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Should celecoxib be contraindicated in patients who are allergic to sulfonamides? Revisiting the meaning of 'sulfa' allergy.

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Abstract

Celecoxib, a selective cyclo-oxygenase-2 inhibitor, is a diaryl-substituted pyrazole derivative containing a sulfonamide substituent. Because of this structural component, celecoxib is contraindicated for use in patients who have demonstrated allergic reactions to sulfonamides. However, there is a lack of data demonstrating cross-reactivity among sulfonamide medications. A sulfonamide is any compound with an SO2NH2 moiety. The major difference between sulfonamide antimicrobials and other sulfonamide-containing medications such as furosemide, thiazide diuretics and celecoxib, is that sulfonamide antimicrobials contain an aromatic amine group at the N4 position. This allows for division of the sulfonamides into 2 groups: aromatic amines (i.e., sulfonamide antimicrobials) and nonaromatic amines. In addition, sulfonamide antimicrobials contain a substituted ring at the N1-position; this group is not found with nonaromatic amine-containing sulfonamides. Adverse reactions to sulfonamide antimicrobials include type I, or immunoglobulin (Ig) E-mediated reactions, hypersensitivity syndrome reactions, and severe skin reactions such as toxic epidermal necrolysis. The aromatic amine portion of the sulfonamide antimicrobial is considered to be critical in the development of latter 2 reactions. In susceptible individuals, the hydroxylamine metabolite is unable to be detoxified leading to a cascade of cytotoxic and immunological events that eventually results in the adverse reaction. Since celecoxib does not contain the aromatic amine, adverse reactions such as hypersensitivity syndrome reactions and toxic epidermal necrolysis would not be expected to occur at the same frequency as they do with sulfonamide antimicrobials. Similarly, for IgE-mediated reactions, the N1-substituent and not the sulphonamide moiety is important in determining specificity to antibodies. Celecoxib and other nonaromatic amine-containing sulfonamide medications do not contain the N1-substituent. Cross-reactivity among the various

sulfonamide-containing medications has also not been substantiated by published case reports. In fact, conflicting information exists in the literature. Reports showing lack of cross-reactivity balance the few case reports suggesting cross-reactivity. Cross-reactivity between sulfonamide medications should be based on scientific data, including chemistry, metabolism, immune responses and clinical data. Based on the current information, there is no documentation for cross-reactivity between sulfonamide antimicrobials and other sulfonamide medications, such as celecoxib.

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