

THE TRIPLE WHAMMY – A DANGEROUS TRIO

1. ACE inhibitor or angiotensin II receptor antagonist ('sartan')
2. Diuretic
3. Non-steroidal anti-inflammatory drug (NSAID) or COX-2 inhibitor ('coxib')

- ▶ THIS COMBINATION MAY PREDISPOSE VULNERABLE PATIENTS TO RENAL FAILURE - AVOID IF POSSIBLE
- ▶ INDIVIDUALLY OR COMBINED, THESE MEDICINES ARE INVOLVED IN 50% OF IATROGENIC RENAL FAILURE CASES
- ▶ TRIPLE WHAMMY-INDUCED RENAL FAILURE FATALITY RATE IS 10%
- ▶ RISK FACTORS INCLUDE ADVANCED AGE, PRE-EXISTING RENAL IMPAIRMENT AND DEHYDRATION
- ▶ PATIENTS TAKING THESE COMBINATIONS SHOULD SEEK MEDICAL ADVICE IF THEY BECOME UNWELL
- ▶ BE AWARE THAT TAKING OVER THE COUNTER NSAIDS CAN PRECIPITATE THE TRIPLE WHAMMY

Triple Whammy – 'three simultaneous deleterious blows with compounded effect'¹. This combination of medicines can result in significant patient harm; the rate of fatalities from renal failure is estimated at 10%. Used individually or combined, these three medicines are involved in more than half of reported iatrogenic acute renal failure cases².

Older patients are especially vulnerable to the Triple Whammy because they often have a degree of pre-existing renal impairment^{2,3}. Other reasons include: sensitivity to the renal effects of NSAIDs, being prone to diuretic-induced dehydration and hypotension, and inadequate fluid intake³. However, anyone with renal impairment is at risk, especially if dehydrated.

Dehydration from vomiting/diarrhoea is a trigger for renal failure; minor illness can place susceptible patients at risk if they are taking *whammy* combinations². Advise patients to avoid hypovolaemia (drink plenty of water) and to seek medical advice if they become acutely unwell⁴. Prescribers may also wish to **consider stopping NSAIDs/'coxibs'** in these circumstances and to monitor patients' renal function/serum potassium levels³.

The Triple Whammy should be avoided whenever possible - extreme caution should be exercised if it is used in patients with renal impairment^{2,4}. Remember that the

control of hypertension by ACE inhibitors and diuretics and their beneficial effects in heart failure are antagonised by NSAIDs¹. The toxicity from *whammies* may not be dose-dependent⁵.

Care is needed to avoid the Double Whammy. The concurrent use of NSAIDs + diuretics is associated with a 2-fold increase in the risk of hospitalisation for heart failure when compared with diuretics alone¹. Combination ACE-inhibitor/angiotensin II receptor antagonists + diuretics (e.g. Inhibace Plus[®]) are useful products, but remember patients on these are two-thirds of the way to the *Triple Whammy*. Advise these patients to avoid self-medicating with over the counter NSAIDs.

REFERENCES

1. Thomas M. Diuretics, ACE inhibitors and NSAIDs - the triple whammy. The Medical Journal of Australia 2000;172:184-5
2. ACE inhibitor, diuretic and NSAID: a dangerous combination. Australian Adverse Drug Reactions Bulletin 2003;22(4):14-5
3. Savage R. A Dangerous Trio. Prescriber Update 2002;23(2):20
4. Beware the triple whammy! Australian Adverse Drug Reactions Bulletin 2006;25(5):18
5. Loboz K, Shenfield G. Drug combinations and impaired renal function - the 'triple whammy'. British Journal of Clinical Pharmacology 2004;59(2):239-43

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