

Use of unlicensed drugs in a Swiss Pediatric University Hospital and associated prescribing error rates

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Introduction

Unlicensed drugs are medicines without marketing authorization in a given country. [1]. These may be either imported drugs, or medicines which are prepared by a hospital pharmacy or by another licensed manufacturer (formula drugs). In pediatrics, these drugs are often used due to the lack of suitable formulations, dosages, or specific substances. However, unlicensed drugs carry a higher risk of prescription errors [2] due to the absence of proper labeling and dosing instructions. Our aim was to describe unlicensed use and to investigate whether unlicensed drugs were more prone to prescribing errors than licensed drugs.

Conclusion

Unlicensed drugs are frequently prescribed in hospital care in pediatrics. About every tenth drug prescription on general wards in the University Children's Hospital Zurich is an unlicensed drug (10.8%). One third of patients received at least one unlicensed drug. Imported and formula drugs each account for about half of the unlicensed prescriptions. Oral liquid solutions were the most frequently prescribed drug form in unlicensed drugs. Prescribing errors occur more often in unlicensed drugs than in licensed drugs, and formula drugs had the highest rate of prescribing errors (36.4 errors per 100 prescriptions)

compared to imported and licensed drugs. Because unlicensed drugs showed a significantly higher rate of prescribing errors, licensed drugs are favorable in terms of medication safety and should be prescribed whenever possible. If no licensed drug is available, imported drugs should be favored over formula drugs due to lower prescribing error rates. To increase medication safety in pediatrics in Switzerland, efforts are necessary to increase the number of suitable licensed drug formulations for pediatric patients, including developing new innovative drug formulations for children.

Patients & Methods

We conducted a sub-analysis of a retrospective single-center observational study, which previously investigated the influence of a computerized physician order entry (CPOE) on prescribing errors in pediatrics [3]. We analyzed 5022 prescriptions for a total of 1000 patients from 2018 and 2019 on pediatric general wards. Patients were divided into 4 age groups according to the EMA classification (table 1).

Newborn (term newborn infants)	0 – 27 days
Infants	28 days – 23 months
Children	2 – 11 years
Adolescents	12 – 18 years

Table 1: age groups

All drugs were assigned if they were licensed or unlicensed. The unlicensed drugs were further divided into imported drugs or formula drugs. The galenic drug formulations were categorized into 5 main classes, which comprised several similar drug forms (table 2).

rectal forms	suppositories and other rectal forms
oral liquid forms	suspensions, solutions, syrups, etc.
oral solid forms	tablets, capsules, soft capsules, etc.
i.v. solutions	i.v. conc. solutions, powder for the preparation of an iv solution, i.v. infusion solutions, etc.
other	nasal sprays, topical ointments, solutions for intravesical instillation, etc.

Table 2: drug forms

Medication review was performed on all patients to assess prescribing errors. Errors were categorized according to the PCNE classification (Pharmaceutical care network Europe), and their severity according to the NCC MERP index (National coordinating council for medication error reporting and prevention). Errors with a severity of E-I were classified as potentially harmful errors. The validity of the captured data was ensured through a second review of 5% of patients by another clinical pharmacist. Consequently, interrater reliability could be assessed. Rates of unlicensed drugs versus licensed drugs and rates of prescribing errors, were compared by t-test or chi-square-test as appropriate.

Results

The 1000 patients were prescribed 5022 medicines, of which 544 (10.8%) were prescriptions of unlicensed drugs. 5.1% were imported drugs and 5.7% were formula drugs (Figure 1). 340 Patients (34%) received at least one unlicensed drug. Newborns had the highest proportion of unlicensed drugs (15.8%), and adolescents the lowest (7.1%). Oral liquid forms were the most frequently prescribed drug form in formula drugs, whereas the most frequently prescribed imported drug form were rectal forms (see Figure 2).

Figure 1

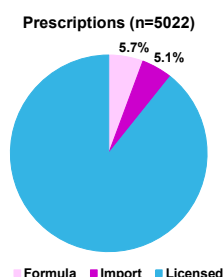


Figure 2

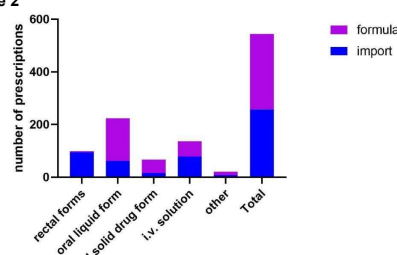
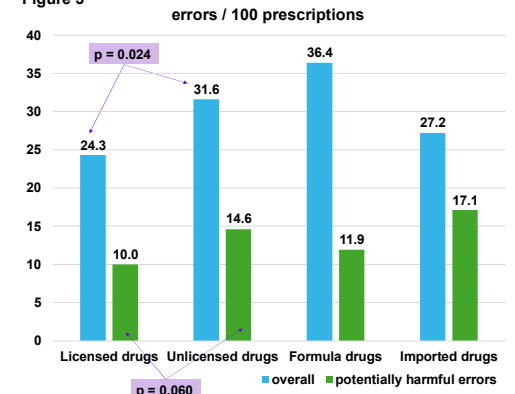


Figure 3 shows that use of unlicensed drugs was associated with statistically significantly more prescribing errors than use of licensed drugs: 31.6 errors per 100 prescriptions (95% CI: 26.1 – 37.0) versus 24.3 errors per 100 prescriptions (95% CI: 22.3 – 26.2), $p = 0.024$. Particularly formula drugs were prone to errors with 36.4 errors per 100 prescriptions (95% CI: 28.4 – 44.2) in formula drugs, vs. 24.5 errors per 100 prescriptions (95% CI: 22.6 – 26.3) in non-formula drugs (licensed in Switzerland or another country), $p = 0.012$.

Figure 3



Most of the errors were of minor severity. A closer analysis of potentially harmful errors revealed a rate of 14.6 errors per 100 prescriptions (95% CI: 10.9 – 18.3) for unlicensed drugs, compared to 10.0 errors per 100 prescriptions (95% CI: 8.7 – 11.3) for licensed drugs ($p = 0.060$).

