

# ALLERGY Net

ALLERGY 2010 DOI: 10.1111/j.1398-9995.2009.02320.x

© 2010 JOHN WILEY & SONS A/S

CONTRIBUTIONS TO THIS SECTION WILL NOT UNDERGO PEER REVIEW, BUT WILL BE REVIEWED BY THE ASSOCIATE EDITORS

## Aspirin tolerance in patients with NSAID-hypersensitivity

W. S. J. Malskat, C. van der Tas,  
A. C. Knulst, C. A. F. M. Bruijnzeel-Koomen,  
H. Röckmann\*

**Keywords:** aspirin; drug hypersensitivity; nonsteroidal anti-inflammatory drugs; oral drug challenges; tolerance.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are frequently used analgetic therapeutics worldwide and are known to cause about 21–25% of all the adverse drug reactions (1, 2).

The common mechanism of action, inhibition of cyclooxygenases (COX), seems to explain the

observed cross-reactivity between non-selective COX-1/2 inhibitors and tolerability of selective COX-2 inhibitors. Assuming that cross-reactivity exists mainly between COX-1 inhibitors, oral challenges with COX-2 inhibitors are often primarily carried out in case of a drug reaction to a COX-1 inhibitor, to identify a safe alternative NSAID (3). This practice may however result in unnecessary avoidance of potentially useful nonselective NSAIDs, while treatment options in the management of pain, inflammation, and anticoagulation are already limited. The aim of this study was to determine the tolerance of aspirin (a nonselective COX inhibitor) in 14 patients with proven

hypersensitivity to nonselective COX inhibitors.

To all patients, diagnosed with NSAID-hypersensitivity in our clinic between 2003 and 2009, whom passed a challenge with a selective COX-2 inhibitor ( $n = 50$ ), we offered an additional challenge with aspirin. Of these 50 patients, 18 were willing to undergo this challenge. Patients with hypersensitivity to three or more NSAIDs, known hypersensitivity to aspirin, or current use of aspirin without symptoms, were excluded ( $n = 4$ ). Fourteen patients could participate in this study (Table 1). Mean age of the study group was 49 years, 78.6% were women. All patients experienced at least one episode of hypersensitivity symptoms (consisting of urticaria ( $n = 10$ ), angioedema ( $n = 7$ ), dyspnea, ( $n = 2$ ) and/or anaphylactic shock ( $n = 8$ )), subsequent to ingestion of one ( $n = 13$ ) or more ( $n = 1$ ) NSAID(s).

The diagnosis was based on a detailed and reliable history ( $n = 11$ ), or an oral challenge with the culprit drug in cases with a doubtful history ( $n = 3$ ).

Single blind placebo-controlled aspirin challenges were performed. The oral challenge protocol, adapted from EAACI guidelines (4), consisted of oral administration of placebo on the first and aspirin on the second day. Aspirin was given in five increasing doses: 10 mg with a time interval of 30 min, 44 mg, 117 mg, and 312 mg with an interval of 60 min, and 500 mg after an interval of 120 min. Patients were observed for at least 3 h after the last dose. A challenge test was considered to be positive at the presence of pruritis and erythema, urticaria, angioedema, dyspnea or 30 mmHg drop in systolic blood pressure (SBP).

No reactions to placebo were observed. Eleven (78.6%) of the 14

**Aspirin is tolerated in 78.6% of the patients with NSAID-hypersensitivity.**

**Table 1** Clinical features and results of oral aspirin challenges

| Patient number | Sex/age | Co-morbid disorders | Culprit drug | Type of reaction | Manner of diagnosis | Oral challenges |  |
|----------------|---------|---------------------|--------------|------------------|---------------------|-----------------|--|
|                |         |                     |              |                  |                     | Aspirin         |  |
| 1              | F/41    | NS                  | ibu          | An               | PH                  | Neg             |  |
| 2              | F/49    | NS                  | ibu          | U                | PH                  | Neg             |  |
| 3              | F/52    | NS                  | dic          | U/D/An           | PH                  | Neg             |  |
| 4              | M/21    | NS                  | prop, ibu    | U/A              | PH/C                | Neg             |  |
| 5              | F/53    | NS                  | ibu          | U/A/An           | PH                  | A               |  |
| 6              | M/62    | CU                  | dic          | U                | PH                  | A               |  |
| 7              | F/50    | NS                  | dic          | An               | PH                  | Neg             |  |
| 8              | F/48    | NS                  | nap          | U/An             | PH                  | Neg             |  |
| 9              | F/56    | NS                  | nap          | U/A              | PH                  | A               |  |
| 10             | F/63    | NS                  | dic          | D                | C                   | Neg             |  |
| 11             | F/43    | NS                  | dic          | A/An             | PH                  | Neg             |  |
| 12             | F/49    | As                  | dic          | U/A/An           | C                   | Neg             |  |
| 13             | M/53    | NS                  | dic          | U/An             | PH                  | Neg             |  |
| 14             | F/55    | NS                  | ibu          | U                | PH                  | Neg             |  |

NS, none specific; CU, chronic urticaria; As, asthma; ibu, ibuprofen; dic, diclofenac; prop, propyfenazon; nap, naproxen; An, anaphylaxis; U, urticaria; D, dyspnea; A, angioedema; PH, patient history; C, challenge test; Neg, negative reaction.

patients tolerated aspirin. Three (21.4%) patients experienced mild angioedema, after which the challenge was discontinued. Two of them had symptoms after ingestion of 44 mg (cumulative dose: 54 mg), one after intake of 117 mg (cumulative dose: 171 mg).

We observed that more than three-quarters (78.6%) of the patients tolerated aspirin. This correlates with the study of Asero (5), showing aspirin tolerance in 76% of 117 patients with NSAID-hypersensitivity. In this study, only cutaneous symptoms were observed. This might be attributed to the fact that only patients with a history of a cutaneous reaction were included, in contrast to our study. We included eight (57.1%) patients with a history of anaphylactic shock. Seven of these patients also tolerated aspirin.

Aspirin is tolerated in most (78.6%) of the patients with NSAID-hypersensi-

tivity; limiting of the NSAID-repertoire as a result of hypersensitivity to a single NSAID is unnecessary. Oral challenges should be performed to confirm tolerance.

\*University Medical Centre  
Department of Dermatology  
Heidelberglaan 100  
G 02.124, 3584 CX Utrecht  
The Netherlands.  
Tel.: +31 88755 7388  
Fax: +31 88755 5404  
E-mail: H.Rockmann@umcutrecht.nl

Accepted for publication 3 December 2009  
Allergy 2010  
© 2010 John Wiley & Sons A/S  
DOI: 10.1111/j.1398-9995.2009.02320.x

## References

1. Faich GA. Adverse-drug-reaction monitoring. *N Engl J Med* 1986;**314**:1589–92.
2. Gomes E, Cardoso MF, Praca F, Gomes L, Marino E, Demoly P. Self-reported drug allergy in a general adult Portuguese population. *Clin Exp Allergy* 2004;**34**:1597–601.
3. Weberschock TB, Muller SM, Boehncke S, Boehncke WH. Tolerance to coxibs in patients with intolerance to nonsteroidal anti-inflammatory drugs (NSAIDs): a systematic structured review of the literature. *Arch Dermatol Res* 2007;**299**:169–75.
4. Nizankowska-Mogilnicka E, Bochenek G, Mastalerz L, Swierczynska M, Picado C, Scadding G et al. EAACI/GA2LEN guideline: aspirin provocation tests for diagnosis of aspirin hypersensitivity. *Allergy* 2007;**62**:1111–8.
5. Asero R. Oral aspirin challenges in patients with a history of intolerance to single nonsteroidal anti-inflammatory drugs. *Clin Exp Allergy* 2005;**35**:713–6.