Volume 16 Issue 2 / Fall-Winter 2013

The Renal Pharmacist

Vol 16

Issue 2

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In this issue ...

A biannual Insight into the Renal Pharmacist Network

View from the Chair

As a renal pharmacist, I have been impressed with the scope and range of renal pharmacy practice across Canada. Renal pharmacists work as a part of a interdisciplinary team that includes nephrologists, nurses, community pharmacists and dietitians to care for patients living with kidney disease, mentor and teach students, residents and team members, and perform research and quality improvement projects. As the network chair, I met many of you at the Canadian Society of Nephrology (CSN)/ Société québécoise de néphrologie (SQN) Annual General Meeting and Renal Pharmacists Network (RPN) Nephrology Educational Day in Montreal, PQ in April and know that you have attended RPN Education Evenings in Vancouver, Winnipeg and Toronto this Fall. The RPN website (www.renalpharmacists.net) has speaker's slides and other documents from these events. These events not only provide formal education and but allow us to network and learn from one another. How many of you can say that you came away from an RPN educational event with new insights, ideas, or a fresh perspective to better care for patients in your renal pharmacy practice?!

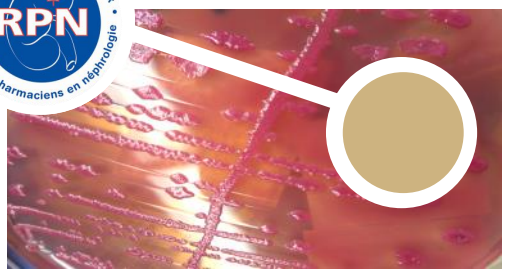
"learn from one another"

The RPN executive is now planning the educational events for 2014. In April 2014, the RPN will be holding our Nephrology Educational Day in partnership with the CSN Annual General Meeting in Vancouver, BC. I want to thank the RPN executive, Robert, Derek, Marisa, Judith, Jenny, Grace, Amy, and Elaine, for their brilliant ideas and contributions this year. Beginning in 2014, we will be expanding the RPN executive committee to include three members at large so that we can better represent renal pharmacists from all parts of Canada on the executive. Robert Bell, outgoing Past-Chair from Quebec, will be our first member at large. We are thrilled that Robert has agreed to continue representing Quebec on the RPN executive! Also, Derek will now be taking on the position of RPN Chair in 2014. Expect great things…

Seasons Greetings,

Piera T. Calissi

RPN Chair



BIOGRAPHY: Carlee Balint

Carlee Balint is a Nephrology and Solid Organ Transplant Pharmacist at the Foothills Medical Center in Calgary, Alberta. She is responsible for acute care inpatients with chronic kidney disease, including those receiving peritoneal dialysis or hemodialysis, as well as kidney, pancreas or liver transplant recipients.

Carlee obtained a Bachelor of Science degree in Pharmacy at the University of Saskatchewan in 2002. After graduating she then completed a Hospital Pharmacy Residency in Saskatoon. She then moved on to Calgary, where she began working with hemodialysis patients as an anemia management pharmacist, and then moved on to inpatient nephrology where she developed the Inpatient Nephrology Pharmacy Service.

Carlee has worked in Nephrology for over 10 years and has more recently expanded her practice to include care of solid organ transplant recipients. Over the past year Carlee has also been actively involved with the RxEACH study. This primary objective of this study is to assess the community pharmacist management of patients with chronic kidney disease patients and high risk for cardiovascular events.

Carlee enjoys teaching and regularly works with University of Alberta pharmacy students and pharmacy residents during their rotations in nephrology and transplant. In addition she has been involved in pharmacy, nursing, and medical resident orientation, and development and maintenance of policies and procedures in all areas of chronic kidney and end stage renal disease.

Carlee is looking forward to the positive impact she can make as the chair-elect of the Renal Pharmacists Network.

Carlee Balint, BSP, ACPR

Highlights: RPN Evening CE 2013, Toronto, ON

Submitted by Jenny Ng, BScPhm, Sunnybrook Health Sciences Centre, Toronto, ON

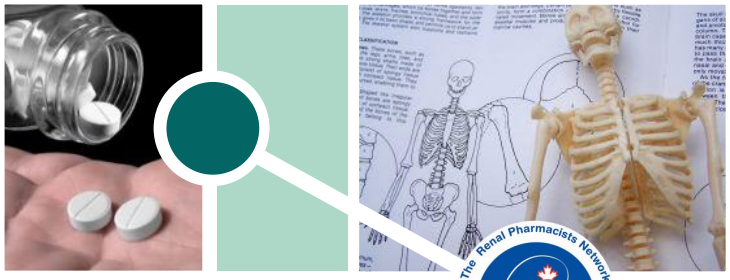
Phosphate Management in CKD

In November a continuing education event was held for renal pharmacists in Toronto. We were fortunate to have Dr. Robert Richardson from University Health Network present to the group an update on phosphate management.

As renal pharmacists we are aware of the association of higher serum phosphate levels with mortality in the CKD population. Despite various guidelines providing variable target levels for bone parameters such as calcium, phosphate and parathyroid hormone (PTH), we recognize in clinical practice how difficult it is to achieve all these targets and the scarcity of evidence to support specific targets in the CKD population.

Dr. Richardson highlighted some recent publications that add to the literature on this topic of discussion and illustrate why there is controversy in this area of practice. In one paper from Block et al. from 2012, it was interesting that when looking at effects of phosphate binders in moderate CKD that those randomized to binders (calcium, lanthanum or sevelamer) had more calcification progression than those on placebo (please see slides posted on RPN website for full details).

Overall for those in attendance, it was a great opportunity for discussion with peers over a thought provoking presentation.



Highlights: RPN Evening CE 2013, Vancouver BC

In November, the RPN hosted an evening continuing education event in Vancouver, BC for renal pharmacists. It was very well attended by hospital and community pharmacists. Dan Martinusen presented on subsequent entry biologics and Clifford Lo presented on glomerulonephritis. Below are brief summaries on their presentations. Please also refer to their presentation slides that are posted on the www.renalpharmacists.net.

The Dilemma of Biosimilars

Submitted by Dan Martinusen, BSc(Pharm), PharmD, Vancouver Island Health Authority, Victoria, BC.

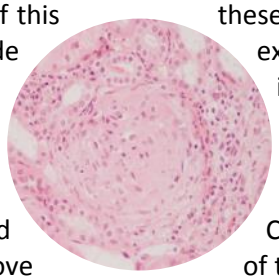
Subsequent Entry Biologics (SEB's) may soon be coming to the Canadian marketplace. Unfortunately, many physicians and pharmacists report no or little knowledge on this topic. Dan Martinusen introduced the topic of biosimilars by providing definitions, molecules likely affected and the potential impact on practice. He further outlined the various layers of complex issues that will need to be addressed by practitioners and funding agencies as these are introduced. SEB's by definition are not generic equivalents but must be similar (not significantly better or worse) to the innovator's molecule. The only advantage, then, would be an expected cost savings of 20-30% off the list price of the innovator molecule. This cost difference may be minimized by value adds currently in existence by the innovator company or those proposed in the future. Further, practicalities of inventory costs, patient safety issues and the infrastructure to differentiate these products at the patient level all will be associated with a system cost. Dan also provided an overview of the various manufacturing steps to produce a biologic drug and noted which steps were proprietary to each manufacturer and how the regulatory body (Health Canada) proposes to evaluate the SEB against the innovator. To date, Europe has seven years of experience with SEBs (or "Biosimilars " in Europe) while the United States and Canada are just venturing into this realm. He explored the market penetration of various SEB classes into Europe with explanations for the variations seen. Health Canada has stated that SEBs are not bioequivalent and does not support interchangeability nor

substitution. Interchangeability and substitutability are in jurisdiction of the provinces and perhaps with hospital P&T committees. Hence, nephrology pharmacists will play a role in guiding / advising on those SEBs relating to nephrology with respect to how, when or perhaps if they should be introduced into practice. To this end, Dan Martinusen, along with Nicole Tsao (pharmacoeconomist) and BC RPN members Judith Marin, Clifford Lo and Marianna Leung have been awarded a research grant from the CSN to provide a Canadian nephrology perspective to this issue that will be presented at CSN in Vancouver in April".

GN and Tonic: Glomerulonephritis Treatment Guidelines

Submitted by Clifford Lo, PharmD, MHA, BCPS, Fraser Health Authority, Surrey, BC.

Glomerulonephritis is a group of rare kidney diseases with only 267 new cases diagnosed per year in British Columbia. If left untreated, it can lead to kidney failure and the requirement for transplantation or dialysis. In a 2013 survey of all adult nephrologists in British Columbia, it was found that there was considerable variation in prescribing patterns between practitioners. For example, 19% of surveyed nephrologists would prescribe prednisone or a calcineurin inhibitor to a patient with focal segmental glomerulosclerosis with proteinuria of 2 g/day despite the 2012 KDIGO guidelines recommending no immune therapy. The goal of this talk was to provide nephrology pharmacists with an overview of glomerulonephritis and its treatment, including its expected efficacy and toxicities in order to improve outcomes for patients with glomerulonephritis. Specifically, membranous nephropathy was discussed since it is the most common cause of nephrotic syndrome in Caucasians, IgA nephropathy was discussed since it is the most common cause of glomerulonephritis in the world, and lastly ANCA associated vasculitis and lupus nephritis were discussed since nephrology pharmacists often become involved in these cases due to the need for expensive immunosuppressant medications. The treatment of glomerulonephritis is evolving quickly in British Columbia with development of the first of its kind in Canada, the glomerulonephritis network and registry under the Provincial Renal Agency. Look forward to new and innovative strategies that the British Columbia Provincial Renal Agency undertakes as our understanding and treatment improves for this subset of kidney patients.



Highlights: RPN Evening CE 2013, Winnipeg, MB

In September, the RPN hosted an education evening in Winnipeg. Hospital pharmacists across Manitoba, specializing in renal disease attended the event. Peter Thomson presented on the topic of anticoagulation in chronic kidney disease. He described the thrombosis risk in CKD, the risk and benefit with warfarin use specifically in the CKD population as well as the evidence available with the new oral anticoagulants in renal impairment. A brief summary follows below.

Anticoagulation in Chronic Kidney Disease – Are the New Oral Agents OK?

Submitted by Peter Thomson B.Sc.(Pharm), Pharm.D., Clinical Resource Pharmacist, Winnipeg Regional Health Authority Medicine Program, Clinical Associate Professor, Faculty of Pharmacy, University of Manitoba

The landscape of oral anticoagulation has changed with the arrival of three new oral anticoagulants. Since their arrival, thousands of Canadians have received these agents for either treatment of VTE or prevention of VTE following orthopedic joint replacement or prevention of stroke or systemic embolization (SE) from atrial fibrillation (AF). Unlike warfarin, all three newer oral agents are given in fixed doses with no anticoagulation monitoring in most clinical situations. Product monographs do provide advice on dose adjustment for renal insufficiency.

Although severe renal dysfunction is an exclusion criteria in clinical trials, many patients have received these agents in varying degrees of renal insufficiency. This discussion focuses on the evidence in the public domain for outcomes

of patients with CKD who have received these anticoagulants prevention in atrial fibrillation. Atrial fibrillation is commonly thought as a disease of the old. Its prevalence increases with age. There is evidence that the prevalence of atrial fibrillation also increases in CKD with rates of 13 – 27 % reported in CKD stage 5 patients. In addition to a higher prevalence, CKD is associated with a higher rate of both stroke and major bleeding (Reincke et al 2009). Hence, anticoagulation in CKD is a higher risk, higher reward scenario.

In non-valvular atrial fibrillation, there is one large phase III trial with each of the newer agents compared with warfarin. There is also one which compares apixaban with ASA in those unsuitable for warfarin. Each of these trials are different and comparing each of the new agents to each other based on these trials is fraught with assumptions which are likely to be inaccurate. In the case of renal insufficiency, there are important distinctions, particularly when comparing dabigatran to the two anti Xa inhibitors. In the dabigatran trial (RE-LY), subject were randomized to one of three groups; one of two doses of dabigatran (110 mg and 150 mg bid) and warfarin. The dose of dabigatran was not adjusted based on increased risk for bleeding or drug accumulation (renal function, older age, low body weight). In both the rivaroxaban and apixaban trials each agent were compared to warfarin and the dose of the newer agents were adjusted for risk factors. There is much debate on the statistical versus clinical benefit between the new agents versus warfarin in non-valvular AF. In the overall patient population, a consistent signal from all three the phase III trials is an approximate 10% reduction in overall mortality and at least 50% reduction in intracranial bleeds with any of the three new agents over warfarin. A clinical question is if these signals are also seen in the subset of patients with CKD.

As with any of the subgroup analysis these trials have undergone, results need to be interpreted with caution. Any suggestions of trends should be thought of hypothesis generating and may be underpowered for the clinical endpoint in question. In total, just over 50,000 patients participated in the three large AF trials comparing a newer oral anticoagulant to warfarin. Table 1 provides a summary of the major efficacy and safety outcomes in the CKD population studied from the large clinical trials. Approximately 18 % of patients had advanced CKD (based on the Clcr in Table 1). A baseline Clcr of $\leq$ 25 – 30 mL/min was an trial exclusion criteria (varies between trials). There is very little data in that subset of patients at this time.

From Table 1, compared to the overall study populations (data not presented here), the there is no evidence to suggest that the overall advantages in efficacy or safety of the newer agents over warfarin is not maintained in the CKD population. This is not due to the new oral agents not causing more major bleeding in CKD – in fact they do. In all four trials, with either warfarin or a newer anticoagulant, higher rates of both stroke and major bleeding were seen in those with CKD.

Inherently, one would think that a drug that is not renally

Table1. Newer Oral Anticoagulants vs. Warfarin in Non-Valvular Atrial Fibrillation

Trial	Total Pts	CKD pts (Clcr cut off)	Outcome CKD Subgroup Only	
			Stroke/ SE	Major Bleed
Dabigatran (RE-LY)	18,133	Clcr < 50 (n = 3554)	2.70%/yr Warf 2.32 %/yr Dabi 110 mg 1.53 %/yr Dabi 150 mg	5.49 %/yr Warf 5.45 %/yr Dabi 110 mg 5.50 %/yr Dabi 150 mg
Rivaroxaban (ROCKET-AF)	14,264	Clcr 30–49 (n = 2950)	3.44/100 pt yrs Warf 2.95/100 pt yrs Riva	4.70/100 pt yrs Warf 4.49/100 pt yrs Riva
Apixaban (ARISTOTLE)	18,201	Clcr < 50 (n = 3017)	2.67 %/yr Warf 2.11 %/yr Apix	6.44 %/yr Warf 3.21 %/yr Apix
vs. ASA				
Apixaban (AVERROES)	5599	Clcr < 25–49 (n = 1198)	5.8 %/yr ASA 2.5 %/yr Apix	2.5 %/yr ASA 3.2 %/yr Apix

(Hijazi Z 2013; Fox KAA 2011; Hohnloser SH 2012; Connolly SJ 2011)

cleared and is monitored would provide important efficacy and safety advantages in CKD over drugs which are (at least partially) renally eliminated and given in a fixed dose. To date, the evidence we have from the AF trials with dabigatran, rivaroxaban and apixaban suggests this assumption may not necessarily be true. What is clear is that anticoagulation in CKD is associated with a higher risk of stroke and bleeding – with any anticoagulant. All three of the newer anticoagulants appear to be at least as safe and effective as warfarin. They should be considered therapeutic options when anticoagulation is considered in stage 1-3 CKD. Until more data is available, they should not be used in severe CKD.

A recommended checklist for each of the newer oral anticoagulants is available through the Rx Files website at:

Apixaban-CLOT-Checklist - Link:
http://www.rxfiles.ca/rxfiles/uploads/documents/CLOT-Apixiban-Checklist-Final-CPP.pdf

Dabigatran-CLOT-Checklist - Link:
http://www.rxfiles.ca/rxfiles/uploads/documents/CLOT-Dabigatran-Checklist-Final-CPP.pdf

Rivaroxaban-CLOT-Checklist - Link:
http://www.rxfiles.ca/rxfiles/uploads/documents/CLOT-Rivaroxaban-Checklist-Final-CPP.pdf

References:

- Connelly SJ, Ezekowitz MD, Yusuf S et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation (RE-LY) N Engl J Med 2009
- Connelly SJ, Eikelboom J, Joyner C et al. Apixban in Patients with Atrial Fibrillation (AVERROES). N Engl J Med 2011
- Fox KAA, Piccini JP, Wojdyla D et al Prevention of stroke and systemic embolism with rivaroxaban compared with warfarin in patients with non-valvular atrial fibrillation and moderate renal impairment. Eur Heart J 2011
- Granger CB, Alexander JH, McMurray JJV et al. Apixaban versus Warfarin in Patients with Atrial Fibrillation (ARISTOTLE) N Engl J Med 2011
- Hart RG, Diener HC, Yang S et al. Intracranial Hemorrhage in Atrial Fibrillation Patients During Anticoagulation With Warfarin or Dabigatran: The RE-LY Trial. Stroke 2012
- Hijazi Z, Hohnloser SH, Oldgren J et al. Efficacy and Safety of Dabigatran Compared with Warfarin in Relation to Baseline Renal Function in Patients with Atrial Fibrillation: A RE-LY Trial Analysis. Circulation 2013
- Hohnloser SH, Hijazi Z, Thomas L et al. Efficacy of apixaban when compared with warfarin in relation to renal function in patients with atrial fibrillation: insights from the ARISTOTLE trial. Eur Heart J 2012; 33: 2821-30
- Patel MR, Mahaffey KW, Garg J et al. Riveroxaban versus Warfarin in Nonvalvular Atrial Fibrillation (ROCKET-AF). N Engl J Med 2011
- Reinecke H, Brand E, Mesters R et al. Dilemmas in the Management of Atrial Fibrillation in Chronic Kidney Disease. J Am Soc Nephrol 2009

Conflict of Interest: In the past 2 yrs the author has either been sponsored to speak at education event, introduced speakers or attended advisory meeting or provided advice to: AstraZeneca Canada, Bayer Canada, Boehringer Ingelheim Canada, Bristol Myers Squibb Canada, Paladin Labs Inc., Pfizer Canada, Sanofi Aventis Canada, Takeda Canada

Upcoming Conferences:

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National Kidney Foundation:
2014 Spring Clinical Meeting
April 22-26, 2014,
MGM Grand, Las Vegas, USA
For further information:
www.kidney.org

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Canadian Society of Nephrology
Annual General Meeting,
April 24-26, 2014.
Vancouver, BC, Canada.
For further information:
www.csnscn.ca

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American Society of Nephrology:
Kidney Week,
November 11-16, 2014,
Philadelphia, PA, Canada.
For further information:
www.asn-online.org




Save the Date!
Renal Pharmacist Network
Annual Nephrology Education Day 2014

in Vancouver, BC., April 24, 2014 in conjunction with the
Canadian Society of Nephrology Annual General Meeting 2014
In Vancouver, BC. April 24 - 26, 2014.

The RPN will be holding their
Annual Nephrology Education Day on April 24, 2014
prior to the CSN meeting and will be partnering again with CSN to
offer educational sessions during the CSN conference.

Please stay tuned for more details about the RPN Nephrology Education Day
including agenda and registration deadlines, www.renalpharmacists.net.
More information on the CSN conference agenda
will be available at www.csnscn.ca.

Canadian Society of Nephrology has launched its official journal!

CANADIAN JOURNAL OF KIDNEY HEALTH AND DISEASE
Journal Canadien de la Santé et de la Maladie Rénale

Now accepting submissions! Please check out the website www.cjkhd.org
Congratulations to our Renal Pharmacists,
Lori Wazny (University of Manitoba) and Marisa Battistella (University of Toronto)
who are on the prestigious Editorial Board!

Apply for
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Pharmacist annual memberships are only $100.00! CSN Member Pharmacists
also get a discounted rate for registration at the CSN conference!
www.csnscn.ca.




What's New in the Nephrology Literature? A Focus on Renal Pharmacotherapeutics...

Click on the title to go to the PubMed link

Congratulations to all the Canadian Renal Pharmacists with recent publications highlighted below!

Please send any articles of interest to
renalpharmacistsnetwork@gmail.com

KDIGO: Lipid Management in Chronic Kidney Disease: Synopsis of the Kidney Disease: Improving Global Outcomes 2013 Clinical Practice Guideline.
Tonelli M, Wanner C; for the Kidney Disease: Improving Global Outcomes Lipid Guideline Development Work Group Members.
Ann Intern Med. 2013 Dec 10. doi: 10.7326/M13-2453.

The new Lipid guidelines have been published by KDIGO! These evidence-based guidelines will be sure to change your practice.

Standards of clinical practice for renal pharmacists.
Raymond CB, Wazny LD, Sood AR.
Can J Hosp Pharm. 2013 Nov;66(6):369-74.

This article describes the unique pharmacy practice model in the Manitoba Renal Program and outlines a detailed set of Standards of Clinical Practice, including steps involved in the review of patients with CKD for drug therapy problems. These standards are an invaluable tool to standardize patient care, set priorities, develop competency assessment criteria, inform performance appraisals for renal pharmacists and educate new staff and students.

New models of chronic kidney disease care including pharmacists: improving medication reconciliation and medication management.
*St Peter WL, **Wazny LD**, Patel UD.*
Curr Opin Nephrol Hypertens. 2013 Nov;22(6):656-62. doi: 10.1097/MNH.0b013e328365b364.

This review discusses successful models of care for CKD patients that incorporate pharmacist care in team-based models. Growing evidence indicates that pharmacists reduce medication-related problems, increase medication adherence and improve patient outcomes in CKD patients.

Pain assessment and management in hemodialysis patients.
*De Castro C, Murphy L, **Battistella M.***
CANNT J. 2013 Jul-Sep;23(3):29-32; quiz 33-4.

This review paper describes the barriers to adequate pain management specifically in the hemodialysis population, discusses pain assessment tools and outlines the strengths and limitations of the renal adaptation of the World Health Organization (WHO) analgesic ladder.

Review of available intravenous iron preparations in hemodialysis.
*Palmer K, Cameron K, **Battistella M.***
CANNT J. 2013 Apr-Jun;23(2):51-4; quiz 55-6.

This review paper compares and contrasts the different intravenous iron preparations available in Canada (iron dextran, iron sucrose, iron gluconate, ferumoxytol).

Cost Analysis of an Intravenous to Subcutaneous Epoetin α Conversion.
***Wazny LD, Raymond CB, Sood AR**, Eng A, Verrelli M.*
Am J Nephrol. 2013 Dec 11;38(6):496-500.

This original study describes the significant cost reduction of converting from intravenous to subcutaneous epoetin alpha in 4 large in-center hemodiaysis units. Doses of epoetin alpha decreased by 12.6% with a yearly cost savings of $1,135 USD per patient.

The Renal Pharmacists Network would like to thank the following sponsors for their continued support and generous contributions.

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