Hospital pharmacy team supporting the valproate pregnancy prevention programme

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Abstract

Title

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Introduction

In 2018, the Medicines and Healthcare Products Regulatory Agency changed the licence for valproate medicines so these must no longer be prescribed to women or girls of childbearing potential unless they are on a Pregnancy Prevention Programme. The MHRA, and other organisations, have advised healthcare professionals, including pharmacists, on actions that should be taken. We introduced a hospital pharmacy department guideline on how pharmacists can help implement the valproate Pregnancy Prevention Programme.

Method

This was a quality improvement programme within a district general teaching hospital of approximately 750 beds using an electronic prescribing system across all wards. This system was searched retrospectively for females aged 8-55 years who were prescribed valproate during their inpatient stay and any intervention notes or discharge medicines reconciliation notes were extracted from the system for the different phases of the programme.

Results

Over the three distinct phases of this programme, the recording of notes on the system for these females prescribed valproate as an inpatient improved from two out of 17 in phase 1, ten out of 13 in phase 2, and seven out of seven in phase 3. However, the nature of the notes that were recorded did not improve to any great extent.

Conclusion

This small quality improvement programme has shown some improvement in the recording of pharmacist contact with these females on valproate during the different phases. In particular, at the end of phase 3 all seven patients had an electronic note about the valproate Pregnancy Prevention Programme on our system. However, in none of these seven instances had that note been entered in such a way that it would appear in the discharge paperwork.

Keywords: valproate, pregnancy prevention programme, quality improvement.

Introduction

Sodium valproate is licensed in the EU for treating generalised, partial or other forms of epilepsy, and it has also been used to treat bipolar disorder and to prevent migraine. Children born to women who take valproate during pregnancy are at significant risk of harm. If valproate is taken during pregnancy, up to 4 in 10 babies are at risk of developmental disorders, and approximately 1 in 10 are at risk of birth defects.

In 2018, the European Medicines Agency recommended that sodium valproate should not be used during pregnancy unless no other effective treatment is available, and that it must not be used in women able to have children, unless the conditions of a pregnancy

prevention programme (PPP) are met.[1] Healthcare professionals who seek to prescribe valproate to their female patients must make sure patients are enrolled in the PPP. This includes the completion of a risk acknowledgement form when their treatment is reviewed by a specialist, at least annually.

The Royal Pharmaceutical Society quick reference guide lists the materials to support the PPP, including a patient card (to be given by pharmacists to all female patients who are dispensed valproate medicines to inform them of the risks); patient guide (to be provided to girls (of any age) and women of childbearing age (or their parent/caregiver/responsible person)) taking any medicine containing valproate; and a guide for Healthcare Professionals (for all prescribers, pharmacists, and other healthcare providers involved in the care of women of childbearing age (WCBA) using valproate medicines).[2]

It is expected that the specialist team and primary care will be providing information about the teratogenic risks associated with the use of valproate, the actions necessary to minimise the risks to patients, and ensure patients have an adequate level of understanding of the risk. However, in our trust we decided that there is a potential role for the hospital pharmacy team in supporting with this important patient safety issue. In making this decision, we were mindful of the Guide for Healthcare Professionals which has a section 'Actions for pharmacists' (see Box 1).[3]

The initial hospital pharmacy department guideline envisaged that when WCBA on valproate have been identified at the stage of medicines reconciliation or had been flagged on the Pharmacists Friend, a prioritisation and alerting tool used to identify clinical issues that may need pharmacy intervention (Figure 1), the pharmacists will be in a position to undertake one of three actions (Box 2).

Our electronic prescribing and medicines administration (EPMA) system (WellSky International, Basildon, UK) allows a variety of notes to be entered which have different functions. Most of these are episodic in nature and are archived once the patient is discharged from hospital. Dispensing notes are commonly used to convey additional instructions relevant to the dispensing of the patient's medicines. A discharge medicines reconciliation (DMR) note contains information for patients, GPs and community pharmacists regarding information around medication changes that occurred during the admission and any required follow up, and is automatically transferred to the discharge paperwork. A Pharmaceutical Care Plan (PCP) note is used to document important medication changes throughout the patient journey and reasons why these have occurred. It is possible to retain selected notes so that they are displayed on each new episode of care. This is particularly useful for notes that are of continuing relevance such as identifying high risk patients who should only receive 7 day supplies of medicines, or patients who receive blister pack medicines. Such a retained dispensing note should also mean that the same patient is not asked the same questions about the VPPP on their next admission.

Our guideline (Box 2) stipulated a retained dispensing

Ensure the Patient Card is provided every time valproate is dispensed.

Remind patients of the risks in pregnancy and the need for highly effective contraception.

Remind patients of the need for annual specialist review.

Ensure the patient has received the Patient Guide.

Dispense valproate in the original package. In situations where repackaging cannot be avoided always provide a copy of the package leaflet and add a sticker with the warning to the outer box.

If a woman of childbearing potential is not aware of the need for contraception and has not been seen by her GP/Specialist in the past year, dispense their medicine and refer them to their GP (including by contacting the GP if necessary).

Box 1. Actions for pharmacists

note titled 'VPPP', the presence of which will remove the alert from the Pharmacists Friend. It is the DMR note that is transmitted to primary care. Following the results from Phase 2 of this project, a surveillance report was also introduced, enabling active prescription surveillance in real time such that patients prescribed valproate are identified along with patient name, date of birth, hospital number, inpatient location in the hospital, drug name. This is monitored twice daily by a senior pharmacist and relevant alerts forwarded to the ward pharmacy team.

The aim of this project was to ascertain if interventions that had been put in place since the first evaluation of the impact of the guideline had improved the service provided by the pharmacy team.

Method

This was a quality improvement programme within a district general teaching hospital of approximately 750 beds using an EPMA system across all wards. The electronic prescribing system was searched retrospectively for females aged 8-55 years who were prescribed valproate during their inpatient stay and any intervention notes or DMR notes were extracted from the system. This search was undertaken for three distinct time periods or Phases corresponding

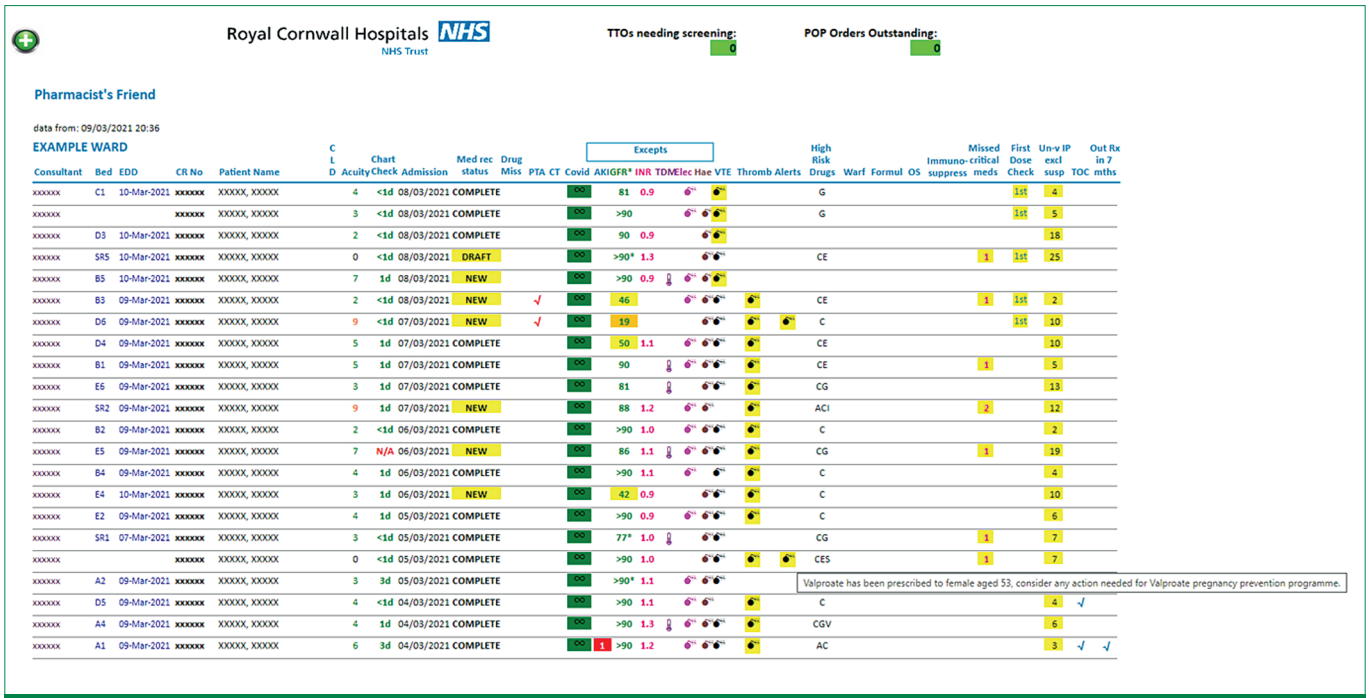

Figure 1. Simulated image of the Pharmacists Friend

- If WCBA (aged 8 – 55 years) then consider providing the patient card and patient booklet. For females outside this age range on valproate consider providing the patient card only.
- Confirm with the patient / carer that they know of the PPP and have received the relevant patient information. Make a retained dispensing note (VPPP) on the e-prescribing system to capture our action as part of the valproate PPP.
- If the patient /carer does not know of the PPP and it is appropriate to hand over the patient information then do so. Make a retained dispensing note (VPPP) on the e-prescribing system, and a discharge medicines reconciliation (DMR) note as well.
- If the patient /carer does not know of the PPP and it is not appropriate to broach this subject (e.g. patient with severe neurodevelopmental problems) make a retained dispensing note (VPPP) on the e-prescribing system, and a DMR note as well.

Box 2. Possible actions for hospital pharmacists

to different interventions undertaken (Table 1): for January to July 2020, for August to mid-October 2020, and for November 2020 to February 2021 (see Table 1). Patients admitted into and discharged from the emergency department were excluded because there is no routine pharmacy service to the emergency department to review these patients PPP status.

Ethics

Health Research Authority criteria about research and service evaluation were considered. This was a retrospective assessment involving no changes to the service delivered to patients, and we used the NHS Health research authority tool (http://www.hra-decisiontools.org.uk/research/index.html) which helped confirm that no ethical approval was required for this project.

Results

Over the three distinct phases of this project the number of WCBA identified via EPMA prescribed valproate as an inpatient was 17 in phase 1, 13 in phase 2, and seven in phase 3 (Table 2). All of these patients had undergone a medicines reconciliation process which had been recorded on EPMA and hence patients were known to pharmacy staff. Four of the 13 patients from phase 2 had also been admitted during phase 1 though none had attracted a note in that first phase. Five of the seven patients in phase 3 had also previously been admitted (two during phase 1 and three in phase 2).

In Phase 1, only two (12%) of 17 patients had a note entered on EPMA mentioning VPPP. One was the required DMR note, and the other instance occurred at medicines reconciliation stage and recorded from the summary care record (SCR) that the surgery had contact with the patient.

In Phase 2, there were ten (77%) of 13 patients with a note entered by the pharmacist on EPMA. Of these, five were correctly recorded both as a dispensing note and a DMR note. Of the other five, three were recorded incorrectly as a PCP, and two solely as a DMR note. Hence, in total seven of these ten were entered as a DMR note and would have been

Results obtained at the end of	Intervention in place
Phase 1 January to July 2020	Initial guideline announced, Pharmacist Friend flags inpatients on valproate
Phase 2 August to mid October 2020	Remind staff of guideline and reinforce standardisation of how notes are to be recorded
Phase 3 November 2020 to February 2021	Surveillance report introduced

Table 1. Timeline of different phases and interventions in place

Medicine at admission	Phase 1	Phase 2	Phase 3
Female aged 8-55 years prescribed valproate as inpatient	17	13	7
Mean age (range) years	40 (11-54)	38 (10-54)	44 (10-54)
Evidence that pharmacy team had noted valproate was prescribed	17	13	7
Evidence of PPP mentioned in any note / intervention	2	10	7

Table 2. Results from the different Phases

transmitted to primary care at discharge. One of the PCP notes identified that valproate was about to be stopped and therefore no need to transmit information about VPPP to primary care.

In phase 3, there were seven (100%) of seven patients with a note entered on EPMA. Of these, two were solely as a dispensing note, and five as a PCP note. Not one of these notes was entered as a DMR note. Examples of the notes from the different phases made by the pharmacists are shown in Box 3.

Discussion

Over the time period of our programme we found that there was some improvement in the recording of pharmacist contact with WCBA on valproate during the different phases. In particular, at the end of phase 3 all seven patients had an electronic note about the VPPP on our EPMA system. However, in none of these seven instances had that note been entered in such a way that it would appear in the discharge summary for transmission to the GP or community pharmacist (if appropriate). This requires further feedback and education to the pharmacist team. Although we have not specifically asked pharmacists, we believe the main driver for the improvement in the recording of notes was down to the introduction of the surveillance report rather than the pre-existing prompt on the Pharmacists' Friend as the former acts as more of an active 'nudge' to the pharmacist.

Though there is global and national interest in the use of electronic systems to facilitate prioritisation of clinical pharmacy services for patients on high-risk medications, there remains some uncertainty on how to implement this.[4] Sodium valproate has featured in a systematically designed and internationally agreed pharmaceutical care complexity screening tool, but this appears to be because it is classed as a high risk medication rather than specifically because of the VPPP.[5] There is a growing body of research into the use of clinical decision support systems such as surveillance alerts for improving medication safety, however there appears to be limited evidence for the type of surveillance report we used to prompt pharmacist action. For example, one study found no incremental benefit of pharmacy surveillance of acute kidney injury patients over a previously implemented clinical decision support alert.[6]

It is clear from a benchmarking study of acute trusts that 94% of organisations had an action plan in place to mitigate the risks associated with the use of valproate products; 65% of organisations had a pharmacy system that directed pharmacy teams to check for childbearing potential when dispensing valproate products; and 77% of organisations with electronic prescribing and medicines administration had systems that gave warnings when valproate products were prescribed. Other hospitals have quite a structured detailed checklist to be used.[7]

The increased risks associated with valproate treatment during pregnancy had led to the effectiveness of the regulatory requirements being closely studied in various countries and in different healthcare settings.[8,9,10,11,12] One English study looking at general practice consultation data concluded that despite the MHRA recommendations, valproate prescription in association with a lack of recorded advice as well as continuing prescription outside of MHRA guidance may continue to place women and their children at risk of exposure during pregnancy.[13]

1. Learning Difficulties Pt. Counselled with staff nurse re importance of not getting pregnant whilst on sodium valproate.
2. Pt confirmed that no plans of having children - very clear about this. Reiterated when Pt being discharged.
3. Patient states she is post-menopausal so valproate prevention programme not discussed.
4. Discussed valproate pregnancy prevention with the patient she is on desogestrel daily - patient is fully aware and signs a form annually with the GP for continued pill supply.
5. Offered counselling, Patient aware of Pregnancy prevention. PMH of Hysterectomy.

Box 3. Examples of VPPP notes for five patients

Another English study in a hospital neurology service reported that documented patient education was improved by introducing standardized sex-specific text passages for insertion into clinical correspondence.[14]

Two studies from the UK describe some of the issues that may face pharmacy teams in that parents or carers feel the guidance is not appropriate for women with epilepsy who have learning difficulties.[15,16] A small number of patients in our hospital based project would be expected to be women with learning difficulties (as shown in Box 3). Angus-Leppan and colleagues surveyed clinical specialists throughout the United Kingdom responsible for the prescription of valproate and/or completion of the MHRA risk acknowledgement form.[17] The authors reported that some patients commented to their nurses and doctors that they were grateful to have time dedicated to explaining the risks associated with valproate and that such information should be delivered face to face, allowing patients to ask questions and explore their options. Though we do not know the depth or the detail of the discussion that occurs between our hospital pharmacists and the patients or carers, it is delivered face to face. The Cumberlege report heard from families who did not receive information about the risks of treatment with sodium valproate during pregnancy.[18] This prevented women from making informed choices about their treatment and family planning options and has led to life-long impacts on their families. A survey by epilepsy charities found one in ten (11%) women who are currently taking the epilepsy medicine valproate are unaware of the possible risk of birth defects if taken in pregnancy. Furthermore, one in five (18%) don't know that, when taken in pregnancy, the medicine could also cause learning and developmental delays in children.[19]

As regards the role of the wider pharmacy workforce, an audit from the Company Chemists Association, published in November 2019, found that just 40% of the 6,480 audited pharmacy teams issued warning cards when dispensing sodium valproate.[20] To support community pharmacy involvement in the valproate PPP, an audit looking at adherence to the PPP was included as part of the NHS England community pharmacy contractual framework pharmacy quality scheme in 2019/2020.[21] The General Pharmaceutical Council intends to use inspections to raise awareness of and improve compliance with the PPP in pharmacies.[22]

Limitations of this study include those inherent to the single-centre, retrospective nature of our study conducted at a district general hospital. Hence, applicability to other hospitals may be limited. Our quality improvement interventions were targeted at pharmacists only rather than the wider hospital healthcare workforce. Our project was not blinded, potentially introducing observer bias. However, we would expect any such bias to be relatively limited, since our departmental guidelines provide a rigorous basis for assessing the action undertaken by the pharmacists. We also recognise that WCBA on valproate who were admitted into the emergency department did not have the opportunity to receive a pharmacist-led discussion on the VPPP. We have not been able to formally establish how these discussions were received by patients. Likewise, because so few of the notes flowed through to primary care we do not know how useful they would be to colleagues in that healthcare setting, and currently such notes do not transmit to the patient's specialist. We have also not implemented any similar action for other potentially teratogenic medicines.

Conclusion

Hospital pharmacy services can improve compliance with requirements of the valproate pregnancy prevention programme. These discussions can aid patient choice and increase understanding of the risks to women of childbearing age, although may be more difficult in patients with learning difficulties depending on the availability of carers or other support. Electronic prescribing systems provide a mechanism for real-time alerting of teams to issues such as valproate counselling, although active surveillance by a designated staff member or team may be more effective than passive alerts on a prioritisation tool.

Declaration of interests

The authors have no interests to declare.

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