant with the existing clinical guideline, that incorporates a low proportion of the identified evidence because it did not exist when it was published [\[9\]](#).
-

Could this evidence change in the future?

- The probability of future evidence changing what we know is very high, because of the very low level of certainty of the evidence.
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How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.

The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.

The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.

The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version** [Efficacy of vitamin C for complex regional pain syndrome in extremity surgery](#)

Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here <http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

These summaries follow a rigorous process of internal peer review.

Conflicts of interest

The authors do not have relevant interests to declare.

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