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Less accidental overdoses and intoxications with Thyrax in small children by changing bottle to blister pack

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Highlights

Accidental intake of medicines in children can be prevented to a considerable extent by the use of child-resistant packaging.

The transition from bottle to blister packaging has both the number of accidental Thyrax overdoses if the dose taken decreases in children younger than seven years

The positive effect of the child-resistant packaging seems to be partly lost by parents / guardians who take the medication early from the original package get it.

Preface

The National Poisons Information Center (NVIC) received nearly 44,000 requests for information from medical professionals in 2015 about the possible effects and treatments for poisoning [1]. The synthetic thyroid hormone was levothyroxine in 2015 has been provided to almost half a million Dutch people therefore present in many households [2]. Got it annually NVIC some 170 questions in response to accidental small children taking levothyroxine.

One-time intake of levothyroxine by a child rarely gives complaints. A considerable amount must have been taken before there is a risk of developing symptoms, consistent with an increase in basal metabolic rate. In mild cases (≥ 0.05 mg / kg) this is expressed in a feverish, hyperactive child. With larger overdoses

ABSTRACT

Less accidental overdoses and intoxications with Thyrax in little children because of change from bottle to blister packaging

OBJECTIVE

In December 2013, the largest manufacturer of levothyroxine for the Dutch market (brand Thyrax) started packaging their product from glass bottles into blisters to protect it from environmental influences. We investigated whether this change in the primary packaging influenced the frequency and severity of accidental levothyroxine overdose in young children.

DESIGN AND METHODS

Telephone inquiries to our Dutch Poisons Information Center concerning children under seven years of age exposed to Thyrax were registered between January 2010 and December 2015. The ingested amount of levothyroxine in mg/kg body weight was recorded and the severity of the overdoses was estimated. An unknown dose or an ingested dose of more than 0.05 mg/kg of levothyroxine was defined as a toxic dose. Information about the actual manner of packaging was collected in 2014 and 2015. The number of telephone inquiries before and after the change in the primary packaging were compared using interrupted time series analyses. The decrease in proportions of cases exposed to a toxic dose were compared using a Z-test

RESULTS

The monthly average number of Thyrax overdose cases decreased from 12.1 per month before the change in the primary packaging to 6.4 after (P = 0.04). Furthermore, this decrease was proportionally larger among children exposed to a toxic dose than among children exposed to a non-toxic dose: −66% versus −38%, respectively (P = 0.002). However, in 2015 still 21% of the children with an overdose took these Thyrax tablets out of a bottle.

CONCLUSION

Blister packaging has significantly reduced the number and severity of accidental intake of Thyrax by young children. However, this preventive effect is hampered by parents removing the medication from the blister well be-fore use.

(≥ 0.3 mg / kg) may cause confusion, fever, tachycardia, arrhythmias, tremors and convulsions. If serious overdose, a thyreotoxic crisis may occur.
Possible symptoms sometimes only manifest five to eleven days after taking levothyroxine because it is first must be converted to the more biologically active triiodothyronine [3]. It is therefore important to be so fast possibly after ingestion to estimate whether there is a toxic dose welcomed. If this is the case, then preferably within one activated charcoal for absorption Reduce.

There are a number of brands of levothyroxine on the market, of which at the end of 2015 the Thyrax brand was the largest with 74% had a market share [2]. Thyrax is found in tablets of 0.025 mg, 0.100 mg and 0.150 mg of levothyroxine. Outbound of a child of two years and twelve kilograms are added taking Thyrax so no significant complaints Expected after taking up to 24 of the lightest tablets or up to four of the strongest tablets. Serious effects are with one child of the same age and weight cannot be excluded after intake from 144 of the lightest tablets or 24 of the strongest tablets.

Thyrax Duotab was supplied in glass bottles until the end of 2013 delivered. The former manufacturer went in December 2013 MSD over to blister packs because the drug is on that would be better protected against, among other things moisture action [4]. The bottles were not supplied of a child-resistant closure, the blister pack complies on the other hand, the child safety requirements of a child non-reclosable packaging (written notice from the current manufacturer Aspen Pharma Trading Ltd., July 25 2017). The NVIC has investigated whether the adaptation of the packaging of Thyrax affected the number and the severity of acute, accidental intakes of Thyrax children younger than seven years.

Methods

Data collection

All requests for information to the NVIC are stored in the NVIC database. The telephone information questions about levothyroxine in the period 2010 to have been analyzed with 2015. In addition, the number of children younger than seven years with an acute levothyroxine overdose of the brand Thyrax Duotab counted. The potential severity of the overdose was determined by of the dose taken (none: <0.05 mg / kg, light: ≥ 0.05 mg / kg, moderate / severe: ≥ 0.3 mg / kg of levothyroxine). Once in a while the applicant knows little about the amount taken (package size, tablet strength and / or ingested quantity are unknown). In such cases based on a worst case scenario, with the risk of symptoms. These cases are counted as potential intoxications. For multiple requests for information about the same child, the case is counted once, based on the latter contact as most accurate.

In December 2013, the SmPC text from Thyrax Duotab tablets indicated that they are in blister packs instead of delivered in vials. Since it's time cost before pharmacists actually deliver Thyrax in blister packs to patients, the information phone was checked from the manufacturer onwards what the original packaging of the Thyrax tablets was, or the tablets by the child from the original packaging were met and if there was more information about it the facts could be given. The NVIC informs and advises professional care providers on possible health effects from poisoning, the information about the facts are not always (fully) available in such conversations. There is no further consultation with the parents / been caretakers. When indicated that was a child Had taken Thyrax tablets independently from jar / vial could therefore not always be fully certain whether this was the original packaging.

Statistical analysis

The effect of the adapted packaging on the monthly number of children with accidental Thyrax intake isanalyzed using interrupted time series analysis(ITS) [5.6]. It has been checked whether there was autocorrelation and has been corrected for this. In addition, it has been testedwhether the blister pack affected the severity of theoverdoses. This is done by means of a Z-testtested whether the decrease in the number of children with an intoxication (dose ≥ 0.05 mg / kg) after switchingchildren without intoxication (<0.05 mg / kg). Statisticalanalyzes were performed using SAS version 9.4for Windows (SAS Institute Inc., USA).

Results

Number

The number of children up to and including 6 years that are in contact was recorded with the NVIC after accidental ingestion from Thyrax, averaged between 2010 and 201312.1 per month. After adjusting the package fell the number of questions about Thyrax to the NVIC to an average of 6.4 children per month. This decrease in the number questions per month was significant (change in the intersection with the y-axis, t-value = −1.2; P = 0.04) (figure 1). The number of information questions about children up to and including 6year with the accidental intake of other levothyroxine-containing products was on average 2.0 per month in 2010 to 2013 (SD = 1.3) and in 2014 up to and including2015 on average at 2.5 per month (SD = 1.9).

Ernst

In most cases (71% on average), the amount of Thyrax taken was too low to cause intoxication cause (Figure 2). In the period 2010 to2013 was the number of children with mild intoxication (L)

Figure 1 Monthly number of requests for information after Thyrax intake by children under the age of seven

Red squares: January 2010 to December 2013, blue triangles: January 2014 to December 2015, red line (in the white area): trend line before the adaptation of the packaging, blue line (in gray area): trend line after adaptation of the packaging.

around 30 a year. After adjusting the package that took number in 2014 and 2015 to 13 and 8 per respectively year. The group of children with moderately severe intoxication(M) was on average annually in 2010 up to and including 20136.5 and decreased in 2014 and 2015 to 2 and 3 respectively. The number of questions with unknown dosage (Unknown) also increased after adjusting the packaging, from an average of eight per year in 2010 up to and including 2013 up to two in 2014 and therein 2015 (Figure 2). After adjustment of the packaging the decrease in the number of requests for information about potential intoxication with Thyrax in small children (L + M + Unknown)proportionally greater than the decrease in the number of children without intoxication, respectively –66% and –38% (P = 0.002).

Jar or blister

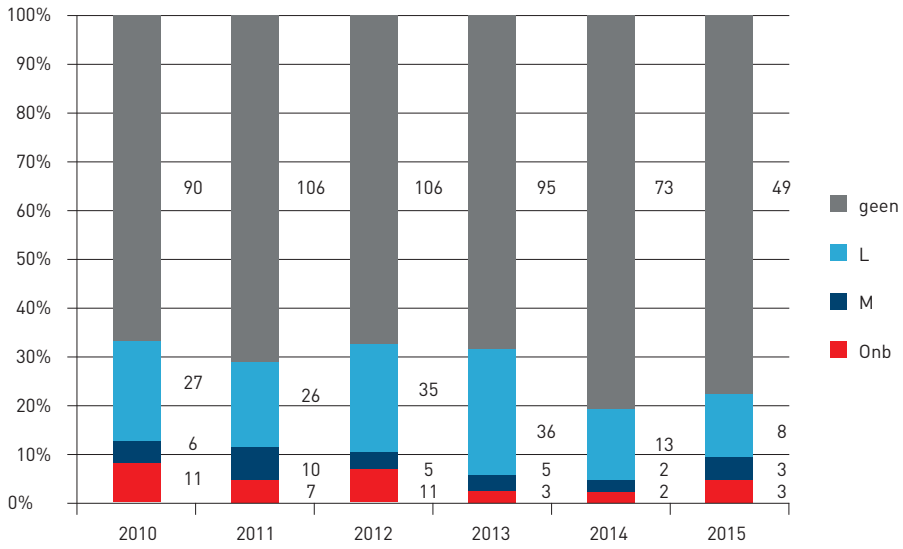
The information about the circumstances was regularly not (fully) available during the telephone consultation. In front as far as the facts were known, it was noticed that the children with an intoxication were more often given a game than a blister (figure 3). They had the tablets were even taken out of a jar in 50% of the cases. In 2015, the second year after the transition to blister packaging, 21% of the cases still stated that the Thyrax Duotab tablets were in a jar. Five times was explicitly indicated that the tablets were taken by the mother were pressed out of the blister and put in a jar (three times in 2014, twice in 2015), the reason this is unknown. In addition, children had to access to tablets that were loose on the table or for example are in a week box.

Beschouwing

The transition to a blister pack has both numbers as the severity of overdoses with Thyraxdecrease the number of children. Since Thyrax Duotabblisters, the NVIC becomes considerably less often consulted about children under the age of seven who take these tablets by accident. In the first year after adjustment, the number of telephone inquiries reduced with 38% and in the second year, the number of requests for information was 56% lower than the number for the change. TheSmall increase in the number of questions about other levothyroxine-containing products may decrease the number of information questions about the accidental intake of Thyraxnot explained by small children. There also hardly seems there must be a switch to other levothyroxine-containing products [2]. This confirms the fact that child-resistant blister pack containing every dose packaged separately, the risk of accidental ingestionsmall children and if this still happens that the dose taken is generally lower [7]. After the transition to blister packaging was the decrease in a number of children with potential intoxication (≥ 0.05 mg /kg) proportionally greater than the decrease in number children without intoxication (<0.05 mg/kg).

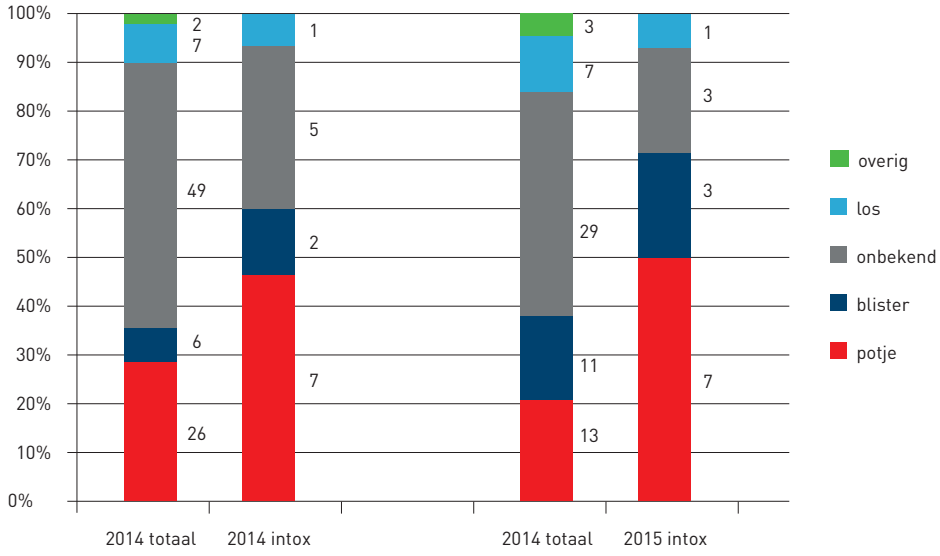
Nevertheless, in 2015, it was still striking(21%) indicated that children are taking Thyraxhad won a game. The childproof feature of the blister pack is destroyed in this way. Patients, and in particular the parents /carers, insufficiently aware of the importance of

Figure 2 Proportions of the potential seriousness of intoxications with Thyrax (per year, for children <7 years)



Proportions are shown per year for children under the age of seven. None: no intoxication, L: mild intoxication (≥ 0.05 mg / kg and <0.3 mg / kg), M: moderately severe intoxication (0.3 mg / kg); Unknown: dose unknown (potential intoxication).

Figure 3 Percentage of reports to NVIC per type of packaging in 2014 and 2015



Total: all questions about Thyrax (<seven years), intox: only questions about potential intoxications (≥ 0.05 mg/kg and dose unknown, <seven years).

the storage of medication in the original packaging until the moment of use so as to reduce the chance of unwanted minimize intake by children. Also, patients who regularly have small children on the floor (for example a babysitter or grandparents) must realize that a blister pack is more child-safe than a jar

or bottle with loose tablets. When the tablets are from one potty is harder to estimate how much tablets have been taken. This will help determine based on the possible severity of the overdose, a worst case scenario is assumed. Outside the turmoil that occurs when children are caught taking

of drugs are involved in potential intoxication also performs medical operations such as taking absorption - reducing measures and monitoring thyroid function, which is a burden on the child. This is possibly prevented by the tablets until the moment of use in the correct packaging. The number increased after the modification of the packaging reports of side effects such that Lareb October 2014 has informed the Medicines Evaluation Board and this the current manufacturer(Aspen Pharma Trading Limited) has requested a DirectSend Healthcare Professional Communication to pharmacists and doctors [8]. This is also broad in the media illuminated. It is therefore not entirely possible to exclude people by repackaging their medication differently tied to prevent further problems.

Conclusion

A blister pack reduces the risk of accidental intake of Thyrax by small children. Also, the amount ingested and thus the seriousness of the intoxications decreases due to the use of child safety litter pack. Thyrax is still used very often in jars, the reason for this is not always clear. If therein the pharmacy room there is a choice for a medicine to make between bulk packaging (jar, bottle) or one blister pack, it is advisable to opt for a blister pack. Especially for patients who have small children, this is important in their household or environment(for example with the babysitter or grandparents). The risk of accidental intake of medicines by small children can be further reduced by (large)to point out to parents/guardians of young children that the packaging of medicines only at the actual must be opened. Any reasons that people have to deviate from this come to light as possible. This allows the pharmacist to work with the patient search for an appropriate solution, such as bidding of a suitable medicine storage box if individual people have difficulty opening the original packaging. Such a conversation can also be used to remind people (again) that it is outside of insight and range of children keep the most effective measure is to prevent accidental drug poison to preventing small children.

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