The Egyptian Journal of Hospital Medicine (April 2018) Vol. 71 (5), Page 3236-3240

Medication Safety Practice in Pediatric Ward

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ABSTRACT
Background: As the medicine advanced, drug therapy became one of the most important and effective therapies in health care system. Which also raises the possibility of its mortality and morbidity. Drug-drug interaction (DDI) is defined as the occurrence of a harmful combination of prescribed drugs in a given patient. DDIs is a known cause of hospital visits, admissions and increases in health care use that could be prevented. In this study, we aimed to detect the DDIs prevalence in pediatric patients in King Abdulaziz university hospital(KAUH), Saudi Arabia.
Methodology: Retrospective cross-sectional study on a sample taken from all pediatric patients at KAUH in Jeddah, Saudi Arabia between January – December 2106, with no exclusion criteria. We extracted the data from KAUH medical files. DDIs, severity and documentation of the DDIs were identified using micromedex. Data entry using microsoft office 2016. Data analysis using SPSS 21 and multivariate regression was done to assess the association of DDI with other factors.
Results: Three hundred and fifty-nine patients were selected with the mean age (SD) 7.06 (5.9), 202 (56.2%) were male. A total of 233 DDIs were identified in 64 (17.8%) of the patients with the mean (SD) 3.64 (3.52). Of all identified DDIs, the severity classification was: major [123 (52.79%)], moderate [67 (28.76%)], minor [37 (15.88%)] and contraindicated [6 (2.58%)]. The documentation of DDIs was excellent [9 (3.8%)], good [89 (38.2%)] and fair [135 (58%)]. Significant association with medications number 5 or more had been suggested.
Conclusion: The prevalence of DDIs although much less than other studies but the higher proportion of major severity. Patients 1-3 years of age and those on 5 or more medications need more strict monitoring as they have more risk to have DDIs.
Keywords: medications, drugs, pediatrics, safety, interactions.

INTRODUCTION

As the medicine advanced, drug therapy became one of the most important and effective therapies in health care system. It also raises the possibility of its mortality and morbidity[1].
In the United States, the economic burden of medication-related morbidity and mortality is as high as $177 billion [2]. Johnson JA estimated the cost of drug-related problems in 2013 about 300 billion in the US [3]. Some studies showed that 85 % of the patients had at least one drug therapy problem and 29 % had five or more drug therapy problems [4]. A research in Saudi Arabia indicated that 4.5 % of hospital admissions was due to drug-related problems [5].
"Administration of an enormous number of medications or administration of several medications at the same time " is the polypharmacy definition stated by WHO [6]. polypharmacy is a common tool in modern medicine especially in patients with chronic diseases, syndromes and elderly [7].
DDI defined as the occurrence of a harmful combination of prescribed drugs in a given patient [8]. DDI in patients with multiple medications is a big concern [9].

An earlier study has suggested that up to 3 % of hospital admissions were due to DDIs [10-12]. DDIs are associated with increased health care use [13]. DDI rates of 32% for pediatric patients and 22% for psychiatric ones [14]. Zurita and Rojop in recent research found that 68 % of a schizophrenic patient at risk of DDI [15]. A meta-analysis conducted by Dechanont demonstrated that the hospital admission rate of DDI was 22.2 % and the hospital visits rate was 8.9% [16]. A recent study done in Saudi Arabia showed that 104 DDI in 57 prescriptions [17]. 49% of hospitalized pediatric were associated with at least one potential DDI [18].

Finally, due to the limited data on DDI prevalence in our region, we aimed to detect the DDIs prevalence in pediatric patients in King Abdulaziz university hospital(KAUH), Saudi Arabia.

METHODOLOGY

Retrospective cross-sectional that was conducted at King Abdul-Aziz university hospital, Jeddah, Saudi Arabia that started from January 2016 – December 2016.
All the admitted pediatric patients were included, sample selection was a systematic random sampling of pediatric patients.

Received:2 /2 /2018 DOI**: 10.12816/0046631**
Accepted:12 /2 /2018

The data were collected from hospital records through data collection sheet. The data sheet made based on previous similar studies on the literature. Age, gender, diagnosis and list of drugs had been taken from hospital records. DDIs had been investigated using micromedex DDI checker.

Age was classified: neonate 0 – 30 days of age, infant 1 month – 2 years, young child 2 – 6 years, child 6 – 12 years and Adolescent 12 – 18 years[6].

Gender was classified into male and female.

The DDIs were classified into: contraindicated, major, moderate, minor and unknown. Major: life-threatening or require medical intervention to minimize or prevent serious adverse effects. Moderate: may result in exacerbation of the patient's condition and/or require an alteration in therapy. Minor: limited clinical effects [19].

The documentation of the interactions was classified into: excellent, good, fair and unknown. Excellent: interaction was established by controlled studies. Good: documentation strongly suggested that the interaction exists. Fair: poor documentation, but pharmacologic considerations lead to suspect the interaction.

The data entered using microsoft excel 2016 then analyzed by SPSS V.21. Categorical variables including primary variables were analyzed using frequency tables. Furthermore, continuous variables were described using mean, standard deviation, and range. The data later was processed in order to find the statistical significance using multivariate logistic regression. For all statistical tests, p values smaller than 0.05 were considered significant.

APPROVAL

This study was approved by the institutional review board of King Abdulaziz University Hospital.

RESULTS

In this study, we aimed to detect the DDIs prevalence in pediatric patients in KAUH, Saudi Arabia.

This research reviewed 380 medical records of 2016 admissions, twenty-one medical records were excluded due to insufficient information.

The mean age (SD) was 7.06 (5.9). Of the total sample, 202 (56.2%) were male and 157 (43.8) were female. (table.1)

Most of the patients were without comorbidities 311 (86.6%). The most common comorbidity was congenital heart disease [4 (1.1 %)] followed by hypothyroidism [3(0.8%)] and Down's syndrome [3(0.8%)].

The most common cause of admission was blood diseases [50 (13.9%)]; thalassemia, sickle cell anemia and acute lymphoblastic leukemia, followed by infectious diseases [36 (10%)] and congenital [34 (9.5%)].

The number of medications was prescribed for those patients in the last admission was 1502 medications with the mean (SD) was 4.18 (4.48). Almost one-third of the patients [116 (32.3 %)] had 5 medications or more, thirty percent of them aged between 1-3 years of age. Forty-four (12.3 %) had no medication at all, 61 (17%) had one medication and 138 (38.4%) had 2-4 medications prescribed for them.

Table 1: characteristic information of the patients and DDIs

		Count	N %	MAJOR	MODERATE	MINOR	CONTRAINDICATED	SUM
				N %	N (%)	N (%)	N (%)	N (%)
GENDER	Male	202	56.30%	60 (25.75)	35 (15.02)	18 (7.73)	0 (0.00)	113 (48.50)
	Female	157	43.70%	63 (27.04)	32 (13.73)	19 (8.15)	6 (2.58)	120 (51.50)
AGE	< 1 yr	33	9.20%	17 (7.30)	5 (2.15)	13 (5.58)	0 (0.00)	35 (15.02)
	1-3 yrs	115	32.00%	58 (24.89)	27 (11.59)	14 (6.01)	6 (2.58)	105 (45.06)
	3-7 yrs	54	15.00%	18 (7.73)	13 (5.58)	4 (1.72)	0 (0.00)	35 (15.02)
	7-12 yrs	64	17.80%	12 (5.15)	6 (2.58)	1 (0.43)	0 (0.00)	19 (8.15)
	>12 yrs	93	25.90%	18 (7.73)	16 (6.87)	5 (2.15)	0 (0.00)	39 (16.74)
Length of stay	1 night	199	55.40%	11 (4.72)	10 (4.29)	4 (1.72)	0 (0.00)	25 (10.73)
	2 night	41	11.40%	4(1.72)	2 (0.86)	3 (1.29)	0 (0.00)	9 (3.86)
	3-7 nights	56	15.60%	25 (10.73)	11 (4.72)	11 (4.72)	0 (0.00)	47 (20.17)
	>7 nights	63	17.50%	83 (35.62)	44 (18.88)	19 (8.15)	6 (2.58)	152 (65.24)
number of	0	44	12.30%	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
	1	61	17.00%	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
	2 – 4	138	38.40%	9 (3.86)	4 (1.72)	7 (3.00)	0 (0.00)	20 (8.58)
	5 or more	116	32.30%	114 (48.93)	63 (27.04)	30 (12.88)	6 (2.58)	213 (91.42)
		359	100.00%	123.00 (52.79)	67 (28.76)	37 (15.88)	6 (2.58)	233 (100)

Using Micromedex to identify interactions between medications revealed that 295 (82.2%) of the patients had no DDI. Two hundred and thirty-three DDIs were identified in 64 (17.8%) of the patients with a mean (SD) of 3.64 (3.52).

Table 2: Side effect of DDI

Side effect	Count	%
CNS depression	17	10.6%
Respiratory depression	16	10.0%
Nephrotoxicity	16	10.0%
QT-interval prolongation	15	9.4%
Hyperkalemia	13	8.1%
Arrhythmias	13	8.1%
Serotonin syndrome	11	6.9%
GI lesion	7	4.4%
Postural hypotension (first dose)	6	3.8%
Ototoxicity	6	3.8%
Hypokalemia	5	3.1%
Bleeding	5	3.1%
Myopathy	4	2.5%
Increase BP	4	2.5%
Hyperglycemia	4	2.5%
Hepatotoxicity	4	2.5%
Cardiotoxicity	4	2.5%
Postoperative paralysis	3	1.9%
Seizure	2	1.3%
Prolong sedation	2	1.3%
Hypotension	2	1.3%
Cardiac depressive effect	1	0.6%

More than half of the interactions were major [123 (52.79%)], moderate [67 (28.76%)], minor [37 (15.88%)] and contraindicated [6 (2.58%]).

The documentation of DDIs was excellent [9 (3.8%)], good [89 (38.2%)] and fair [135 (58%)]. Adverse effects were the outcome of 124 (52.8%) of DDIs such as CNS depression, QT-interval prolongation, arrhythmias, bleeding or nephrotoxicity (table.2). Ninety-eight (41.7%) of the interactions between medications concerns the effect on the other medication; effectiveness, bioavailability, absorption, serum or tissue concentration.

The most common medications involved were midazolam and furosemide. The most common pairs were (midazolam – ranitidine) and (midazolam – chloral hydrate).

A standard logistic regression was performed to study the relationship between the presence of DDIs and the other variables (gender, age, number of medications and length of stay).

No significant association between gender or age and presence of DDIs was found. Although the patient aged 1-3 years were 6 times more likely to have DDIs with near significance p=0.05, association was significant with number of medications of 5 or more (p = 0.002) and with 2 nights stay at hospital (p = 0.001). (table.3)

Table 3: A standard logistic regression between the presence of DDIs and the other variables (gender, age, number of medications and length of stay).

	B	P	OR	95% C.I.for EXP(B)	
Gender					
Male	Reference				
Female	-.513	.129	.599	.309	1.161
Number of meds					
0	Reference				
1	-20.701	.997	.000	.000	.
2-4	-20.677	.997	.000	.000	.
5 ore more	-1.205	.002	.300	.142	.633
Length of stay					
1 night	Reference				
2 nights	-1.597	.001	.202	.082	.498
3-7 nights	-1.166	.054	.312	.095	1.022
> 7 nights	-.697	.107	.498	.213	1.162
Age					
< 1 year	Reference				
1-3 years	1.849	.005	6.357	1.744	23.169
3-7 years	.470	.297	1.600	.661	3.871
7- 12 years	.123	.828	1.131	.373	3.432
>12 years	.081	.875	1.084	.397	2.956

DISCUSSION

Severity

The majority of our sample had major DDI which is supported by similar pediatrics studies such Feinstein 41 % [18] and to a lesser extent by Ismail 34% [21]. Moderate severity interactions of this study were 29.4% which also was supported by Feinstein 28%[18] and the higher proportion found in Ismail 37.8%[21].

Contributing factors:

As our research suggested and supported by **Ismail** study[21] and **Fantaye Teka** [22] that there is no association between the presence of DDIs and gender. On the opposite side, Tragni et al[23] found a relationship between male gender and DDIs in most of DDI pairs. Also, Cruciol-Souza [24] noticed higher risk in the female gender.

Positive correlation of the age with DDIs suggested by retrospective case-control study done at the teaching hospital in Brazil [24] and the increase risk above 50 years of age was also suggested by the Tragni study [23]. Our study found a higher risk in 1-3 years age group. We believe that this is due to a higher number of medications in this age than others. However, van Leeuwen[8] found no association between DDIs and age.

Patients who had five medications or more have a higher risk of DDIs than others as this study suggested and also supported by Fernández de **Palencia Espinosa [25], van Leeuwen [8], Teka [22], Albadr [17], Cruciol-Souza [24], Tragni [23], Holm [1] and Sharma study [20].**

LIMITATIONS

This study did not investigate if the DDIs suggested by Micromedex manifested on the patient, the intervention needed or not. The retrospective design of this study doesn't allow for the follow up of the patients. However, our study provides a great clinical importance of DDIs prevalence and severity that will contribute to improve health care, decrease hospital stay and prevent serious events.

RECOMMENDATIONS

A larger multicentral prospective study needs to be done to detect more accurate prevalence, follow up the patients and record doctors reason for prescribing the medications.

CONCLUSION

In this study, we aimed to detect the DDIs prevalence in the pediatric ward at KAUH. We found that the prevalence of DDIs although much less than other countries, but the higher proportion of major severity was present. Patients 1-3 years of age and those on 5 or more medications need more strict monitoring as they have more risk to have DDIs.

ACKNOWLEDGMENT

We would like to thank Prof. Ahmed S. Ali, Professor of Pharmacology who provided insight and expertise that greatly assisted the research, although he may not agree with all the interpretations/conclusions of this paper. We would also show our gratitude to (Diyaa H.

Bokhary, Nada M. Fussi, Rawan M. Almekhlafi, Mohammed A. Bashanfar, Huda A. Zaher, Abdulrahman S. Batarfi, Ruba A. Al-sanoosy, Aisha S. Aljohani, Basmah A. Alzahrani, Noura A. AlAtwi, Shahad S. Alhibshi, Hamza S. Owaidah) for their help in data collection and revision of earlier versions of this paper, although any errors are our own and should not tarnish the reputations of these esteemed persons.

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