

METHADONE AND LEVOMETHADONE: RISKS AND COSTS ANALYSES



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Background

- Racemic methadone oral solution 10mg/mL is the gold standard in the Opioid Agonist Treatment (OAT).
- Since recently, a levomethadone solution 5mg/mL is available in Switzerland and will decrease the cardiac toxicity.
- However, the risk of errors and confusion in prescriptions, preparation and administration seems to be significant and the costs would be probably higher than the racemic solution.

Objectives

- To analyse the risks of different dosage forms and products formulation from the prescription to the administration of methadone and levomethadone in the Ambulatory Addiction Treatment Centre (AATC) and the General Psychiatry.
- To assess the associated costs for the entire hospital.

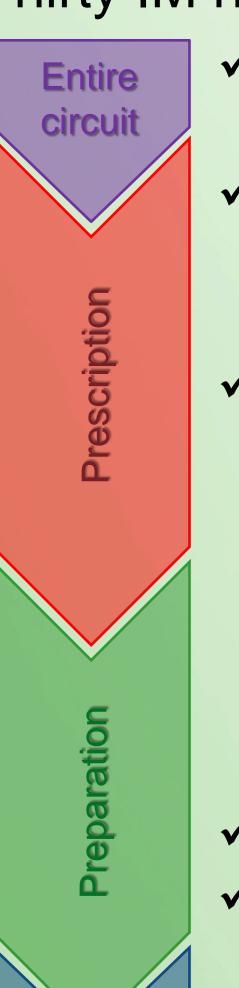
Study Design

- A multidisciplinary team identified and listed the failure modes (FM) and prioritized them based on their criticality indices using the Failure Modes, Effects and Criticality Analysis (FMECA).
- Improvement measures (IM) have been proposed.
- An economic evaluation compared the annual costs between racemic methadone and levomethadone.

Results

Sixty-one FM have been identified. Among the 25 most critical FM (**Table 1**), ten concerned the preparation step, seven the prescription. Three of them involved confusions or errors between methadone and levomethadone.

Thirty IM have been proposed including:



- ✓ An information letter about changes in treatments with OAT;
- ✓ A clinical algorithm defining the use of levomethadone
 in the hospital choosing between methadone and
 SROM, balancing costs and clinical risks (Fig 1 & 2);
- ✓ A basic "bed-scanning" based on coloured stickers
 -prescription sheet and levomethadone bottle in
 orange; slow release oral morphine (SROM) in yellowonce the prescriber wants to change from methadone
 to levomethadone and/or SROM, depending on clinical
 risks of heart rhythm disorders induced by
 prolongation of the QTc interval (see algorithm);
- ✓ A conversion table [mg/volume];
- ✓ The purchase of a balance allowing the doublechecking of prepared doses at the AATC;
- ✓ Five monodoses of methadone for general psychiatry;
- ✓ A checklist of preparation and administration steps.

A systematic switch from methadone to levomethadone will generate an additional annual cost of 60'000 Euros for the hospital.

Conclusions

- This study allows the identification and quantification of the main risks related to methadone and levomethadone in our hospital.
- IM have been proposed taking into account the clinical and pharmacoeconomic aspects.
- A cost-benefit analysis would be a perspective for a better assessment of the impact of levomethadone on morbidity/ mortality and the costs involved.

Table 1: The 25 most critical FM

N°	FM	Who?	CI
1	Error during hospital-outpatient transfer	CHUV	343
2	Error of unit conversion	AATC	336
3	No double-check (or done by the patient only)	CHUV	336
4	Ambulatory-Hospital transmission by oral	CHUV	294
5	Confusion between methadone and levomethadone bottles	CHUV	294
6	Confusion between methadone and morphine bottles	CHUV	294
7	No double-check	AATC	288
8	Modification of the dose by a non-physician	AATC	280
9	Patient doing the labelling (dose; date)	AATC	280
10	Confusion mg-mL	AATC	280
11	Multitude of dosages to prepare	CHUV	252
12	Inadequate environment (distraction by patient, stress, noise)	AATC	252
13	Oral prescription	AATC-PGE	245
14	Selection of an another patient's vial	PGE	245
15	Confusion mg-mL	CHUV	240
16	Wrong understanding of oral prescription	AATC	240
17	No double-check	AATC	240
18	No formal identification of patients	AATC	240
19	Non up-to-date prescription	AATC	216
20	Omission to write dosage changes	AATC	216
21	Confusion between methadone-levomethadone	CHUV	210
22	Transcription by a non-medical staff	AATC	210
23	Preparation by a non-medical staff (risks, legality, etc.)	AATC	210
24	Pump adjusmtent error	AATC	210
25	Selection of the wrong dosage of capsules (13 dosages in stock, look-alike)	AATC	200

Caption: AATC = ambulatory addiction treatment centre, PGE = general psychiatry, CHUV = entire hospital CI = criticality index (occurrence x severity x detectability)

Color code: red = prescription, yellow = transcription, green = preparation, blue = administration

QTc ≥ 500ms **SROM** or positive cardiac history ! renal failure Buprenorphine ! IA CYP3A QTc 450-500ms Urine **SROM**! renal failure or positive cardiac positive for history **Levomethadone*** ! IA CYP3A/2B6/QTc opiates Racemic methadone* QTc < 450ms ! IA CYP3A/2B6/QTc or negative cardiac history depending on the case: without IA CYP3A/2B6/QTc buprenorphine or SROM *Under reserve of medical evaluation of concomitant factors prolonging the QTc;; IA: interaction; ! : caution Fig 1: Algorithm for naive patients with OAT **QTc** ≥ **500ms*** switch to: If QTc always > 500 ms: **SROM** or positive cardiac reassess other risk factors ! Renal failure history QTc = 450-500msIf QTc 450-500 ms switch to: or positive cardiac history **Annual** after change: reassess control: or methadone dose > levomethadone levomethadone QTc, clinic & 100 mg/j versus switch to SROM ! IA CYP3A/2B6/QTc anamnesis or IA CYP3A/2B6/QTc

References

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- 3. OFSP, limitations LS, 2015
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Aknowledgments

*Increased risk of torsades de pointes ; IA: interaction; ! : caution

Fig 2: Algorithm for patients in maintenance therapy

with racemic methadone

QTc < 450ms

or negative cardiac history

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Do not change the treatment

or levomethadone if severe side

effects