COTRIMOXAZOL: HOW FOLATE SUPPLEMENTATION COULD AFFECT TREATMENT EFFICACY

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6ER-011

BACKGROUND AND IMPORTANCE

Cotrimoxazole (CTX) is an association of sulfamethoxazole and trimethoprim which act synergistically to inhibit folic acid (FA) synthesis and block bacterial growth.

It is used in the treatment of bacterial infections and in the prophylaxis of opportunistic diseases like:

Toxoplasma gondii

Pneumocystis jirovecii

In immunosuppressed patients

CTX causes myelotoxicity since it affects the same process in human cells. To prevent toxicity, **FA or folinic acid (FNA) can be administered**. However, there is controversy as to whether this folate supplementation could affect the efficacy of CTX.

OBJECTIVE → **To determine** if the co-administration of CTX and folates compromises efficacy of the treatment.

METHODS

A review of the published evidence on CTX and folate supplementation was conducted.

An initial search was performed in PubMed and Google Scholar using the terms "**cotrimoxazole**" and "**folates**" and "**efficacy**" supported by federal data sheets.

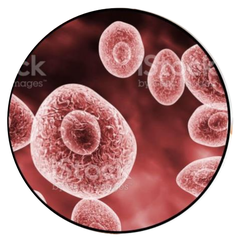
Google Scholar

PubMed

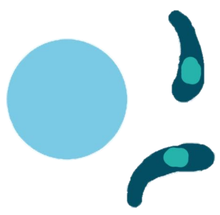
RESULTS

Regarding the use of folates as a supplement in bacterial infections, there is no evidence at all.

Theoretically, as bacteria intrinsically lack of mechanisms to capture exogenous folates, it seems to be more appropriate to use FA in front of FNA due to its **lipophilicity**. This could avoid a possible passage of this molecule through the bacterial wall, that is **lipophilic.**



Pneumocystis jirovecii is permeable to lipophilic folates and lacks an active transport mechanism to incorporate classical folates. Therefore, the administration of FNA, **which is more lipophilic**, could reduce the antifolate activity of CTX, meanwhile, **FA supplements do not affect the activity of CTX.**



In the case of ***Toxoplasma gondii***, the folate of choice is FNA because the microorganism can intake exogenous FA through the BT1 family transmembrane proteins, **which have no affinity for FNA.**

CONCLUSIONS

- In general, **FA supplementation theoretically can be used to prevent myelotoxicity** as it does not interfere with the action of the antibiotic in the case of bacteria.
- However, **in infections caused by more complex eukaryotic organisms** such as other fungi or parasites with lipophilic cell walls or specific transmembrane proteins, each case must be evaluated.

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