Retrospective Review of Emerging Drug Use in a Mother-Child Center in Quebec

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INTRODUCTION

- Unapproved and off-label drug use in children is an important issue, with reported prevalences of 1-33% and 9-34% respectively.
- In a teaching hospital, clinicians are frequently confronted with conditions requiring unlicensed drugs or licensed drugs used off-label
- To overcome the lack of approved drugs, Health Canada created the Special Access Program (SAP)
- Newly approved drugs are often costly and represent a growing part of a teaching hospital budget

Emerging drugs were defined as:

- Drugs unapproved in Canada (without a notice of compliance from Health-Canada)
- Drugs used off-label with limited scientific literature
- Costly drugs (> 300 $CAD / dose)

OBJECTIVE

- **To evaluate the use of emerging drugs within our hospital during a 14-months period**

METHODS

- **Design -** Retrospective study with the identification of emerging drugs used between 2013-01-01 and 2014-02-28 in a tertiary care mother-child teaching hospital with a 500-bed capacity
- **Exclusion -** Conventional oncologic drugs were excluded (the oncology ward already had a decision-making process mainly based on research protocols)
- **Data collection -** Every medical chart was reviewed by a research assistant
- **Variables -** The following variables were collected in patient file (initial prescription): age, dates/hours of written intention to use the drug, prescription and first dose administered, written justification of the treatment
- **Justifications -** Presence/absence of written justification including alternatives used and considered/not used; efficacy and safety endpoints, delays between intention to treat and prescription, and between prescription and first dose administered; a literature review was performed for every emerging drug used for every specific indication of use to determine safety and efficacy endpoints that should be monitored
- **Consent -** Presence/absence of the documentation of consent from parents/patients were collected
- **Statistics -** Descriptive statistics were performed.

RESULTS

- A total of 26 emerging drugs corresponding to 99 prescriptions for 89 patients were identified during this 14-months period
- Top-10 of emerging drug used are summarized in Table I with their indications, Canadian status, local emerging status and number of patients concerned
- Top-10 emerging drugs represents 78.5% of all patients who received emerging drugs during this period
- 42% of drugs were unapproved in Canada
- 27% of drugs were licensed drugs in Canada used off-label with poor scientific literature
- 31% of drugs were costly drugs

Table I. Top-10 emerging drugs used

Substance names	Indications	Canadian status	Local emerging status	Patients concerned n (%)
Aldesleukine (interleukine-2)	. Lymphoblastic leukemia . Myeloblastic leukemia . Neuroblastoma . Atypical myelodysplesia	DIN	OLPD	10 (11.2%)
Stiripentol	. Dravet syndrome . Refractory epilepsy (tonic clonic or myoclonic seizures)	SAP	SAP	10 (11.2%)
Eculizumab	. Atypical hemolytic-uremic syndrome . Chronic glomerulonephritis . Thromboembolic disease (including thrombotic thrombocytopenic purpura)	DIN	$$$ (aHUS) OLPD	8 (9.0%)
Liothyronine (triiodothyronine, injection)	. Neonatal cardiac surgery . Euthyroid-sick syndrome	SAP	SAP	8 (9.0%)
Sargramostim (GM-csf)	. Neuroblastoma	SAP	SAP	8 (9.0%)
Pyridoxal 5-Phosphate	. West syndrome . Refractory epilepsy (focal seizures)	WCS (compounding)	SAP	6 (6.7%)
Rufinamide	. West syndrome . Refractory epilepsy (tonic-clonic seizures)	DIN	OLPD	6 (6.7%)
Cidofovir	. Adenovirus systemic infection after bone-marrow transplant	SAP	SAP	5 (5.6%)
Omalizumab	. Severe allergic asthma . Allergic bronchopulmonary aspergillosis	DIN	$$$ (SAA) OLPD	5 (5.6%)
Canakinumab	. Juvenile idiopathic arthritis	DIN	$$$	4 (4.5%)

Legend: DIN : marketed in Canada, SAP : Special Access Program / not-marketed in Canada, WCS : without Canadian status;

OLPD : off-label drug use with poor scientific literature; aHUS : atypical hemolytic-uremic syndrome; SAA : severe allergic asthma

Table II. Emerging drug prescriptions characteristics

Emerging drugs and criteria of emergence n (%)	26 emerging drugs used . 11 (42%) unapproved in Canada . 7 (27%) licensed drugs used off-label with poor scientific literature . 8 (31%) costly
Different prescriptions n	99
Patients n	89
Median age at the treatment initiation	4 years-old [0-18]
Median treatment duration (if discontinuation by the end of the study)	66 days [1-1435]
Median delay between intention to treat and prescription	2 days [0-333]
Median delay between prescription and first dose administered	0 day [0-404]
Mean number of used/available alternatives n (%)	2.2/3.6 (61%)
Documented consent from parents/patientsn n (%)	19 (19%)
Prescriptions with efficacy parameters identified n (%)	33/99 (33%)
Patients who experienced a positive evolution under treatment n (%)	52/99 (53%)
Prescriptions with safety parameters identified n (%)	10/99 (10%)
Patients who experienced a side effect possibly related to the emerging drug use n (%)	26/99 (26%)

Longer delays were associated with outpatient reimbursement authorization processes

CONCLUSION

- This study describes 26 emerging drugs involving 99 prescriptions (89 patients) and their current challenges, such as the lack of efficacy and safety endpoints defined to ensure the treatment is effective and safe.
- In response to these results, we adopted a new policy concerning emerging drugs prescription and follow-up, including an emerging drug use form to be completed by prescribers and pharmacists when an emerging drug is needed
- This form contains information about the drug, the indication, previous treatments received, literature associated with the requested use, efficacy endpoints (parameters, targets and delays), safety endpoints and confirmation of the consent obtained from parents/patients.

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