

Case story of elderly patient with renal impairment and dose adjustment of analgesics

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INTRODUCTION

Many analgesics or their metabolites are renally excreted. Tailored and safe prescribing of those analgetics require accurate estimates of the renal function.

Creatinine and cystatin C are well-known endogenous biomarkers for GFR estimation.

Creatinine highly dependent on muscle mass, while cystatin C is affected by e.g. inflammation and smoking.

The choice of biomarker, eGFR equation as well as literature source for dosage recommendations can influence the dosing recommendation.

OBJECTIVE

The aim of the present study is to simulate differences in dosing of five different analgesics depending on eGFR biomarker and literature source used for dosages recommendations.

CASE

The case is exemplified with an elderly woman with renal impairment:

- Patient: woman, 81 years, weight 58,2 kg, height 172 cm, BMI 19,7
- Analgesics: Paracetamol, Ibuprofen, Morphine, Oxycodone and Tramadol.
- Biomarkers used for eGFR calculation : creatinine, cystatin C and a combination of the two Crea-Cys C.
- Literature consulted: Pro.Medicin, UpToDate and The Renal Drug Handbook

RESULTS:

eGFR calculated by respectively P-creatinine or P-cystatine or a combination of the two markers:

- eGFR/1,73 m² (CKD-EPI) crea: **70**
- eGFR/1,73 m² (CKD-EPI) comb: **44**
- eGFR/1,73 m² (CKD-EPI) cys C: **29**

eGFR values varies significantly depending on the equation used. Choice of equation was shown to have impact on recommended dose of analgetics. This may have considerable clinical impact in the treatment of the renal impaired patient.

Tabel 1 shows:

Some variation in dose adjustments on Ibuprofen and Oxycodone when using **CKD-EPI creatinine** (eGFR=70).

Variation in dose adjustments on Paracetamol, Ibuprofen, Oxycodone and Tramadol when using **CKD-EPI crea-cys C** (eGFR=44).

Variation in dose recommendations on Paracetamol, Ibuprofen, Oxycodone and Tramadol between information sources using **CKD-EPI cystatin C** (eGFR=29).

The following equations for calculation of eGFR was used (women):

(CKD-EPI) crea > 62 mikromol/l: $144 \times (P\text{-crea}/(0,7 \times 88,4))^{-1,209} \times 0,993^{\text{age}}$

(CKD-EPI) crea-cys C > 62 mikromol/l og > 0,8 mg/l: $130 \times (P\text{-Cr}/52)^{-0,601} \times (P\text{-Cys}/0,8)^{-0,711} \times 0,995^{\text{age}}$

(CKD-EPI) cys C > 0,8 mg/l: $133 \times (P\text{-Cys}/0,8)^{-1,328} \times 0,996^{\text{age}}$

TABEL 1	Pro.medicin	UpToDate	The Renal Drug Handbook
eGFR (ml/min/1,73m²)			
Paracetamol			
70	Dose as in normal renal function	Dose as in normal renal function	Dose as in normal renal function
44	Dose as in normal renal function	Administer every 6 hours	Dose as in normal renal function
29	Injection: adjust doseinterval to minimum 6 hours Tablet: Dose as in normal renal function	Administer every 6 hours	Dose as in normal renal function
Ibuprofen			
70	Use with caution and monitoring of kidney function	Dose as in normal renal function	Dose as in normal renal function
44	Use with caution and monitoring of kidney function	Avoid use in patients with intercurrent disease that increase risk of acute kidney injury	Dose as normal, but avoid if possible
29	Avoid use	Avoid use	Dose as normal, but avoid if possible
Morphine			
70	Dose as in normal renal function	Caution, start with low dose, titrating slowly	Dose as in normal renal function
44	75 % of normal dose, same doseinterval	Caution, start with low dose, titrating slowly	75 % of normal dose "extreme caution with all opiates in patients with impaired renal function"
29	75 % of normal dose, same doseinterval	Caution, start with lower dose, titrating slowly	75 % of normal dose "extreme caution with all opiates in patients with impaired renal function"
Oxycodone			
70	Reduce dose	Initiate at low end of dosage range	Dose as in normal renal function
44	Reduce dose	33-50 % of usual initial dose	Start with 75% of normal dose
29	Reduce dose	33-50 % of usual initial dose	Start with 75% of normal dose
Tramadol			
70	Dose as in normal renal function	Use with caution	Dose as in normal renal function
44	Dose as in normal renal function	Use with caution	Dose as in normal renal function
29	Doseinterval should be increased. Avoid extended release formulations.	Increase doseinterval to every 12 hours. Max. 200 mg/day.	Dose as in normal renal function.

CONCLUSION

In clinical practice renal function estimates is normally based on creatinine. This method has drawbacks especially in elderly frail patients with low muscle mass.

This case shows significant differences in renal function estimation depending on the biomarker. The case emphasizes that, choice of biomarker as well as choice of as literature sourced for dosages recommendations can have significant impact on prescribing of analgesics.