UIT HET NEDERLANDS PLATFORM VOOR FARMACEUTISCH ONDERZOEK 2017;2:A1649

Prisma Symposium, 16 mei 2017

De hier opgenomen abstracts vormen een selectie uit de presentaties op het Prisma Symposium van 16 mei 2017 te Amersfoort.

Citeer als: Prisma Symposium, 16 mei 2017. Nederlands Platform voor Farmaceutisch Onderzoek. 2017;2:a1649.

Opioid-induced constipation and the use of laxative co-medication: an evaluation of patients' experiences and considerations in community pharmacy practice

Frans de Bruin *, Marcel Bouvy and Martina Teichert

* Correspondence: f.debruin@students.uu.nl.

Introduction

Opioid-induced constipation (OIC) is a clinical relevant adverse effect of strong opioids and a prominent cause of potentially avoidable hospital admissions.

Objectives

The study aimed to describe the degree of laxative co-medication in starting opioid users and reasons for not using laxatives concomitantly and to evaluate the influence of laxatives on constipation during opioid use.

Methods

All community pharmacies in the Netherlands were invited to participate in this prospective observational study. First, laxative use was registered using clinical rule (CR) forms in starting opioid users in November and December 2016. Reasons for non-use of laxatives were collected. Secondly, two starting opioid users per pharmacy were invited to complete questionnaires regarding their defecation prior to and during opioid use. The effect of laxatives on constipation was analysed with multivariate regression models.

Results

125 community pharmacies agreed to participate in the study. From those 81 (64.8%) returned the CR forms of 460 patients and completed questionnaires for 75 patients. In total 344 (74.8%) of patients starting with opioids concomitantly initiated laxatives. Main reason to not use laxatives was that either the prescriber or the patient was of the opinion that laxation was unnecessary. Laxative omission showed a non-significant trend to increase the risk of constipation with 40%.

Conclusion

One in four opioid starters did not concomitantly receive a laxative. These patients showed a trend towards an increased risk to develop constipation. Therefore, reluctance to immediately start laxatives should be accompanied with monitoring to prevent constipation, together with lifestyle advise.

Community pharmacy in transition: a work sampling study of community pharmacists using modern smartphone technology

J.M. van de Pol *, S.V. Belitser, G.W.J. Frederix, A.M. Hövels and M.L. Bouvy

* Correspondence: jvdpol@benuapotheek.nl.

Introduction

Community pharmacy is undergoing a transition from compounding and distribution of medicines to the provision of pharmaceutical care. Traditional roles, however, are competing with innovative services. Currently, little is known about how community pharmacists are spending their time in daily practice and to what extent they are able to implement pharmaceutical care related services in daily practice.

Methods

Self-reported work sampling was used to register activities of community pharmacists. A smartphone application was designed specifically for this purpose. The smartphone application alerted participants to register their current activity five times per workday during six weeks. Participants were also asked to complete an online survey on background data.

Results

Ninety-two Dutch community pharmacists provided work sampling data consisting of 7923 registered activities. The results show that 51.5% of time is spent on professional activities, 35,4% on semi-professional activities and 13.1% on non-professional activities. The proportion of time devoted to pharmaceutical care declines during the workweek, whereas time spent on traditional task increases.

Discussion and conclusion

This study shows that work-sampling data collection using smartphone technology is practical and useful. The results show that community pharmacists are spending almost half of their time on activities which could have been delegated to other staff members. It also shows that community pharmacists are being limited in the transition to pharmaceutical care, mostly by the traditional tasks that compete with pharmaceutical care for the pharmacists' time. Based on this study, it seems that community pharmacists are experiencing difficulties making time for pharmaceutical care, probably due to the hampering effect of traditional tasks that still need to be performed. Therefore, community pharmacists take less advantage of the opportunity to be the pharmaceutical expert in daily practice.

Cost-effectiveness analysis of genotype-guided treatment allocation in patients with alcohol dependence using naltrexone or acamprosate

R.L. Sluiter *, W. Kievit, G.J. van der Wilt, A. Schene, M. Teichert, A.M.J.H. Coenen and A. Schellekens

* Correspondence: rene.sluiter@radboudumc.nl.

Background

Alcohol dependence (AD) is a major contributor to the global burden of disease, and has huge societal impact. Recent studies showed that AD patients with a G-allele of the *OPRM1* genotype responded better to naltrexone with reduced relapse rates, compared to AA genotype carriers. Genotype-guided treatment allocation of these patients could potentially improve treatment outcomes. However, the cost-effectiveness of this strategy should be investigated before considering clinical implementation.

Methods

In a Markov model the costs and QALYs of genotype-guided treatment allocation (G-allele carriers received naltrexone; AA homozygotes acamprosate or naltrexone) were evaluated and compared to standard care (random treatment allocation to acamprosate or naltrexone) for one year. Cost-effectiveness was evaluated by Incremental Cost-Effectiveness Ratios (ICERs). Sensitivity analyses were performed to check influence of parameter uncertainty on the results.

Results

The strategy genotype-guided treatment allocation compared to random allocation resulted in incremental costs of €20.85 (95%CI: -105; 147) and incremental effects of 0.005 QALYs (95%CI: 0.000; 0.011) per patient, resulting in an ICER of €4,202.08 (95%CI: 735,000; dominant) per QALY gained. At a willingness to pay €80,000 for one QALY, there was 79% chance that the intervention was cost-effective compared to standard care. Cost-effectiveness outcomes depended most on the risk ratio to relapse after treatment allocation.

Conclusion

Genotype-guided treatment allocation of AD patients to naltrexone, based on *OPRM1* genotype, seemed to be a cost-effective strategy. Additional evidence is needed to confirm these findings.

Discontinuing inappropriate medication in nursing home residents: a cluster randomized controlled trial

Hans Wouters *, Jessica Scheper, Hedi Koning, Chris Brouwer, Jos Twisk, Heleen van der Meer, Froukje Boersma, Sytse Zuidema and Katja Taxis

* Correspondence: j.wouters@umcg.nl.

Background

Inappropriate prescribing is a prevalent problem in nursing home residents that is associated with cognitive and physical impairment. Few interventions have been shown to reduce inappropriate prescribing.

Aim

To examine successful discontinuation of inappropriate medication.

Method

A cluster randomized controlled trial. Fifty-nine wards were randomly assigned to the intervention or to 'care as usual'. The intervention was a Multidisciplinary Multistep Medication Review (3MR) consisting of an assessment of the patient perspective, a medical history, a critical appraisal of medication, a meeting between the elderly care physician and a pharmacist, and execution of medication changes. The primary outcome was successful discontinuation of ≥ 1 inappropriate drug(s), i.e. without relapse or severe withdrawal symptoms and clinical outcomes (neuropsychiatric symptoms, cognitive function and quality of life). Nursing home residents with a life expectancy of > 4 weeks who did not refuse treatment with medication were included. Data were collected at baseline and at 4.5 months of follow-up.

Results

A total of 426 nursing home residents participated (intervention group: n=233 and control group: n=193). Generalized linear mixed models (logit link function) showed that for 91 (39.1%) of the residents in the intervention group ≥1 inappropriate medication(s) could be successfully discontinued versus 57 (29.5%) of residents in the control group (adjusted relative risk: 1.37 (95%CI: 1.02; 1.75). There was no deterioration on clinical outcomes.

Conclusion

The 3MR is effective in discontinuing inappropriate medication in frail nursing home residents whilst probably not compromising their wellbeing.

De ontwikkeling van medicatiebewakingsadviezen voor de contra-indicatie levercirrose

R.A. Weersink *, M. Bouma, D.M. Burger, J.P.H. Drenth, F. Harkes-Idzinga, N.G.H. Hunfeld, H.J. Metselaar, M. Monster-Simons, A.W. van Putten, K. Taxis en S.D. Borgsteede

* Correspondentie: rianne.weersink@healthbase.nl.

Achtergrond

Levercirrose heeft veel impact op de farmacodynamiek en farmacokinetiek van geneesmiddelen, maar het ontbrak aan concrete medicatiebewakingsadviezen voor deze contra-indicatie.

Doel

De ontwikkeling van medicatiebewakingsadviezen bij patiënten met levercirrose.

Methode

Met behulp van systematisch literatuuronderzoek en aanbevelingen van deskundigen zijn adviezen opgesteld over de veiligheid en optimale dosering van geneesmiddelen bij patiënten met levercirrose. Het veiligheidsadvies kon zijn dat een geneesmiddel gebruikt mocht worden bij levercirrose; dat aanbevolen werd een veiliger middel te kiezen; of dat een geneesmiddel vermeden moest worden. De adviezen werden, indien relevant, opgesplitst naar de ernst van de cirrose.

Resultaten

In totaal zijn 209 geneesmiddelen beoordeeld en zijn er 218 medicatiebewakingsadviezen opgesteld. Negen geneesmiddelen hebben twee adviezen vanwege verschillen tussen toedienroutes of indicaties. Van de 218 adviezen is bij 73% (n=159) actie nodig van de voorschrijver of apotheker. Dit gaat om een veiligheidsactie in 92 adviezen, een dosisaanpassing in 31, of beide in 36. De veiligheidsactie bestaat in 42 adviezen (19%) uit het aanbevelen van een veiliger geneesmiddel en in 56 (26%) is de actie afhankelijk van de ernst van de cirrose. Als veiligheidsactie wordt 30 keer (14%) geadviseerd een geneesmiddel niet te gebruiken omdat het onveilig is. De reden hiervoor is een sterk gewijzigde farmacokinetiek (n=9) of farmacodynamiek (n=21) bij patiënten met levercirrose in vergelijking met gezonde controles.

Conclusie

Van de meer dan 200 beoordeelde geneesmiddelen is bij bijna driekwart een actie nodig van voorschrijver of apotheker. Een gewijzigde farmacodynamiek was de belangrijkste reden dat gebruik van een geneesmiddel werd afgeraden.

Development and empirical testing of multisource feedback in the accreditation for community pharmacists

Koen ten Hove, Esmee J. Peters, Annemieke Floor, Reinier Akkermans, Marnix Westein, Martina Teichert and Jozé Braspenning *

* Correspondence: joze.braspenning@radboudumc.nl.

Background

Medical doctors use multisource feedback (MSF) as input for their professional development. We studied the value of such instrument in an accreditation program for community pharmacists.

Objective

Develop and evaluate MSF as part of an accreditation program for community pharmacists, to assess and improve their professional performance.

Method

Two questionnaires (MSF), for professionals and patients respectively, have been developed in a pilot study among 20 community pharmacists. Psychometric properties of the questionnaires were analysed. The written improvement plans of the community pharmacists were evaluated against the MSF input. The feasibility of the accreditation program was studied with a separate questionnaire and a panel discussion.

Results

173 Healthcare professionals (63 staff, 56 pharmacists, 54 general practitioners (GP)/practice nurses (NP), and 70 patients responded. Internal consistency of the items per domain, excluding Health advocate and Manager, was confirmed by sufficient factor loadings (> 0.40) and high Chronbach's alpha's (> 0.76). The total average scores on the items were high, but multilevel analysis showed that pharmacist and staff tend to score lower than the others.

Pharmacists had difficulty formulating SMART improvement plans. MSF was seen as providing realistic feedback (64.2%), new insights (64.2%), and it was recommended to colleague-pharmacists (71.4%).

Conclusion

MSF is valued as part of the accreditation program based on psychometrics and individual judgments. It supports the descriptions of an improvement plan. More data are needed to confirm these preliminary results. Furthermore, information should become available on the actual activities that are undertaken based on the improvement plans.

Implementatie van een mobile health interventie in de apotheek: het apothekersperspectief

Richelle C. Kosse *, Marcel L. Bouvy, Tjalling W. de Vries en Ellen S. Koster

* Correspondentie: r.c.kosse@uu.nl.

Achtergrond

Apothekers hebben een belangrijke rol als zorgverlener om patiënten te begeleiden bij (goed) medicatiegebruik. In de Adolescent Adherence Patient Tool (ADAPT) studie wordt een mobile health interventie – bestaande uit een smartphone app voor patiënten en begeleidingssysteem voor apothekers – getest in apotheken, met als doel therapietrouw van jongeren met astma te verbeteren.

Doel

De ervaringen en wensen van apothekers over de interactieve ADAPT interventie in kaart brengen.

Methode

Als onderdeel van deelname aan de ADAPT studie, werden semigestructureerde (evaluatie)interviews gehouden met 24 apothekers die gewerkt hebben met de ADAPT interventie. Hierbij werd gevraagd naar de positieve punten en verbeterpunten.

Resultaten

Het gebruik van de interventie kostte weinig tijd voor de apotheker; maximaal 5 minuten per week, afhankelijk van de behoefte van de patiënt. De meeste apothekers (80%) gaven aan geen (technische) problemen te hebben ervaren. De chatfunctie met de patiënt, en de vragenlijst om de patiënt te monitoren werden als meest nuttig ervaren. Meer dan de helft van de apothekers vindt dat de communicatie met de patiënt verbeterd is door het gebruik van de interventie, ook hebben ze meer inzicht gekregen in de luchtwegklachten. Bijna alle apothekers (88%) zouden de interventie inzetten als deze in het vergoedingspakket zou zitten, ook voor andere chronische aandoeningen. Er zijn echter wel verbetermogelijkheden, zoals gemakkelijker inloggen en minder updates. Een koppeling met het apotheekinformatiesysteem bevordert ook het gebruik.

Conclusie

Apothekers zijn positief over het begeleiden van jongeren met astma met de ADAPT interventie. Voor verdere implementatie zijn er verbeteringen nodig, zodat de interventie gemakkelijker geïntegreerd kan worden in de dagelijkse werkzaamheden van openbaar apothekers.

Development of a model to predict QTc interval prolongation in patients who use one or more QT-prolonging drugs

A.N. Bindraban, J. Rolvink, F.A. Berger, P.M.L.A. van den Bemt, R.T.M. van der Hoeven, A.K. Mantel-Teeuwisse and M.L. Becker *

* Correspondence: mbecker@sahz.nl.

Background

Healthcare providers receive warnings for interactions between QT-prolonging drugs. It is debatable how these warnings should be managed.

Aim

To develop a model to predict QTc interval prolongation above 500 ms, based on risk factors in patients who use one or more QT-prolonging drugs.

Methods

This study was performed at the Spaarne Hospital (Haarlem/Hoofddorp). We included 19,340 ECGs of adult in- and outpatients who used one or more QT-prolonging drugs. ECGs with a QRS interval > 120 ms were excluded. Independent risk factors were determined using backwards conditional stepwise multivariate logistic regression. Risk scores were assigned to these risk factors based on their regression coefficient. The association between the total risk score and QTc-prolongation was validated in an independent set of ECGs.

Results

The independent risk factors with the accompanying risk scores, are age > 70 years, risk score 1; use of antiarrhythmics, 1; eGFR ≤ 60 ml/min, 2; use of loop diuretics, 3; serum calcium level ≤ 2.14 mmol/l, 3; serum potassium level between 3 and 3.5 mmol/l, 3; maximum past QTc between 480 and 500 ms, 3; serum potassium level ≤ 2.9 mmol/l, 7; and a maximum past QTc of > 500 ms, 7. The area under the ROC curve is 0.71. We also developed a simplified model excluding the maximum past QTc value and serum calcium levels with an area of 0.62.

Conclusion

Patients with higher risk scores have a higher chance of developing QTc interval prolongation. In these patients QT-prolonging drugs should be used more cautiously.

Toepassing van gezondheidsgerelateerde doelen bij een medicatiebeoordeling

Sanne Verdoorn *, Timo Vogelzang, Henk-Frans Kwint, Jacobijn Gussekloo, Jeanet Blom en Marcel Bouvy

* Correspondentie: s.verdoorn@sirstevenshof.nl.

Achtergrond

Onderzoek heeft aangetoond dat medicatiebeoordeling (MBO) farmacotherapie-gerelateerde problemen (FTP's) oplost. Een effect op klinische uitkomsten, zoals kwaliteit van leven, is nog niet aangetoond. Mogelijk door te weinig aandacht voor klachten en doelen van patiënten. Goal Attainment Scaling (GAS) is een hulpmiddel om het behalen van gezondheidsgerelateerde doelen te kunnen meten. Dit meetinstrument wordt gebruikt binnen de DREAMeR-studie (Drug use Resonsidered in the Elderly using goal Attainment scales during Medication Review).

Doel

Onderzoeken of GAS een geschikt meetinstrument is om gezondheidsgerelateerde doelen te kunnen meten binnen medicatiebeoordeling.

Methode

De DREAMER-studie is een gerandomiseerd gecontroleerd onderzoek uitgevoerd in 35 Service Apotheken in Nederland. Patiënten van ≥ 70 jaar met polyfarmacie werden geïncludeerd. Inmiddels zijn 281 MBO's afgerond. Indien mogelijk werden doelen opgesteld. DREAMeR-uitkomstmaten waren: aantal gezondheidsgerelateerde doelen, drie meest voorkomende GAS-onderwerpen, scores op GAS na drie en zes maanden en implementatiegraad van interventievoorstellen voor bijbehorende FTP's.

Resultaten

Bij 242 van 281 MBO's (86%) patiënten in de interventiegroep werden 336 GAS-doelen opgesteld. Drie meest voorkomende GAS-onderwerpen waren: pijnreductie (19%), verminderen aantal medicijnen (14%) en verbeteren mobiliteit (10%). Van de 260 geëvalueerde doelen na drie maanden bleek 50% (deels) behaald, 43% niet veranderd en 7% verslechterd. Na zes maanden was dit respectievelijk 53%, 36% en 11% bij 146 geëvalueerde doelen. De implementatiegraad van interventievoorstellen voor FTP's gerelateerd aan GAS-doelen was 71%, voor niet GAS-gerelateerde FTP's 52% ($p < 0.05$).

Conclusie

Goal Attainment Scaling lijkt een bruikbaar meetinstrument om het behalen van gezondheidsgerelateerde doelen bij medicatiebeoordeling te kunnen meten.

The development of a clinical rule for handling QT-interactions

F.A. Berger *, N.M.S. de Groot, I.H. van der Sijs, M. Heringa, M.L. Bouvy, T. van Gelder and P.M.L.A. van den Bemt

* Correspondence: f.berger@erasmusmc.nl.

Background

The risk of combining QTc-prolonging drugs is unknown making it difficult to interpret these drug-drug interactions. The development of a clinical rule will facilitate the correct handling of these interactions.

Objectives

The primary objective was to develop and validate a clinical rule for handling QT-interactions.

Methods

A clinical rule was developed based on risk factors associated with QTc-prolongation from a prospective study on QT-interactions. Risk points were assigned based on their Log odds ratios. Additional risk factors were added from literature. The risk score model was validated in a hospital and primary care population. The risk score model was applied to both datasets to predict QTc-prolongation as primary endpoint in the hospital population, and to predict an advice for intervention or no intervention as primary endpoint in the primary care population. An expert panel was appointed to formulate this advice in the primary care cases. Sensitivity and specificity were calculated. For safety reasons, a higher sensitivity was preferred.

Results

The clinical rule included age, female sex, cardiac comorbidities, hypertension, diabetes mellitus, renal function, serum potassium levels, loop diuretics and other QTc-prolonging drugs as risk factors. A risk score of ≥ 6.00 was associated with a sensitivity = 0.846, specificity = 0.667 in a hospital population and a sensitivity = 0.932, specificity = 0.540 in a primary care population.

Conclusions

A clinical rule based on a risk score model was developed and validated in both a hospital and primary care population, which might be useful to guide safe prescription practices.

Development and evaluation of an e-learning program on oral anticancer drugs

Lise-Marie Kinnaer, Sandra De Coster, Maaike Desiron, Sarah Moermans, Astrid Sterckx, Charlotte Vermeersch, Elsie Decoene, Ann Van Hecke and Veerle Foulon *

* Correspondence: veerle.foulon@kuleuven.be.

Background

Since anticancer therapy with oral anticancer drugs (OACD) is conducted at home, the role of healthcare professionals (HCPs) from primary care (i.e. general practitioners, community pharmacists and home care nurses) is becoming more important. HCPs from primary care currently lack knowledge and expertise regarding these drugs for an adequate level of care and follow-up.

Aim

This project aims to develop and test an e-learning program for HCPs from primary care to increase their knowledge and expertise with OACD.

Methods

A first version of the e-learning program, consisting of 6 modules, was pilot tested in a small group of HCPs from primary care. Before and after completing the e-learning, HCPs filled in a knowledge test containing 18 multiple choice questions (covering all modules) and a satisfaction survey focusing on comprehensibility of the program and usability in daily practice.

Results

In total 30 HCPs completed both knowledge tests and the satisfaction survey. In all disciplines a significant improvement in knowledge was observed: in general practitioners (n=9) the mean scores increased from 6.3/18 to 11.9/18, in community pharmacists (n=13) from 5.5/18 to 13.5/18 and in home care nurses (n=8) from 4.9/18 to 14.0/18. Participants were positive about the availability of downloadable and practical information. However, they mentioned that the e-learning was extensive and time-consuming.

Conclusion

The results from the knowledge tests show that education of HCPs in the follow-up of patients treated with OACD is highly needed. An e-learning program seems to be an appropriate method to increase the knowledge on OACD.

Nilotinib bij chronische myeloïde leukemie: een lagere dosering met voedsel

Christel Boons *, Yvonne den Hartog, Jeroen Janssen, Anthe Zandvliet, René Vos, Noortje Swart, Harry Hendrikse en Jacqueline Hugtenburg

* Correspondentie: c.boons@vumc.nl.

Achtergrond

Nilotinib, voor de behandeling van chronische myeloïde leukemie (CML), moet tweemaal daags nuchter worden ingenomen. Inname met voedsel verhoogt de biologische beschikbaarheid van nilotinib.

Doel

Onderzoeken of nilotinib 200 mg 2dd ingenomen met voedsel vergelijkbaar is met 300 mg 2dd nuchter ingenomen.

Methode

Interventieonderzoek met een 'pre-test post-test' opzet bij patiënten met CML. De AUC, C_{max} en C_{min} van nilotinib 300 mg 2dd nuchter zijn vergeleken met de AUC, C_{max} en C_{min} van nilotinib 200 mg 2dd ingenomen met voedsel. De concentraties zijn bepaald met de bloedspot methode. Bijwerkingen werden gemeten met een dagboek en 24-uurs ECG-monitoring. Kwaliteit van leven werd gemeten met de EORTC QLQ-C30 en EORTC QLQ-CML24.

Resultaten

Veertien patiënten (58,3 ± 12,6 jaar) hebben deelgenomen. De gemiddelde AUC van nilotinib 200 mg 2dd met voedsel was 11% (ochtendinname) en 18% (avondinname) lager dan de gemiddelde AUC van nilotinib 300 mg 2dd nuchter. De gemiddelde dalspiegels waren, respectievelijk, 10% en 5% lager. Inname van nilotinib met voedsel leidde tot een hogere t_{max}. De intra- en interindividuele verschillen waren voor beide doseerregimes even groot. Er werd geen afwijkend QT-interval waargenomen. De EORTC QLQ-CML24 schaal *symptoomlast* was significant lager na inname van nilotinib met voedsel.

Conclusie

Gezien de beperkte verschillen in de farmacokinetiek van nilotinib 200 mg 2dd met voedsel en nilotinib 300 mg 2dd nuchter en de vergelijkbare intra- en intervariabiliteit, is het zeer aannemelijk dat de werkzaamheid en effectiviteit van de lagere dosering met voedsel overeenkomen met die van de aanbevolen dosering op een lege maag. ■