

## S2k Guideline “Drug Safety in Paediatric Emergencies” – tips for practical application

J. Kaufmann<sup>1,2</sup> · T. Klein<sup>1</sup> · S. Bittner<sup>3</sup> · C. Eich<sup>4</sup>

Representing the Expert Group of AWMF-S2k-LL 027/071<sup>5</sup>

► **Citation:** S2k Guideline “Drug Safety in Paediatric Emergencies” – tips for practical application  
Anästhesiologie 2022;63:34–41. DOI: 10.19224/ai2021.034

### Summary

Medication errors represent a threat to patients of all ages. Errors occur more frequently with children than with adults because age-group-specific features must be considered, an individual calculation of the dose will be necessary, and the emergency team cannot be familiar with the dose to be administered. Especially in emergency situations, it is necessary to administer drugs holding a high potential for life-threatening complications within a short period of time. Even the wrong placing of a comma when calculating a dose of epinephrine might easily result in a life-threatening tenfold error. Preclinically, it is often impossible to provide specialised paediatric emergency teams. This article analyses the process of drug administration with the typical pitfalls, presents successful interventions and the recommendations of the S2k guidelines on medication safety in paediatric emergencies coordinated by the Association of the Scientific Medical Societies in Germany (AWMF).

### Introduction

The World Health Organization (WHO) ranked medication errors due to injectable drugs as number one on their list of the five most significant safety-relevant topics in medicine (“High5s”) [1]. Children are particularly at risk of medication errors in emergency situations, because, for them, an individual dose must be calculated and a “typical” dose simply

does not exist [2]. Serious errors are not of rare occurrence and are life threatening, for example, in case of epinephrine used for resuscitation [3,4].

### Case Report in Brief

An emergency rescue service was called to the home of an 8-month-old infant whom the parents found lifeless in its bed. Bag-mask ventilation was successful, pulses were palpable under chest compressions. The emergency physician succeeded in inserting an intraosseous needle and gave three administrations of 2 mg epinephrine each. Resuscitation failed. The emergency physician’s protocol did not state the child’s body weight, a forensic pathology inquiry later revealed a measured weight of 8 kg.

### Safety Culture

The case described above originates from the data acquired in the scope of a nationwide study on the improvement of medication safety in paediatric emergencies owing to the support of a length-related dosing aid [5]. The most important statement in this context is that errors do happen, which is not meant as a reproach to the medical practitioner but is a central elementary prerequisite for any improvement of patient safety (“to err is human”) [6]. It is not enough to be aware of the general principle. Instead, it must be very concretely accepted by every single medical practitioner, because only by accepting one’s own fallibility can

- 1 Children’s Hospital Cologne
- 2 Faculty for Health, University Witten/Herdecke
- 3 University Hospital Münster
- 4 Auf der Bult Children’s Hospital, Hanover
- 5 In addition to the authors mentioned:  
Prof. Dr. med. Wolfgang Rascher, Prof. Dr. rer. nat. Antje Neubert, Dr. med. Martin Krebs, Prof. Dr. med. Robert Schwab, Dr. med. Florian Reifferscheid, Bianca Rösner, Dr. med. Reinhold Merbs, Dr. med. Hubert Rädinger, Lothar Ullrich, Prof. Dr. med. Karl-Peter Ittner, Dr. med. Philipp Jung, Prof. Dr. med. Johannes Winning, Marco K. König, Frank Flake, Priv.-Doz. Dr. med. Florian Hoffmann, Julia Rebbert, Dr. Annette Mund

### Conflict of interest

Priv.-Doz. Dr. Jost Kaufmann holds a Europe-wide patent for the development of the Paediatric Emergency Ruler (PaedER; [www.notfalllineal.de](http://www.notfalllineal.de)), however, relinquished any right of compensation for its marketing. The other authors report of having no conflict of interest.

### Keywords

Medication Errors – Prehospital Paediatric Emergency Care – Patient Safety – Weight Estimation – Off-label Use

the implementation of safety structures be assured. The traditional claim made by people outside the system and by the physicians themselves on their alleged infallibility is still an existing problem [7]. The inconsistent acceptance of individual fallibility is identifiable in the literature [8]. For example, experienced physicians less often allowed themselves to be assisted by a simple chart when they dosed emergency medications and continued to make serious mistakes, compared to inexperienced or medical students who applied doses without errors by using the chart [9].

#### NOTE

Humans make mistakes and a complex system such as medicine should be adapted in a way that makes it easy to make the right decisions, and hard to make mistakes.

Standard operating procedures (SOPs) and checklists help to standardise processes and thus avoid errors as early as during a stage of preparation. In addition, they make essential pharmacotherapy information visible for the entire team. Regular trainings in simulations, which include these SOPs and checklists, will improve the chances of a safe and error-free realisation. All initiatives designed to improve drug safety should concentrate on building and/or reinforcing the safety culture and enhancing the competence of the team responsible for treatment. However, care must also be taken to achieve a high level of acceptance in practice. This can only be reached if the recommendations and specifications do not overtax the users [10], are adapted sensitively to the situation, and give users the opportunity to initiate reasonable modifications and optimisations [11].

#### Incidences

In the case reported, an epinephrine dose of 250 µg/kg had been administered, hence 25 times more than the recommended dose of 10 µg/kg body weight. A tenfold higher dose corresponds to a tenfold-error, which is already life-threatening [3,4].

#### CAUTION

An overdose of epinephrine might be life-threatening.

In prehospital treatments in the USA, incorrect drug doses were documented in every third drug administered and in 60 % of all cases when epinephrine was the drug administered [12]. In this and one other study from Germany, the average overdose of epinephrine exceeded the recommended dose by a factor of eight [5]. A tenfold-error was prescribed and prepared in 3 % of cases also in the scope of simulated resuscitation scenarios in a paediatric emergency room [13]. In summary, children are regularly endangered by medication errors.

#### The New Guideline, Objectives and Implementation

A group of 22 experts from 15 professional societies, professional associations and advocacy groups appointed and coordinated by the German Society of Paediatrics and Adolescent Medicine (DGKJ) has released recommendations in a formal consensus based on available evidence in order to improve the quality of pharmacotherapy and thus patient safety in cases of paediatric emergencies [14]. They also identified threats and mechanisms which arise from special paediatric conditions or might lead to medication errors in paediatric emergency situations. More important yet, however, is that many actions could be recommended, most of which are applicable at short notice and with simple means and increase patient safety in paediatric emergencies. The guideline can be downloaded free of charge in versions of various detailedness from the AWMF website (S2K-LL Reg.-No. 027–071; [www.awmf.org](http://www.awmf.org)).

#### Qualification, Training and Increase of Vigilance

The qualification and professional training of the staff, particularly their paediatric expertise as well, will naturally have a positive influence on the quality of

the medication. However, demanding as a consequence that every provider of paediatric emergencies must possess paediatric expertise is not feasible. But a staff with no background in the field will also be capable of treating children safely in acute situations if well prepared. This requires, above all, clear, simple recommendations for action, the knowledge and use of aids as well as training of simulation scenarios [15]. Training and advanced training courses should be implemented as an integral part of any overall concept [16–27]. This was also revealed in studies in which inspecting the prescribers as the sole measure resulted in making less mistakes. It was not even crucial whether the inspector had stood nearby [28] or whether an “invisible” inspection had been carried out [29]. In either case, it may be assumed that the prescribers were merely more vigilant in their prescriptions. Therefore, apart from the immediate learning effect of trainings, surely an increased vigilance for the sensitive subject of medication safety will have a very central role to play.

#### NOTE

Training courses on medication safety for children will increase the knowledge and the vigilance of the prescribers.

#### The Importance of Body Weight

The case presented also shows how important it is to know and consider the weight of a child during its treatment. In a major city in Germany, only 0.5 % of all emergency physician protocols documented the body weight of children who had received intravenous medication [5]. This was surely partly due to the circumstance that the emergency physician protocols used almost everywhere in Germany only rarely offered a field for making an entry of body weight. In the major city mentioned above, a field to enter a body weight was included in the protocol 10 years ago, whereupon the rate of weight documentations has risen to 30 % [30].

**NOTE**

A safe medication in paediatric emergencies begins with the registration or the length-related estimation of the body weight.

In addition, a bundle of measures had been continuously implemented. The rate of false doses displaying deviations of more than 300 % from the recommended dose decreased by 55 % for all drugs examined, and by 78 % for epinephrine [30]. This shows that an improvement of drug safety which actually reaches the child is possible and that paying more attention to the child's body weight can make a significant contribution to that end. If the body weights are wrong, overdosing and underdosing will be inevitable consequences.

### Body Weight Estimations and Length-related Dosing Aids

As confirmed by a meta-analysis, a weight reported by the parents as being known should be used (not one which has been estimated upon request). Otherwise, length-related estimations are superior to those related to age [31] and pertinent systems should be available [32]. Another important advantage of length-related weight estimations is that they allow for determining the normal weight, a practicable approximation to the ideal weight which is perfect for emergency medications, but difficult to calculate.

**CAUTION**

The dosage of drugs which have a narrow therapeutic range (e. g. sedatives and analgesics) relative to a measured weight might be the cause of overdoses in case of adiposity and should therefore be oriented to the ideal weight.

Using such length-related systems, which also offer drug dosages in addition to the weight estimations, is especially recommended in the prehospital sector [32]. They prevent calculation errors and make suggestions for the right sizes of

materials (e. g. ventilation masks, laryngeal masks, endotracheal tubes, etc.).

The weight of a child is mostly known in the inner-hospital setting. Emergency plans adapted to the child's weight should nowadays be used without exception at paediatric wards. The doses should not only be reported in mg for weight-related doses, but also the applied volume should be reported in ml of the respective clearly defined drug concentration. For reasons of clarity, the selection of the drugs in such an emergency plan should be limited to the most urgent and time-critical emergency medication (resuscitation, emergency narcosis including relaxation, arrhythmias).

### Prevention of Overtreatment

It happens that children may receive a stronger drug therapy than absolutely necessary due to their actual situation. For example, external circumstances might tempt an overtreatment, for example, the kind of the planned transportation. A "protective intubation", hence an intubation which is not acutely necessary but considered on account of the prevailing circumstances might result in death or most serious incapacities due to arising complications. The guideline therefore encourages to avoid "overtreatment" by exploiting supportive actions and improving the external circumstances. Conversely, this does not mean that "undertreatment" should be generally encouraged but – in difficult situations and in case of children with serious underlying diseases – it will actually be safer to avoid a too strong impact on vital functions due to analgesics or sedatives.

**NOTE**

Sometimes "doing nothing as much as possible" might be the right decision ("primum non nocere").

Particularly children with sleep apnoea due to severe obstructions of the upper respiratory tract, limited muscular strength or serious neurological development impairments are highly at risk

of suffering severe complications from treatment procedures which are normal for other children [33–35]. An appropriate hospital has experience with children with serious basic diseases and possesses the special instruments needed. Prehospital treatment can therefore not always proceed on the same safety level as in a hospital, for example, as far as the airways are concerned. As a rule, all children who receive medication with a potential impact on vital functions – and especially those with serious underlying diseases – must be closely monitored, at least with pulse oximetry and an electrocardiogram.

The guideline group also agreed that support of the child by reference persons would have a highly positive impact on the child's self-perception and on limiting the situational stress intensity, due to the usually strong bond they have with the child. For example, the administration of sedatives can often be avoided in the comforting presence of a reference person and there is even a demonstrable effect on pain perception [36]. An age-adequate position (e. g. warm, soft and spatially limited) can also produce a positive effect. To be more specific, for example, a child with strained breathing sitting in the lap of its mother, who holds an oxygen mask might possibly be stable for transport, whereas when strapped down and fixated on a stretcher without the mother, the resulting excitement might induce decompensation. Yet it was not possible in the scope of a guideline to formally recommend a deviation from the rules of securing patients during transport, despite the fact that the legal situation (Art. 21a STVO Sect.1 No. 5) permits a deviation in case of necessary medical treatment. The legal responsibility for transport lies with the driver of the vehicle.

**NOTE**

Against the backdrop of a considerable medical advantage and in the sense of increasing patient safety, the most favourable transport modality should be discussed with the vehicle driver in each individual case.

Figure 1



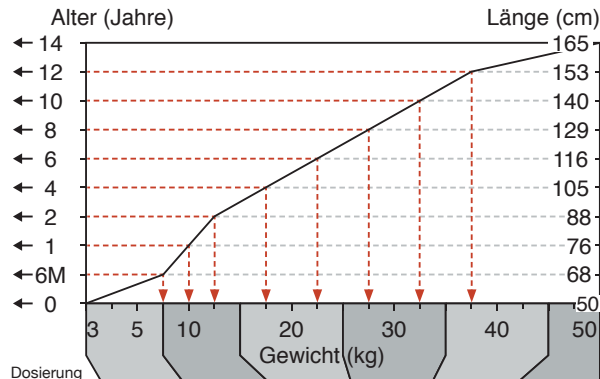
# Pädiatrische Notfallkarte

© F. Hoffmann, München; O. Heinzel, Tübingen, ÄLRD Bayern

Alle Dosierungen wurden nach bestem Wissen und Gewissen sorgfältig recherchiert und hier aufgeführt, entbinden jedoch den Anwender nicht davon, die Dosierungen vor der Anwendung zu überprüfen bzw. an den Zustand des Patienten anzupassen. Es kann keine Gewähr für die Richtigkeit übernommen werden! Einige der aufgeführten Medikamente sind bzgl. Indikation, Dosierung oder Applikationsweg nicht zugelassen.

Larynxmaske	ET-Tubus	
Größe #	Länge oral (cm)	Größe ID (mm)
3,0	20	7,0*
3,0	19	6,5*
3,0	18	6,0*
2,5	16	5,5*
2,5	15	5,0*
2,0	14	4,5*
2,0	13	4,0*
1,5	12	3,5*
1,5	11	3,5 ohne Cuff
1,0	9	3,0 ohne Cuff

\* Tubus mit kleinem distalen Cuff, Druckmessung obligat (max. 20 cm H<sub>2</sub>O)!  
Tubus ohne Cuff ½ Nummer größer wählen.



		Dosierung	Gewicht (kg)					
Reani- mation	Adrenalin (1 ml = 1 mg + 9 ml NaCl) i.v.	0,01 mg/kg	0,5 ml	1 ml	2 ml	3 ml	4 ml	5 ml
	Adrenalin-Perfusor (1 ml = 1mg + 49 ml NaCl) i.v.	0,1 µg/kg/min	1-2 ml/h	3 ml/h	6 ml/h	9 ml/h	12 ml/h	15 ml/h
	Amiodaron (150 mg/3 ml) als Bolus i.v.	5 mg/kg	0,5 ml	1 ml	2 ml	3 ml	4 ml	5 ml
	Defibrillation (Einzelschock)	4 J/kg	20 J	40 J	80 J	120 J	160 J	200 J
Anaphy- laxie	Adrenalin pur (1 ml = 1 mg) i.m.	0,01 mg/kg	0,1 ml	0,1 ml	0,2 ml	0,3 ml	0,4 ml	0,5 ml
	Dimetinden (4 mg/4 ml) i.v.	0,1 mg/kg	0,5 ml	1 ml	2 ml	3 ml	4 ml	5 ml
	Prednison rektal	100 mg-Supp.	altersunabhängig 100 mg					
Volu- men	Prednisolon (250 mg/5 ml) i.v.	2 mg/kg	0,2 ml	0,4 ml	0,8 ml	1,2 ml	1,6 ml	2 ml
	Balanzierte VEL (Bolus) i.v.	20 ml/kg	100 ml	200 ml	400 ml	600 ml	800 ml	1000 ml
Analgo- sedierung	HAES 6% i.v.	5 ml/kg	25 ml	50 ml	100 ml	150 ml	200 ml	250 ml
	Esketamin (1 ml = 25 mg + 9 ml NaCl) i.v.	0,5 mg/kg	1 ml	2 ml	4 ml	6 ml	8 ml	10 ml
	Fentanyl (50 µg/ml) i.v.	1,0 µg/kg	0,1 ml	0,2 ml	0,4 ml	0,6 ml	0,8 ml	1 ml
	Midazolam (1 ml (= 5 mg) + 4 ml NaCl) i.v.	0,1 mg/kg	0,5 ml	1 ml	2 ml	3 ml	4 ml	5 ml
	Esketamin* (25 mg/ml) nasal	2 mg/kg	0,5 ml	0,9 ml	1,7 ml	2,5 ml	3,3 ml	4,1 ml
	Fentanyl* (50 µg/ml) nasal	1,5 µg/kg	0,3 ml	0,4 ml	0,7 ml	1 ml	1,3 ml	1,6 ml
	Midazolam* (15 mg/3 ml) nasal	0,3 mg/kg	0,4 ml	0,7 ml	1,3 ml	1,9 ml	2,5 ml	3,1 ml
	Midazolam (1 ml = 5mg) + 4 ml Nacl i.v.	0,1 mg/kg	0,5 ml	1 ml	2 ml	3 ml	4 ml	5 ml
Krampt- anfall	Midazolam* (5 mg/ml) nasal	0,2 mg/kg	0,3 ml	0,5 ml	0,9 ml	1,3 ml	1,7ml	2,1 ml
	Esketamin (25 mg/ml) i.v.	1 mg/kg	0,2 ml	0,4 ml	0,8 ml	1,2 ml	1,6 ml	2 ml
Narkose	Fentanyl (50 µg/ml) i.v.	3 µg/kg	0,3 ml	0,6 ml	1,2 ml	1,8 ml	2,4 ml	3 ml
	Midazolam (15 mg/3 ml) i.v.	0,2 mg/kg	0,2 ml	0,4 ml	0,8 ml	1,2 ml	1,6 ml	2 ml
	Propofol 1% (10 mg/ml) i.v.	3 mg/kg	1,5 ml	3 ml	6 ml	9 ml	12 ml	15 ml
	Propofol 1% (10 mg/ml) Perfusor i.v.	6 mg/kg/h	3 ml/h	6 ml/h	12 ml/h	18 ml/h	24 ml/h	30 ml/h
	Rocuronium (50 mg/5 ml) i.v.	1 mg/kg	0,5 ml	1 ml	2 ml	3 ml	4 ml	5 ml
	Succinylcholin (100 mg/5 ml) i.v.	1,5 mg/kg	0,4 ml	0,8 ml	1,6 ml	2,4 ml	3,2 ml	4 ml
	Vecuronium (1 mg/ml) i.v.	0,1 mg/kg	0,5 ml	1 ml	2 ml	3 ml	4 ml	5 ml
	Adrenalin pur (1 mg = 1 ml) inhalativ ggf. wdh.	3-5 ml	3 ml	4 ml	5 ml	5 ml	5 ml	5 ml
Atemwegs- obstruktion	Prednisolon (250 mg/5 ml) i.v.	2 mg/kg	0,2 ml	0,4 ml	0,8 ml	1,2 ml	1,6 ml	2 ml
	Prednison rektal	100 mg	altersunabhängig 100 mg					
	Salbutamol – Fertiginhalat (1,25 mg/2,5 ml) inhalativ ggf. wdh.	3-5 ml	2,5 ml	5 ml	5 ml	5 ml	5 ml	5 ml
Sonst.	Ceftriaxon (2 g/20 ml) i.v. (Meningitisdosis)	max 100 mg/kg	5 ml	10 ml	20 ml	20 ml	20 ml	20 ml
	Glukose 40% i.v.**	200-400 mg/kg	5 ml	10 ml	20 ml	30 ml	30 ml	30 ml

\* über MAD\* (LMA Deutschland), 0,1 ml Füllungsvolumen bereits eingerechnet  
\*\* verdünnt anwenden

ARBEITSGEMEINSCHAFT  
DER BAYERISCHEN  
SOZIALVERSICHERUNGSTRÄGER

INM

ÄLRD

LMU  
KLINIKUM  
DER UNIVERSITÄT MÜNCHEN

GAIA  
Wissenschaftlicher Arbeitskreis  
Kinderanästhesie  
PAEDSIM®  
Teamtraining für Kindernotfälle e.V.  
Version 07-2017



### Calculations

The correct weight-related dosage in paediatric patients is almost without exception not comparable with the dosing of adults and to some extent varies considerably among different paediatric age groups. For this reason, the prescribing caregiver should either know or, at least, be able to reliably determine the right body-weight-related dosage of the emergency medication for the individual patient, for example, by taking a look into the summary tables of the guideline or the “Children’s Formulary” (see Chapter “Off-label Use”).

The underlying calculation of the dose is the step in the pharmacotherapy of paediatric emergencies in which life-threatening errors most frequently occur. For example, tenfold-errors occur on a regular basis [2]. However, it is remarkable and positive that by a systematic literature search one may come to the conclusion that all measures which reduce the cognitive requirements also reduce the rate and intensity of dosage errors [37].

Simulations revealed that just using a simple table can prevent 66 % [9] and 90 % [38] of all tenfold-errors when epinephrine is used for resuscitation. In a study on “real” prehospital paediatric emergency treatments, a length-related system with dosage recommendations prevented errors with deviations of more than 300 % in 9 out of 10 cases [5].

#### CAUTION

Due to the considerable risk and the chance to improve safety, dangerous medications (e. g. epinephrine, analgesics) should never without prior reassurance be administered by a supporting system.

The overdose in the case report presented could also have been prevented this way. An easy and quick look into a table or ruler will increase the safety of patients. One example of such a useful tabular aid used in a paediatric emergency is shown in Figure 1.

### Communication structure

Information could get lost during the transmission of the prescription, or transmission errors might occur. Both setbacks can be remedied by standardising and confirming the receipt of the transmission [11,37]. The transmission of a prescription should proceed in writing, if possible, preferably on a standardised sheet [39–41]. This particularly applies to prescriptions with a high risk potential (e. g. potassium, catecholamines, insulin, epinephrine). Oral prescriptions in emergency situations should be done in a structured manner and repeated and confirmed by everyone involved. The amount of each drug to be administered must always be stated. If experienced staff are familiar with the current medical situation, it will suffice only to state the name of the drug and the intended dose application [11]. The person in charge of administration repeats the name of the drug and the dose to be administered (“closed-loop” communication).

#### NOTE

Only after all team members have signalled their consent (“closed-loop” communication) that everything is correct, should the medication be administered.

Approximately 70–80 % of all medical incidents do not result from medical ignorance, but from insufficient team performance. This has been known for over 20 years (“To err is human” [6]). Reasons for this could be, for example, communication deficits or a wrong role behaviour or a misunderstanding [42]. Each team member should always have the chance to express doubts about the prescriptions (“speaking up”) [6]. Prior to each drug administration, all involved must observe the 5-R Rule with high vigilance and equally.

#### 5-R Rule

- Right patient?
- Right medication?
- Right dose?
- Right time?
- Right route of application?

A good communication structure should be practically trained on a regular basis (for example, in simulations). It should also be established in clinical routine apart from emergency situations, which extremely increases the probability that it will then be applied in emergency situations as well. Critical Incident Reporting Systems (CIRS) are an important component of communication and should enable an anonymous report of critical incidents. These reports must be discussed constructively by an interdisciplinary expert group and solution proposals elaborated. A CIRS should be an established standard in every medical facility by now.

### Sorting and Labelling of Medication

Confusions when selecting the right medication might happen especially when names sound similar or ampoules look alike (“sound-a-like” and/or “look-a-like”; collectively abbreviated as SALA). Especially unfavourable in this regard is when easily confusable medications are stored closely together, hence confusions might be caused only by a slightly changed grip into an ampullary. If alternative options exist, similar sounding or similar looking drugs should be avoided or, at least, be kept distinctly separated at their place of storage. Each medication should have its own clearly defined place of storage (e. g. in an ampullary or solid case). If sufficient space is available, any medication with a high potential of hazard or confusion should be separated as clearly as possible.

### Preparation of Medication

As a rule, dilutions should be avoided whenever a precise and safe application of an undiluted solution is possible. In many cases, a precise application of the undiluted injection solution can be done by using small syringes (e. g. 1 ml syringe with 0.01ml scale). Afterwards sufficient rinsing, e. g. with a 0.9 % NaCl solution, must be ensured.

Another possibility to avoid own dilutions is the use of pharmaceutically preloaded syringes (“ready-to-use syringes”) for which there is now an increasing supply in Germany. For example, there are epinephrine (adrenalin) syringes for resuscitation with a concentration of 100 µg/ml, used nearly everywhere in Germany and otherwise only to be obtained by dilution, available in a total volume of 10 ml. Should dilution be inevitable, then a clear instruction should be available for its preparation. The target syringe containing the medication must be immediately labelled, using labels which conform with ISO 26825 and also indicate the concentration of the solution [43]. The calibration scale should not be pasted over, so that the exact application of the desired volume is not hindered. The intended target concentration should be chosen in such a manner that any further calculations and dosages can be done as easily as possible (e. g., 1, 10 or 100 units per ml).

When preparing a drug for intramuscular (IM) administration, the syringe should be emptied to such an extent that only the total amount to be administered shall remain in the syringe. For the technical handling of an IM injection with a puncture angle perpendicular to the body surface and thumb operation of the plunger provides a worse condition for the controlled forward movement of the syringe’s plunger and increases the probability of an accidental administration of a too large volume.

### “Off-label Use”

The guideline group also felt strongly about formulating a clear statement on “off-label use” in paediatric emergency medicine. Many drugs which had been applied successfully and without causing problems in paediatric and adolescent medicine for years have no formal marketing authorisation, despite the fact that many years of clinical experience and evidence for their safe use has been documented in the literature. Representative for the entirety of paediatrics, only 46 % of all significant drugs in the USA had a formal authorisation for paediatric

use in 2021 [44]. When it comes to neonatology, this rate is considerably lower and ranges at about 20 % [45]. All previous political efforts to improve this situation remained without relevant success, for which reason no change of the status quo is to be expected in the near future.

Irrespective of their authorisation status, for many drugs there is comprehensive evidence which documents their effective and safe application to children. In many cases, these drugs are even considered to be the first choice in certain indications and patient groups. One example for this is fentanyl which is formally approved only for children of 2 years of age and older [46], but for decades has been the opioid most often used in neonatology for analgesedation worldwide [47]. Pharmacokinetic data and valid dosage recommendations are even available for both premature and full-term babies [48,49], but they never have been used in a marketing authorisation.

Consequently, as for the prehospital and in-hospital treatment of paediatric emergency cases, therapy decisions should be based on scientific evidence and experience and not depend on the authorisation status alone. An “off-label use” is neither improper, illegal nor contraindicated, but may represent the best possible therapy for many cases. The “off-label use” should be discussed with the persons having care and custody of the children. Those who apply emergency medication to children and adolescents, especially in “off-label use”, should seek information on the current safety instructions released by pharmacovigilance early in time (e. g., Red Hand Letters, Newsletters of the Drug Commission of the German Medical Association (AkdÄ), the Bulletin of the German Federal Institute for Drugs and Medical Devices, BfArM).

### NOTE

A fundamental renunciation of “off-label use” puts children at risk and makes appropriate treatment impossible.

In a project financed by the Federal Ministry of Health, a European harmonised database was created on the foundations of the best possible evidence as a reference for dosage recommendations. It can be retrieved free of charge at [www.kinderformularium.de](http://www.kinderformularium.de) and is continually updated. Its intention is to improve drug therapy in children and adolescents, harmonise dosage recommendations nationwide and worldwide, and make information easily accessible and free of charge to users [50]. In the guideline, excerpts of the information gathered here have been summarised in tables for the most important emergency medications.

### Annotation

This special publication is based on the recommendations of the S2k Guideline “Drug Safety in Paediatric Emergencies” which has been published under AWMF Registration No. 027/071 in March 2021 on the website of the AWMF ([www.awmf.org](http://www.awmf.org)). A matching representation of the guideline’s content has also been published in the association journal of the German Society of Paediatrics and Adolescent Medicine (Deutsche Gesellschaft für Kinder- und Jugendmedizin, DGKJ), the “Monatsschrift Kinderheilkunde” [Paediatrics Monthly Letter] cited as follows: Kaufmann, J., Neubert, A., Hoffmann, F. et al. Wichtige Aspekte zur Medikamentensicherheit bei Kindernotfällen. Monatsschr Kinderheilkd (2021). <https://doi.org/10.1007/s00112-021-01328-0>. © 2021, Springer Medizin Verlag GmbH, a part of Springer Nature. All rights reserved. Reprinted with kind permission.

### References

1. Leotsakos A, Zheng H, Croteau R, Loeb JM, Sherman H, Hoffman C, et al: Standardization in patient safety: the WHO High 5s project. *International Journal for Quality in Health Care* 2014;26:109–116
2. Kozer E, Scolnik D, Keays T, Shi K, Luk T, Koren G: Large errors in the dosing of medications for children. *N Engl J Med* 2002;346:1175–1176

3. Perondi MB, Reis AG, Paiva EF, Nadkarni VM, Berg RA: A comparison of high-dose and standard-dose epinephrine in children with cardiac arrest. *N Engl J Med* 2004;350:1722–1730
4. Sharman M, Meert KL: What is the right dose of epinephrine? *Pediatr Crit Care Med* 2005;6:592–594
5. Kaufmann J, Roth B, Engelhardt T, Lechleuthner A, Laschat M, Hadamitzky C, et al: Development and Prospective Federal State-Wide Evaluation of a Device for Height-Based Dose Recommendations in Prehospital Pediatric Emergencies: A Simple Tool to Prevent Most Severe Drug Errors. *Prehosp Emerg Care* 2018;22:252–259
6. Kohn LT, Corrigan JM, Donaldson MS: *To Err is Human: Building a Safer Health System*. Washington, DC: National Academy Press 1999
7. Sexton JB, Thomas EJ, Helmreich RL: Error, stress, and teamwork in medicine and aviation: cross sectional surveys. *Bmj* 2000;320:745–749
8. Kaufmann J, Schieren M, Wappler F: Medication errors in paediatric anaesthesia—a cultural change is urgently needed! *Br J Anaesth* 2018;120:601–603
9. Kaufmann J, Engelhardt T, Steinwegs I, Hinkelbein J, Piekarski F, Laschat M, et al: Der Einfluss von Ausbildung und Erfahrung auf Dosierungsfehler bei pädiatrischen Notfallmedikamenten – eine interventionelle Fragebogen-Studie mit tabellarischer Hilfe. *Anaesth Intensivmed* 2019;60:164–172
10. Jain D, Sharma R, Reddy S: WHO safe surgery checklist: Barriers to universal acceptance. *J Anaesthesiol Clin Pharmacol* 2018;34:7–10
11. Kaufmann J, Wolf AR, Becke K, Laschat M, Wappler F, Engelhardt T: Drug safety in paediatric anaesthesia. *Br J Anaesth* 2017;118:670–679
12. Hoyle JD, Davis AT, Putman KK, Trytko JA, Fales WD: Medication dosing errors in pediatric patients treated by emergency medical services. *Prehosp Emerg Care* 2012;16:59–66
13. Kozer E, Seto W, Verjee Z, Parshuram C, Khattak S, Koren G, et al: Prospective observational study on the incidence of medication errors during simulated resuscitation in a paediatric emergency department. *BMJ* 2004;329:1321
14. Kaufmann J, Rascher W, Neubert A, Eich C, Krebs M, Schwab R, et al: S2k – Leitlinie 027/071 „Medikamentensicherheit bei Kindernotfällen“ AWMF 2021; <https://www.awmf.org/leitlinien/detail/II/027-071.html>
15. Kaufmann J, Laschat M, Wappler F: Präklinische Versorgung von Kindernotfällen. *Anaesth Intensivmed* 2020;61:26–37
16. Davey AL, Britland A, Naylor RJ: Decreasing paediatric prescribing errors in a district general hospital. *Qual Saf Health Care* 2008;17:146–149
17. Campino A, Lopez-Herrera MC, Lopez-de-Heredia I, Valls-i-Soler A: Educational strategy to reduce medication errors in a neonatal intensive care unit. *Acta Paediatr* 2009;98:782–785
18. Kidd L, Shand E, Beavis R, Taylor Z, Dunstan F, Tuthill D: Prescribing competence of junior doctors: does it add up? *Arch Dis Child* 2010;95:219–221
19. Costello JL, Torowicz DL, Yeh TS: Effects of a pharmacist-led pediatrics medication safety team on medication-error reporting. *Am J Health Syst Pharm* 2007;64:1422–1426
20. Larsen GY, Parker HB, Cash J, O’Connell M, Grant MC: Standard drug concentrations and smart-pump technology reduce continuous-medication-infusion errors in pediatric patients. *Pediatrics* 2005;116:e21–25
21. Stewart M, Purdy J, Kennedy N, Burns A: An interprofessional approach to improving paediatric medication safety. *BMC Med Educ* 2010;10:19
22. Otero P, Leyton A, Mariani G, Ceriani Cernadas JM, Patient Safety Committee: Medication errors in pediatric inpatients: prevalence and results of a prevention program. *Pediatrics* 2008;122:e737–743
23. Leonard MS, Cimino M, Shaha S, McDougal S, Pilliod J, Brodsky L: Risk reduction for adverse drug events through sequential implementation of patient safety initiatives in a children’s hospital. *Pediatrics* 2006;118:e1124–1129
24. Condren M, Honey BL, Carter SM, Ngo N, Landsaw J, Bryant C, et al: Influence of a systems-based approach to prescribing errors in a pediatric resident clinic. *Acad Pediatr* 2014;14:485–490
25. Koren G: Trends of medication errors in hospitalized children. *J Clin Pharmacol* 2002;42:707–710
26. Manias E, Kinney S, Cranswick N, Williams A, Borrott N: Interventions to reduce medication errors in pediatric intensive care. *Ann Pharmacother* 2014;48:1313–1331
27. McClelland RE, Jr., Catt C, Davis JT, Morvay S, Merandi J, Lewy D, et al: An internal quality improvement collaborative significantly reduces hospital-wide medication error related adverse drug events. *J Pediatr* 2014;165:1222–1229. e1221
28. Subramanyam R, Mahmoud M, Buck D, Varughese A: Infusion Medication Error Reduction by Two-Person Verification: A Quality Improvement Initiative. *Pediatrics* 2016;138
29. Campino A, Lopez-Herrera MC, Lopez-de-Heredia I, Valls ISA: Medication errors in a neonatal intensive care unit. Influence of observation on the error rate. *Acta Paediatr* 2008;97:1591–1594
30. Kaufmann J, Uhl S, Singer E, Eifinger F, Klein T, Lechleuthner A, et al: Improving Pediatric Drug Safety in Prehospital Emergency Care-10 Years on. *J Patient Saf* 2021; Epub ahead of print
31. Wells M, Goldstein LN, Bentley A: The accuracy of emergency weight estimation systems in children—a systematic review and meta-analysis. *Int J Emerg Med* 2017;10:29
32. Van de Voorde P, Turner NM, Djakow J, de Lucas N, Martinez-Mejias A, Biarent D, et al: European Resuscitation Council Guidelines 2021: Paediatric Life Support. *Resuscitation* 2021;161:327–387
33. Niesters M, Overdyk F, Smith T, Aarts L, Dahan A: Opioid-induced respiratory depression in paediatrics: a review of case reports. *Br J Anaesth* 2013;110:175–182
34. Jay MA, Thomas BM, Nandi R, Howard RF: Higher risk of opioid-induced respiratory depression in children with neurodevelopmental disability: a retrospective cohort study of 12 904 patients. *Br J Anaesth* 2017;118:239–246
35. Wappler F: [Current aspects of anaesthesia in neuromuscular diseases]. *Anesthesiol Intensivmed Notfallmed Schmerzther* 2003;38:495–499
36. Bembich S, Cont G, Causin E, Paviotti G, Marzari P, Demarini S: Infant Analgesia With a Combination of Breast Milk, Glucose, or Maternal Holding. *Pediatrics* 2018;142:e20173416
37. Kaufmann J, Laschat M, Wappler F: Medication errors in pediatric emergencies: a systematic analysis. *Dtsch Arztebl Int* 2012;109:609–616
38. Bernius M, Thibodeau B, Jones A, Clothier B, Witting M: Prevention of pediatric drug calculation errors by prehospital care providers. *Prehosp Emerg Care* 2008;12:486–494
39. Broussard M, Bass PF, 3rd, Arnold CL, McLarty JW, Bocchini JA Jr: Preprinted order sets as a safety intervention in pediatric sedation. *J Pediatr* 2009;154:865–868
40. Kozer E, Scolnik D, MacPherson A, Rauchwerger D, Koren G: Using a pre-printed order sheet to reduce prescription errors in a pediatric emergency department: a randomized, controlled trial. *Pediatrics* 2005;116:1299–1302

41. Larose G, Bailey B, Lebel D: Quality of orders for medication in the resuscitation room of a pediatric emergency department. *Pediatr Emerg Care* 2008;24:609–614
42. Calhoun AW, Boone MC, Porter MB, Miller KH: Using simulation to address hierarchy-related errors in medical practice. *Perm J* 2014;18:14–20
43. Sybrecht GW, Prien T: Arzneimittelsicherheit: Standard-Spritzenaufkleber in der Akutmedizin. *Dtsch Arztebl* 2010;107:A1031–1032
44. Sachs AN, Avant D, Lee CS, Rodriguez W, Murphy MD: Pediatric information in drug product labeling. *Jama* 2012;307:1914–1915
45. Pandolfini C, Bonati M: A literature review on off-label drug use in children. *Eur J Pediatr* 2005;164:552–558
46. Fachinformation Fentanyl, Firma JANSSEN-CILAG 2004
47. Hünslers C, Roth B: Analgesiedierung in der pädiatrischen Intensivmedizin. *Intensiv up2date* 2009;5:229–247
48. Koehntop DE, Rodman JH, Brundage DM, Hegland MG, Buckley JJ: Pharmacokinetics of fentanyl in neonates. *Anesth Analg* 1986;65:227–232
49. Santeiro ML, Christie J, Stromquist C, Torres BA, Markowsky SJ: Pharmacokinetics of continuous infusion fentanyl in newborns. *J Perinatol* 1997;17:135–139
50. Zahn J, Wimmer S, Rödle W, Toni I, Sedlmayr B, Prokosch H-U, et al: Development and Evaluation of a Web-Based Paediatric Drug Information System for Germany. *Pharmacy* 2021;9:8.

### Correspondence address



**Priv.-Doz. Dr. med.  
Jost Kaufmann**

Children's Hospital of the Clinics of  
the City of Cologne gGmbH  
Amsterdamer Straße 59  
50735 Köln, Germany

Phone: 0049 221 8907 15199

Fax: 0049 221 8907 5264

Mail: [jost.kaufmann@uni-wh.de](mailto:jost.kaufmann@uni-wh.de)

ORCID-ID: 0000-0002-5289-6465