



Therapeutics Today

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*Nollaig Shona dár léitheoirí go léir!
Happy Christmas to all our readers!*



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Thank you very much! Thank you to all who have acted as reviewers for our NMIC publications in 2020, especially during this extremely difficult year. We would also like to wish our reviewers, those who have contacted our service in 2020, and all the readers of our publications, a very safe and happy Christmas. We wish you all a happy and a very welcome

2021 and hope that it will be a less challenging year for all.



Prescribing cascade: calcium channel blockers (CCBs) and diuretics in older adults with hypertension (HT).

CCBs which are commonly prescribed for HT, are known to be associated with an increased risk of peripheral oedema. Peripheral oedema has an incidence ranging from 2 to 25% depending on the CCB type (most common with amlodipine), dosage and duration of therapy. Peripheral oedema due to CCB may result in the prescribing of a diuretic for symptom relief, however CCB-induced oedema is not due to fluid overload. The treatment of a euvolaemic patient with a diuretic puts the patient at increased risk of overdiuresis, which results in adverse outcomes including electrolyte imbalance, acute kidney injury, urinary incontinence and falls, especially in older adults. **A prescribing cascade occurs when an adverse drug event (ADE) (e.g. CCB-induced oedema) is misinterpreted as a medical condition resulting in the initiation of another drug to treat it.** There is limited evidence of the rate of occurrence of the CCB-diuretic prescribing cascades in the literature. A Canadian population-based, retrospective cohort study assessed whether older adults with HT who were newly dispensed a CCB were more likely to be subsequently dispensed a loop diuretic than: 1) individuals who were newly dispensed an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB), and 2) individuals who were newly dispensed an unrelated medication (*JAMA Internal Medicine* 2020;180(5):643-651). The study was performed using linked health administrative data from health insurance programs of community dwelling individuals with hypertension ≥ 66 years who were newly exposed to CCBs (amlodipine, felodipine, nifedipine, diltiazem hydrochloride and verapamil hydrochloride) or the comparator drugs from September 2011 to September 2016; the dates of analysis were from September 2018 to May 2019. Exclusion criteria included a diagnosis of heart failure or end-stage renal disease in the previous year, hospitalisation within 1 month preceding the index date and those dispensed an antihypertensive drug or a diuretic in the previous 12 months. The index date was defined as the date of first dispensing of a CCB or comparator drug and the primary outcome was a patient being dispensed a loop diuretic. Variables included age, sex, income, medical history, health system use and concurrent drug therapies. The final cohort included 41,086 individuals with HT who were newly dispensed a CCB, 66,494 who were dispensed an ACEI or ARB and 231,439 individuals in the general comparator group. **The study found that, by 90 days those that were newly dispensed a CCB had a higher cumulative incidence of receiving a loop diuretic than those in the comparison groups (1.4% vs 0.7% [ACEI or ARB] and 0.5% [general comparators], $P < 0.001$).** After adjustment, those who were newly dispensed a CCB were dispensed a loop diuretic at higher rates compared to those in the ACEI/ARB comparator group over 3 time periods (Hazard ratio [HR] 1.68; 95% CI, 1.38 to 2.05 for 1 to 30 days; HR 2.26; 95% CI, 1.76 to 2.92 for 31 to 60 days; and HR 2.40; 95% CI, 1.84 to 3.13 for 61 to 90 days), and similar results were found with those in the general comparator group (HR 2.51; 95% CI, 2.13 to 2.96 in the first 30 days; HR 2.99; 95% CI, 2.43 to 3.69 in the subsequent 30 days and HR 3.89; 95% CI, 3.11 to 4.87 in the 3rd month). The rates of loop diuretic dispensing remained elevated throughout 1 year of follow-up. Limitations of the study include the absence of an indication for the medication and the lack of a diagnostic code for the peripheral oedema (i.e. the authors could not confirm that the loop diuretic was used to treat CCB-induced oedema). The authors of the study conclude that many older adults with HT who are newly dispensed a CCB subsequently receive a loop diuretic, and that the results of the study stress the need to raise awareness of this prescribing cascade.

[Editor's note: this article was also reviewed by the *Drug and Therapeutics Bulletin* 2020; DOI: 10.1136/dtb.2020.000067. The DTB advises that prescribing cascades are an important contributor to problematic polypharmacy and that it is important to identify and interrupt prescribing cascades to reduce the risk of preventable adverse events.]



Recent Irish College of General Practitioners (ICGP) clinical guides.

The Quality and Safety in Practice Committee of the ICGP recently published an updated clinical "Asthma – Diagnosis, Assessment and Management in General Practice", a "Guide for Providing Care for Lesbian, Gay and Bisexual Patients in Primary Care" and a guide on "Early Episode Psychosis Diagnosis and Management from a GP perspective". These clinical guides are freely available on the ICGP website (www.icgp.ie).



Updated Flipbook of Medication Safety Minutes.

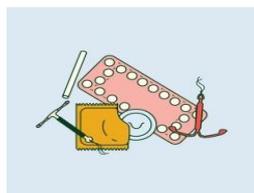
Readers are reminded of the "Medication Safety Minute" which is a collaborative project undertaken by two hospital consultants and the Medication Safety Facilitator (a pharmacist) in St James's Hospital. Each 'Minute' highlights a key medication safety message, which is formatted as a question and answer, and designed to be reviewed in 1 minute or less! Topics covered to date include drug interactions and adverse effects with commonly used medications such as clarithromycin, warfarin, direct oral anticoagulants and statins, plus dose adjustments required in renal impairment. These bite-sized messages which may also include short videos are published every week and available via **Twitter @medsafetymin**. A selection of previously published "Minutes" is also available as an electronic flipbook. This 6th edition of the Flipbook which contains 90 Medication Safety Minutes (including new and existing Minutes, has been updated to reflect current evidence/best practice guidance) and is available at: <http://online.fliphtml5.com/hkta/ivqg/>.



Update to HSE Antibiotic Prescribing website.

As readers are aware the HSE antibiotic prescribing website is a very useful evidence-based antimicrobial resource (www.antibioticprescribing.ie). The website has been recently updated and contains the following sections:

- 1) **Conditions and Treatments** (a list of conditions and treatment guidelines)
- 2) **What's New** (updates and new content)
- 3) **Paediatric Prescribing** (guidelines based on weight and height)
- 4) **Dental Prescribing** (guidelines on dental prescribing and treatment)
- 5) **COVID-19 Acute Respiratory Infection** (prescribing guidance in suspected or proven infection)
- 6) **Prescribing in Renal Impairment** (guidelines on antimicrobial dosing in renal impairment)
- 7) **Antimicrobial Stewardship Audit Tools** (improve and measure the appropriate use of antimicrobials)
- 8) **Tips on Penicillin Allergy** (tips on verifying penicillin allergy)
- 9) **Antimicrobial Resistance and Infection Control team (AMRIC) key messages** (antimicrobial safety alerts and advice issued by AMRIC)
- 10) **Safe Prescribing** (guidelines on prescribing safely)
- 11) **Prescribing in Pregnancy** (prescribing antimicrobials in pregnancy and lactation)
- 12) **Prescribing in Long-term Care Facilities**

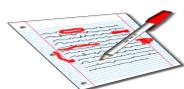


Contraception Guidelines.

Readers are reminded that the UK Faculty of Sexual and Reproductive Healthcare (FSRH) publish useful guidelines on contraception. The FSRH Clinical Effectiveness Unit (CEU) recently published an updated statement on the provision of contraception during the COVID-19 pandemic (www.fsrh.org). While it is essential to maintain effective contraceptive services during the pandemic, it is recommended to avoid unnecessary face-to-face contact for contraceptive provision, as much of the contraceptive consultation process can be achieved remotely. It is important

that individuals at highest risk of unplanned pregnancy can access the most effective contraceptive method. Remote assessment for emergency contraception (EC) should be prioritised so that EC can be offered as soon as possible after unprotected intercourse (UPI) to maximise effectiveness. The prescription of combined hormonal contraception (CHC) requires assessment of medical eligibility, blood pressure (BP) and BMI; this may be achieved remotely with self-reported BP and BMI. The desogestrel progestogen only pill (POP) is ideal for remote provision as no physical examination is required. The available evidence suggests that the risk of pregnancy in the 4th year of use of the etonogestrel implant (ENG-IMP) and the 6th year of use of a 52mg levonorgestrel-releasing intrauterine system (LNG-IUS) is likely to be very low, therefore the FSRH suggests that replacement of these contraceptive agents can be delayed for up to 1 year (up to 4 years use for the ENG-IMP and 6 years use for the LNG-IUS), in order to avoid unnecessary risk of coronavirus transmission. Women should be advised that contraceptive effectiveness is not guaranteed during the additional year and they may wish to use additional contraceptive agents (e.g. condoms or POP). However, it is important to note that if the LNG-IUS is being used for endometrial protection as part of hormone replacement therapy (HRT), it must be either changed at 5 years or a combined HRT preparation commenced. The full CEU statement is available on

<https://www.fsrh.org/documents/fsrh-update-provision-of-contraception-during-covid19/>.



Correction in Management of Osteoporosis Bulletin 2020.

In the 2020 NMIC bulletin on Management of Osteoporosis, Volume 26; Number 1, incorrect relative risk reduction (RRR) information was provided for denosumab; we had stated that "Denosumab reduces the incidence of vertebral, non-vertebral and hip fractures (RRR of 68%, 40% and 20% respectively) in postmenopausal women.", when the correct information is that "Denosumab reduces the incidence of vertebral, non-vertebral and hip fractures (RRR of 68%, 20% and 40% respectively) in postmenopausal women." We have updated the bulletin with the correct information on our website

<https://nmiccomms.newsweaver.com/izn877i20c/e6pzmvpnbiy>.