

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

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What are the effects of adding azathioprine to corticosteroids in polymyositis?

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Abstract

The treatment of polymyositis is based on corticosteroid therapy, with addition of azathioprine for non responsive cases or as an attempt to diminish corticosteroids requirements. However, there is no clear evidence of its benefit in controlling symptoms. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified only one systematic review including one pertinent randomized trial. We generated a summary of findings following the GRADE approach. We concluded there is uncertainty if azathioprine improves or not muscular strength in polymyositis because the certainty of the evidence is very low.

Problem

Corticosteroids constitute the standard treatment for dermatomyositis and polymyositis. Given their multiple short and long term side effects there is interest in other immunomodulators, such as azathioprine, especially for non-responsive cases or as an attempt to diminish corticosteroids requirements. However, there is no clear evidence of its benefit in controlling symptoms, and it also carry important side effects.

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), a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages

- There is uncertainty if azathioprine improves or not muscular strength in polymyositis because the certainty of the evidence is very low.
- As far as we know there are no ongoing trials evaluating this question

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found one systematic review [1] including only one pertinent randomized controlled trial [2].
What types of patients were included	The study included adults with polymyositis diagnosed with Bohan and Peter criteria and positive muscle biopsy Patients with previous corticosteroid or immunosuppressive therapy were excluded.
What types of interventions were included	Azathioprine 2mg/kg qd plus prednisone 60 mg qd, compared with prednisone 60 mg qd.
What types of outcomes were measured	Improvement in muscular strength evaluated in each muscular group (score from 0= no deficit, to -140= maximum deficit), serum creatine kinase, muscular biopsy (0= normal, to 36= maximum inflammation).

Summary of findings

The information on the effects of azathioprine is based on one randomized controlled trial [2] including 16 patients.

- There is uncertainty if azathioprine improves or not muscular strength in polymyositis. The certainty of the evidence is very low.

Addition of azathioprine to corticosteroids for polymyositis				
Patients	Polymyositis			
Intervention	Azathioprine plus corticosteroids			
Comparison	Corticosteroids			
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITHOUT azathioprine	WITH azathioprine		
	Difference: patients per 1000			
Muscular strength (scale from 0 to 72 points)	1.1 points more	6.5 points more	MD 5.4 (-13.08 to 23.88)	⊕○○○ ^{1,2} Very low
	Difference: 5.4 points more (Margin of error: 13.1 points less to 23.9 points more)			
Adverse effects	The only study does not report adverse effects		--	No information

MD: Mean difference.
Margin of error = 95% confidence interval (CI).
GRADE: evidence grades of the GRADE Working Group (see later in this article).

The risk **WITHOUT azathioprine** is based on the risk in the control group of the trials. The risk **WITH azathioprine** (and its margin of error) is calculated from relative effect (and its margin of error).

1 The study has high risk of bias (randomization and allocation concealment unclear and high risk of selective reporting).
2 The result is imprecise, including both important benefit and harm.

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

- The study included patients with polymyositis meeting Bohan and Peter criteria, so the evidence found is applied directly to this group. It is clinically reasonable to extend this findings to patients with dermatomyositis with muscular involvement.
 - It does not clearly apply to pediatric patients or patients with other rheumatologic diagnosis or presenting overlap syndrome.
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About the outcomes included in this summary

- The outcomes presented are those considered critical for decision-making, according to the authors of this summary. We did not find clinical guidelines or studies about the relative importance of the outcomes for this condition.
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Balance between benefits and risks, and certainty of the evidence

- It is not possible to estimate the risk/benefit given the existing uncertainty. Considering the intervention has side effects and costs its use outside of the context of a clinical trial is questionable.
-

What would patients and their doctors think about this intervention

- Given the absence of a clearly established alternative treatment, it is possible some clinicians will consider using this drug, especially in refractory patients. Some patients putting more value on the hypothetical benefit than on the risks and costs, may be inclined to use it too. In these cases, it is extremely important to inform the patient about the certainty of the evidence.
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Resource considerations

- Given the uncertainty about the benefits, it is not possible to make a judgment about the cost/benefit.
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Differences between this summary and other sources

- Our summary is in agreement with the only systematic review identified.
 - We did not identify guidelines that are recognized by a substantial proportion of experts in the topic.
-

Could this evidence change in the future?

- The probability of this information changing with new studies is very high because the certainty of the evidence is very low.
 - Unfortunately, we did not identify any ongoing study addressing this question.
-

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** [Corticosteroids plus azathioprine versus corticosteroids alone for polymyositis](#)

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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