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Sulfasalazine-induced taste disorders

Introduction

Sulfasalazine in an azo ester of sulfapyridine and 5-aminosalicylic acid (mesalamine, 5-ASA). H^+-azoreductase, a bacterial enzyme present in the colon, splits sulfasalazine into equimolar amounts of sulfapyridine and 5-aminosalicylic acid. Sulfapyridine is thought to be responsible for its anti-rheumatic properties, 5-ASA is thought to be the major therapeutically active part in the treatment of ulcerative colitis. The Medicines Evaluation Board approved sulfasalazine in March 1969. Nowadays it is approved for the indications *ulcerative colitis, Crohns disease and progressive rheumatoid arthritis* [1].
Dose related nausea and vomiting are common as well as headache, abdominal pain, anorexia and reversible oligospermia. Adverse reactions are frequent and the discontinuation rate for this reason can be as high as 30% [2]. Gastro-intestinal adverse reactions occur more commonly in slow acetylators, and these patients should receive lower doses [2].

Reports

Until September 2002 the Netherlands Pharmacovigilance Centre Lareb received seven reports concerning sulfasalazine in suspected association with taste disorders. An overview of the reports that have been received by Lareb is provided in Table 1. Although paracetamol, indomethacin, ibuprofen, diclofenac and misoprostol as concomitant medication have been associated with taste disorders, the time of onset of the suspected ADRs in these patients is strongly suggestive for a relationship with sulfasalazine [3].

Other sources of information

Literature

A search in the Medline database revealed limited information concerning the occurrence of taste disorders associated with sulfasalazine. Series of case-reports have been published one and two decades ago [4,5].
Dysgeusia (metallic taste, changes in sweet taste sensations) has been reported to occur in patients with inflammatory bowel disease, ankylosing spondylitis and reactive arthritis treated with sulfasalazine [4,5,6]. Total ageusia for sweet taste was reported in a patient with Crohn's disease [5].

Databases

The database of the WHO Collaborating Centre for Drug Monitoring currently contains 6069 possible ADRs during the use of sulfasalazine. An association with taste loss was suggested in 45 reports. With a Reporting Odds Ratio of 4.1 (95% CI 3.0-5.5) this combination is disproportionally represented.
Analysis of the Netherlands Pharmacovigilance Centre Lareb database revealed a Reporting Odds Ratio of 5.5 (95% CI 2.2-13.5) for ageusia, and 1.5 (95% CI 0.4-5.9) for dysgeusia.

Table 1. Overview of reports received by Lareb concerning taste disorders in suspected association with sulfasalazine

No	Age	Sex	Indication	Dose [mg/day]	Concomitant	Suspected ADRs	Latency	Therapy adjustment	Outcome
1	46	F	rheumatoid arthritis	2000	levonorgestrel/ethinylestradiol, betahistine, prednisolone, meloxicam	no taste, paraesthesia mouth	weeks	Dose not changed	Unknown
2	44	M	psoriatic arthritis	2000	diclofenac	severe taste loss	26 days	Drug withdrawn	Recovered
3	59	F	unknown	1000	meloxicam	taste disorder, stomatitis, oedema mouth	days	Drug withdrawn	Unknown
4	54	M	rheumatoid arthritis	Not reported	ibuprofen, prednisolone	taste loss, salty taste	19 days	Dose reduced	Unknown
5	38	F	rheumatoid arthritis	1000	fluticasone (pulmonal)	taste alteration	10 days	Drug withdrawn	Unknown
6	50	M	unknown	1000	ferrosulfate, indomethacin, paracetamol, omeprazole, misoprostol	taste loss, taste alteration	7 days	Dose not changed	Unknown
7	28	F	rheumatoid arthritis	1000	indomethacin, cyproterone/ethinylestradiol	taste loss, smell present	5 weeks	Already withdrawn due to allergic reaction after 4 weeks	Unknown

Mechanism

The patho-physiology of sulfasalazine-induced taste disorders is not clearly understood [3,7,8]. Some published cases showed a dose-response relationship between drug administration and dysgeusia. It has been hypothesised that alteration of gastrointestinal tract bacteria, produced by sulfasalazine, may interfere with the absorption of a factor, perhaps zinc, which is necessary for normal taste [4].
However in another published case the immediate improvement in taste after cessation of sulfasalazine suggests that this drug may have caused the taste disturbance via a more direct mechanism than an alteration of gastrointestinal tract bacteria [5].

Conclusion

Over the years the Netherlands Pharmacovigilance Centre Lareb has received several reports of taste disorders associated with the use of sulfasalazine. This association is supported by a few previous publications in the literature and the WHO database.

References
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