Rarely a triple whammy in general medicine

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The 'triple whammy'—the combination of an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), a diuretic and a non-steroidal anti-inflammatory drug (NSAID)—is a well-documented and often avoidable precipitant of acute kidney injury (AKI).[1] The Health Quality and Safety Commission New Zealand (HQSCNZ) recently updated the Atlas of Healthcare Variation, adding the 'triple whammy' in people aged 65 as a measure of potentially harmful polypharmacy.[2] The Atlas reports the frequency of the combination in patients aged 65 and over using community dispensing data. In 2016, the 'triple whammy' was dispensed to 3.2% (21,286) of elderly people in New Zealand and 2.3% (1,887) in Canterbury.[3] Further, an unknown number of patients purchased NSAIDs over-the-counter in addition to their regular ACEI/ARB and diuretic. The frequency of the 'triple whammy' in New Zealand hospitals is unknown. We examined hospital rates of co-prescribing ACEIs/ARBs, diuretics and NSAIDs in general medicine at Christchurch Hospital.

The aim of this study was to determine the incidence of the 'triple whammy' in general medical inpatients.

Methods

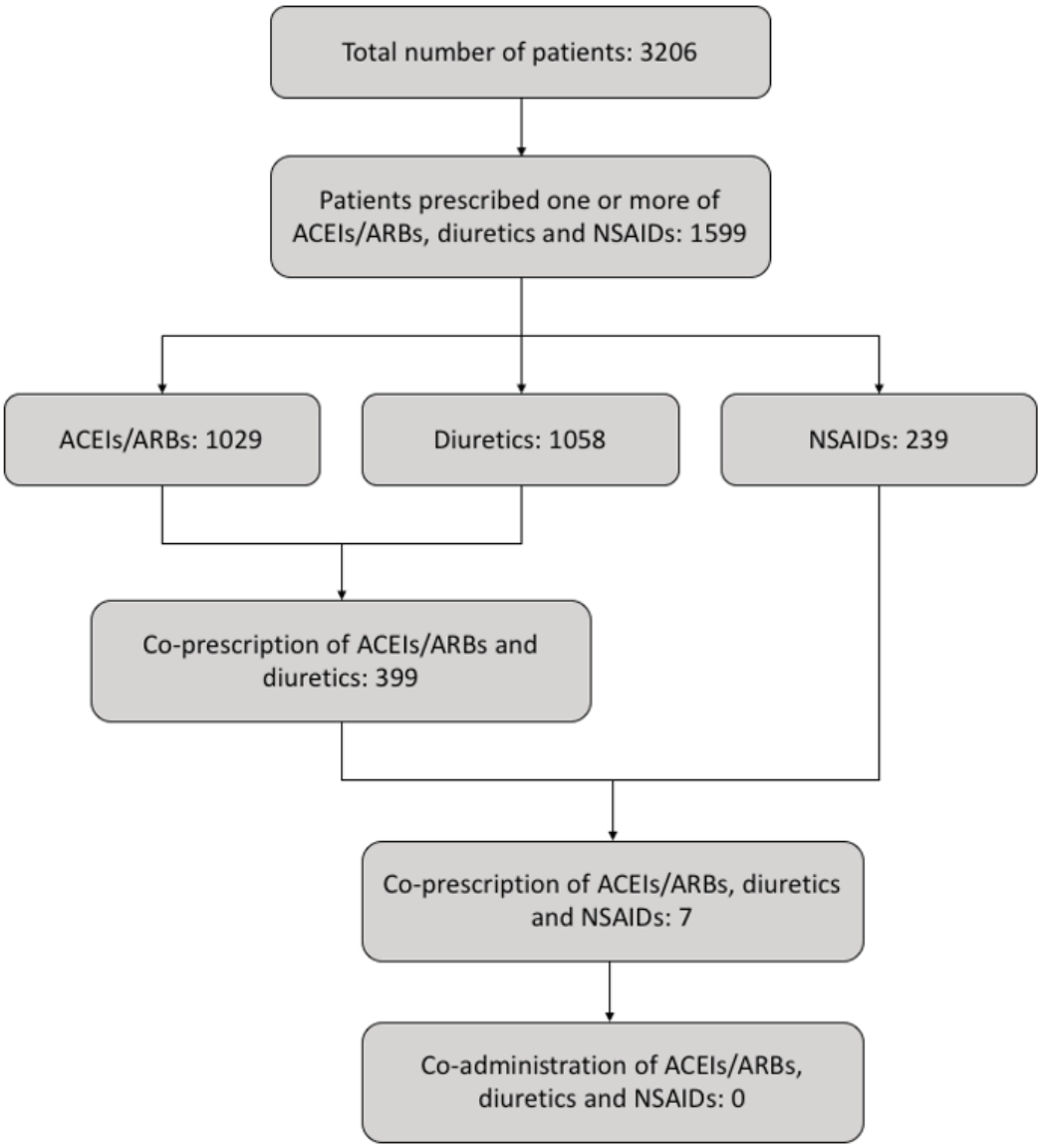
A retrospective cohort study of patients discharged from the Department of General Medicine at Christchurch Hospital between 1 August and 31 October 2017. Prescribing data were extracted from the electronic prescribing record (MedChart®) and analysed using Tableau Desktop®. The data were filtered by medication name to identify all records which included ACEIs/ARBs, diuretics and NSAIDs, and instances of co-prescribing were identified. The prescribing and administration records, discharge summaries, and laboratory results of each patient prescribed the 'triple whammy' were manually reviewed. The additional data extracted included: medication dose (amount and frequency); medication administration (some NSAIDs were prescribed to be administered as required or PRN); current medicines at discharge; and drug-related AKI. For the same time-period discharge coding data were screened for AKI due to medicines. The data were analysed using descriptive statistics using Microsoft Excel®.

Results

A total of 3,206 patients were discharged from general medicine and prescribed medicines during the study period (Figure 1). The median age (range) was 76 years (15–104), 71% were 65 years or older and 53% were female. One or more 'triple whammy' medicines were prescribed to 1,599 patients (50%). This comprised 1,029 prescribed ACEIs/ARBs (33%), 1,058 (33%) prescribed diuretics and 239 (7.5%) prescribed NSAIDs. The combination of an ACEI/ARB and a diuretic was prescribed to 399 (12%) patients of which seven (0.2% of the total and 1.7% of those prescribed ACEI/ARB and diuretic) were also prescribed an NSAID.

Of the seven patients prescribed the 'triple whammy', two were taking ACEIs/ARBs, diuretics and NSAIDs on admission as their regular medicines. In both cases the NSAID was ceased on admission. A further two were taking regular NSAIDs on admission that were ceased prior to inpatient prescription of new ACEI and diuretic. Three patients were prescribed the 'triple whammy' as inpatients. These three patients were on regular ACEI and diuretic and were subsequently prescribed regular or PRN NSAID. However, in all three cases no doses of NSAIDs were administered during admission nor were they prescribed on discharge.

Figure 1: General medicine inpatient prescribing patterns of ACEIs/ARBs, diuretics and NSAIDs.



During the study period there were 12 patients admitted to general medicine with AKI due to medicines. Three of these were coded as being due to diuretics and two as due to NSAIDs. The remaining seven were attributed to other agents. A further four patients developed AKI as inpatients, all coded as being due to diuretics; none of these received the 'triple whammy'.

Discussion

The incidence of pain increases with age and multi-morbidity,[4] as does the incidence of hypertension and heart failure treated with ACEIs/ARBs and/or diuretics. Less use of NSAIDs is not necessarily better because NSAIDs can provide effective analgesia, particularly for musculoskeletal pain,[5] and the alternatives are either less effective (for example paracetamol)[6] or associated with other potential harms (for example opioids).[7] Co-prescription of ACEIs/ARBs and diuretics is not an absolute contraindication to the use of NSAIDs but increases the risk of AKI.[8] While this study did not detect any cases of AKI due to inpatient co-prescription of the 'triple whammy', coding data demonstrated that drug-induced AKI can be caused by one or a combination of the 'triple whammy' medicines.

It should be noted that the method used to record the 'triple whammy' in this

inpatient study is not the same as used by HQSC to record co-prescribing in the community. Hence direct comparison of co-prescribing rates cannot be made. However, given the reported incidence of the 'triple whammy' in the community, this study suggests that patients admitted under general medicine are less likely to be prescribed the 'triple whammy' than those in the community. This could be because inpatients are generally frailer and more co-morbid, leading to more prescriber caution with NSAIDs. Further, in hospital there is usually more than one doctor, as well as a nurse and sometimes a pharmacist involved before a medicine is administered, each of whom can intervene. Of note, there are no electronic drug interaction alerts related to this combination in the electronic prescribing system at Christchurch Hospital (MedChart®). This study is limited to a three-month period in general medicine and cannot be extrapolated to all inpatients.

This study demonstrates the utility of data produced by electronic prescribing. Unlike paper charts, data from e-prescribing software recorded electronically can be easily analysed for audit purposes. The method used for this current study could be applied to other medicines, other departments or other hospitals, providing opportunity for comparison and collaboration towards safer prescribing practices.

There was no co-administration of ACEIs/ARBs, diuretics and NSAIDs to inpatients in general medicine during the study. The incidence of inpatient co-prescription was 2 per 1,000 admissions to general medicine and there was no co-prescription on discharge. The incidence of AKI attributable to the 'triple whammy' was zero during the three-month period.

Competing interests:
Nil.

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