Panacea Journal of Medical Sciences 2020;10(3):337–342

Content available at: https://www.ipinnovative.com/open-access-journals

Panacea Journal of Medical Sciences

Journal homepage: www.ipinnovative.com

Original Research Article

Study of utilisation pattern of fixed dose drug combinations used in pediatric patients at a tertiary care teaching hospital of Eastern India

Aparajita Mohapatra[1], Rajlaxmi Upadhyay[1,*], Rajendra Kumar Panda[2], Manas Ranjan Upadhyay[3], Trupti Rekha Swain[4]

[1]*Dept. of Pharmacology, S.C.B. Medical College and Hospital, Cuttack, Odisha, India*
[2]*Dept. of Pharmacology, MKCG Medical College And Hospital, Brahmapur, Odisha, India*
[3]*Dept. of Pediatrics, FM. M.C.H, Balasore, Odisha, India*
[4]*Dept. of Pharmacology, SLN. M.C.H, Koraput, Odisha, India*

ARTICLE INFO

Article history:
Received 07-11-2020
Accepted 03-12-2020
Available online 29-12-2020

Keywords:
Fixed dose combinations (FDC)

ABSTRACT

Introduction: Fixed dose combinations (FDC) enhance the efficacy of individual drugs, decrease the chances of drug resistance, improve patient compliance and also decrease the pill burden on the patients. Irrational prescribing of FDCs is a major health concern.
Aims & Objectives: To study the utilisation pattern of fixed dose drug combinations used in paediatric patients
Materials and Methods: The study was conducted during September 2014 to October 2015 in paediatric patients visiting the OPD of a tertiary care teaching hospital of eastern India. After obtaining informed consent, prescriptions were collected from OPD every Thursday from 10 A.M. to 1P.M. and data analyzed and evaluated as per W. H. O. prescribing indicators.
Results: 1380 prescriptions were collected and analysed. It was found that most FDCs were antibiotics, multivitamins formulations, analgesic-antipyretic combinations, cough and cold preparations.
Conclusion: There is an increasing trend towards prescribing FDCs. Many of the FDCs are not included in the WHO Model list of essential medicines and the National List of Essential Medicines. Assessment of prescribing pattern in medical care facilities helps in identifying problems regarding rational use and to propose interventions.

1. Introduction

Drug utilisation studies are powerful tools to ascertain the role of drugs in medical practice. Assessment of the prescribing pattern of drugs in the pediatric out patient department(OPD) helps to identify problems regarding rational use of drugs and to propose interventions where needed.[1] The ultimate goal of drug utilisation research is to assess whether drug therapy is rational or not. Fixed-dose combination (FDC) is defined by WHO as "A combination of two or more active ingredients in fixed ratio of doses".[2] Most drugs should ideally be prescribed as single compounds, but doctors prescribe a lot of FDCs forwarding the argument of better patient compliance.[2] The 5^{th} essential medicines list of WHO for children (April 2015) has 341 essential medicines which includes only15 FDCs.[3] The 1^{st} Indian Academy of Pediatrics List of Essential Medicines for Children of India (Oct 2011) has 134 essential medicines out of which 13 are FDCs.[3] Apart from this, hundreds of irrational FDCs are being marketed in India under more than 1000 brand names. Hence the knowledge about prescribing pattern of FDCs is important for better health outcomes. Tertiary care hospitals have a dual role to play in terms of educating post graduate students and providing health care facilities to the patients. Infants and children presenting to the pediatric

* *Corresponding author*.
E-mail address: drrajlaxmi@yahoo.co.in (R. Upadhyay).

https://doi.org/10.18231/j.pjms.2020.070

OPD are mainly suffering from nonserious illness, usually suffering from self-limiting conditions.[4] They are many a times treated inappropriately and inadequately resorting to polypharmacy. There are a large number of studies and data flooded with the pros and cons of prescribing FDC drugs in adults but very few studies are there to assess the usefulness and advantage or the prescribing pattern of FDCs used in pediatric patients.

Hence the present study was conducted with the following objectives:

1. To study the Drug Utilisation Pattern of Fixed Dose Combination of Drugs Used in Pediatric Patients using the WHO prescribing indicators, which in this study includes parameters like.

- To find out the percentage of utilization of fixed dose combination products, among all prescribed medicines in pediatric patients.
- How many drugs were from the National and WHO Essential Medicine List,
- How many of the medications were prescribed in generic names and how many in brand names,
- The various routes of administration of those medications,
- The cost of those combination medicines against their individual counterparts, wherever feasible and
- To study the demographic profile of patients attending the OPD.

2. Materials and Methods

2.1. Study Design and Ethical consideration

This is a cross-sectional and observational study in a tertiary care pediatric hospital of Eastern India. Informed consent was obtained from the guardians or relatives of the pediatric patients in local language. This study is approved by the Institutional Ethics committee.

2.2. Sample size and data collection

A total of 1380 prescriptions of patients attending pediatric OPD was collected over a period of 14 months from September 2014 to October 2015 out of which 1131(81.96%) were legible and hence analysed. Data was collected on every Thursday during OPD timing from 10 am to 1 pm.

2.3. Selection criteria

Selection of the prescriptions were done as per the following criteria.

2.4. Inclusion criteria

1. Prescriptions of all pediatric patients under the age of 14 years and of either sex visiting the OPD during the study period.
2. Prescriptions which were legible.

2.5. Exclusion criteria

Patients are excluded from the study for any of the following reasons-

1. Prescriptions of patients who did not give consent.
2. Prescriptions of the indoor patients coming to outdoor.
3. Prescriptions containing medication from other systems of medicine.

2.6. Study procedure

All data were collected in a prescribed proforma and entered in a master chart from where it was analysed as per WHO core indicators(5)and then entered in a master chart from where it was analysed.

2.7. Data analysis

The following data were recorded and analysed

1. Patient details like: age, sex, date of OPD visit, disease condition(s), age-wise disease trend.
2. Presenting complaints of patients.
3. Diagnosis of patient disease.
4. The number of FDCs prescribed .
5. The number of drugs prescribed.
6. The names of drugs prescribed for their disease conditions.
7. The individual constituents of FDCs,
8. Whether the FDCs is in the WHO Essential Medicine List 2011 and National List of Medicine , India 2011.
9. Whether the prescribing of FDC was using a generic name
10. The pharmacological system to which the drugs belonged.
11. Routes by which drug was given.
12. Formulation of each drug.
13. Comparison of the prices of those fixed dose drug combinations as against their individual counterparts
14. Various age groups in which various FDCs were prescribed
15. Which group of medications contained more FDCs.

2.8. Statistical analysis

All the data obtained were calculated as percentage of total FDC

3. Results

Total 1380 prescriptions were collected from the patient's relative / guardian with consent. 249 prescriptions were illegible and were discarded from the study. Maximum

number of patients came to the OPD in the month of August, followed by June and July i.e. 121,119 & 112 respectively. The least number of patients came to OPD in the month of March and April.

Table 1: Age-wise distribution of FDCs.

Age group	No. of prescriptions	No .of formulations	No. of FDCs	Percentage of total FDCs
<1 yr	252	1004	501	49.9%
1yr to < 6yrs	576	1751	917	52.37%
6yrs to <12 yrs	267	1059	557	27.33%
>12 yrs	36	145	63	43.44%
Total	1131	3959	2038	51.46%

Table 1 Of the total 3959 formulations prescribed to the 1131 patients, 2038 (51.46%) were fixed dose combination and rest 1921 (48.54%) were single drugs. Most of FDC prescription were encountered in children between 1yrs to <6 years of age.

Table 2: Sex distribution of study population

Sex	Number
Male child	714
Female child	414
Ambiguous genitalia	3
Total	1131

Out of 1131 prescriptions 714 are male child, 414 female child and 3 were mixed genitalia.

Table 3: Drug categories among the FDCs

S. No.	Drug categories	Number	Percentage of total FDCs
1	Antimicrobials	496	25.33
2	Multivitamins + nutritional supplements	446	22.62
3	Anticold medications	271	13.84
4	Analgesic-antipyretics	91	4.65
5	Antihistaminics	74	3.78
6	Digestive enzymes	25	1.28
7	antispasmodics	94	4.8
8	ors	182	9.3
9	Cough syrups	201	10.27
10	Appetizer	78	3.98
	Total	1958	100%

Total number of orally prescribed drugs is equal to 1958, antimicrobials are the most commonly prescribed FDC drugs.

Table 4: FDCs used as Topical preparations.

S.No.		Trade name	Number	Percentage of total FDCs
1	Ear drop	Candibiotic	13	16.25
2	Nasal drop	Hynasal	26	32.50
3	Ointment for mixed dermatosis	Zincoderm/ cosvate gm	30	37.50
4	Mouth paints	Orahelp/oraflora	11	13.75
	Total		80	100%

Ointment for mixed dermatosis (30 out of 80) are the most frequently prescribed topical preparations.

Table 5: Formulation in Generic / Trade name (n=1131)

	Number of medications	Percentage of total FDCs
Generic name	1428	36.07%
Trade name	2531	63.93%
Total	3959	100%

Out of 1131 prescriptions containing 3959 mediations, 1428 drugs were in generic name and 2531 drugs in trade name.

Table 6: Antimicrobial agents prescribed as FDCs

S. No.	Combinations	Total number	Percentage of total FDCs
1	Cefixime +probiotics	19	3.83
2	Cefpodoxime + pot. clavulanate	37	7.45
3	Amoxycillin+clavulanate	156	31.45
4	Ofloxacin+ornidazole	91	18.34
5	Sulfamethoxazole+ pyrimethamine	59	11.90
6	Artemether+lumefantrine	79	15.93
7	Artesunate & sulfadoxine+ pyrimethamine	39	7.87
8	Albendazole+ivermectin	16	3.23
	Total	496	100%

Most commonly prescribed antimicrobial is amoxycillin +clavulanate , 31.45% of total FDCs

Table 7: Prescribed FDC in Essential Medicine List

Total FDCs	EML	Not in EML
2038	417(20.46%)	1621(79.54%)

Out of 2038 FDCs 20.46% drugs were from the EML, 79.54% drugs not from EML

Table 8: Number of Constituents per FDCs (n=2038)

No. of constituents	Total no of FDCs	Percentage of total FDCs
2	798	39.15%
3	659	32.33%
4	145	7.11%
5 and more	446	21.8%
Total	2038	100%

Most of the FDCs have 2 drug combinations

Table 9: Comparison of prices of few FDCs against their individual components.

S. No.	FDC in trade name	Price of FDC	Price of individual components	Total price of individual component	Percentage Difference
1	Syp. Neuro-M	Rs 15.75	1)Mecobalamine-Rs 20.50 2)Folic acid-Rs 15.00	Rs 35.50	125.39%
2	Syp. Bandy-plus	Rs 15.23	1)Albendazole-Rs 19.50 2)Ivermectin-Rs 15.50	Rs 35.00	129.81%
3	Syp. Shelcal	Rs 50/-	1)Calcium-Rs 28.75 2)Vitamin-D3-Rs 33.50	Rs 62.25	24.5%
4	Syp.Telekast-L Kid/ Montec-LC	Rs 25.00	1)Levocetirizine dihydrochloride-Rs 15.00 2)Montelukast-Rs 28.30	Rs 43.30	73.2%
5	Syp.O2/ Oflomac Oz	Rs 45.00	1)Ofloxacin-Rs 42.20 2)Ornidazole-Rs 29.50	Rs 71.50	58.89%
6	Syp. Cefolac	Rs 45.00	1)Cefixime-Rs 55.00 2)Lactobacillus-Rs 20.00	Rs 75.00	66.67%
7	Syp. Ibugesic-plus	Rs 21.15	1)Ibuprofen-Rs 22.00 2)Paracetamol-Rs 17.00	Rs 39.60	87.23%
8	Syp. Drotin plus	Rs 50.00	1)Drotaverine-Rs 25.50 2)Paracetamol-Rs 35.75	Rs 61.25	22.5%

The Table 9 shows the comparison of prices of few FDC against their individual components. The percentage difference was calculated by the formula as the difference of the two values divided by the average of the two values, that is "Total price of individual components of drugs minus price of the FDC divided by average of the two values multiplied by 100."

All the FDCs were cheaper than the total of the price of the individual components.

Table 10: Comparative table of FDC use in this study and MAMC

No. of Constituents in FDCs	Our Study	Akhil Dahiya, MAMC
2	39.15%	33.5%
3	32.33%	5.3%
4	7.11%	15.2%
5 &>5	21.8%	45.9%

Table 10 This shows that in this study FDCs with two drug constituents are more frequently prescribed.

Of the total 2038 FDCs prescribed, 1958(96.07%) were prescribed by oral route, rest 80(3.93%) were prescribed by topical routes. 25.33 % out of all FDCs were antibiotic combinations followed by multivitamin and nutritional supplements 22.62%.

4. Discussion

The present study entitled "Study of the utilisation pattern of fixed dose combination of drugs used in paediatric patients" was conducted over a period of 14 months at a tertiary hospital at Cuttack, Odisha and data was collected in observational, cross-sectional manner in the OPD. A total of 1131 prescriptions met the inclusion criteria.

This study revealed a male preponderance (63.13%) over females (36.6%) as similar to a study conducted by S.P.Londhe et al from Rajkot, which showed 55% were males & 45% were females.[4] Similarly Laveesh M R et al in a study analysed 540 patients out of which 298(55.18%) were males and 242(44.81%) were females.[5]

This study shows the average number of formulations per prescription is 3.5. Akhil Dahiya from MAMC had conducted similar type of study in New Delhi which showed average number of drugs per prescription was 3.93±1.73.

In this study, the most commonly prescribed FDCs were antimicrobial agents (25.33%) followed by multivitamins & nutritional supplements (22.78%). This finding is in accordance with the study conducted by Rayasam S.P. et al in which antibiotics were most commonly prescribed FDCs.[6] Similar study done by Lande S.P. et al from Rajkot, Gujarat showed that antibiotics are the most commonly prescribed FDCs(23%).[4] Laveesh MR et al in his study found 25.37% of prescriptions contain antimicrobial agents. Akhil Dahiya in his study showed antimicrobial agents are the second most frequently prescribed FDCs constituting 22.9% of the total FDCs prescribed(7). A large number of studies in children where FDCs are evaluated have shown antimicrobials are the most commonly prescribed like in a study by Dimri S, Tiwari P, Basu S and Parver V.R. showing antibiotics as prescribed in 29.1% of prescriptions.[6]

Multivitamins and nutritional supplements are the second most commonly prescribed FDCs (22.78%) in this pediatric outdoor. But a study by Balat et al, from Gujarat showed maximum number of FDCs were nutritional supplements(20.2%).[7] Akhil Dahiya from MAMC, New Delhi in his study showed that majority of FDCs prescribed belonged to vitamins & minerals(53.5%) which is much

higher than our study.[8] A study conducted by Rajanish Kumar Sankdia and Mehul Agarwal in a teaching hospital in Bhopal showed B-Complex was the most commonly prescribed FDC unlike in this present study where antimicrobial are the most commonly prescribed FDC(10).

The Drug Controller General of India (DCGI) has banned the use of vit B1, vit B3 and vit B12 in combination for human use as it has no therapeutic advantage over the individual drug,[7] so also a FDC of Vit B1, Vit B6 and Vit B12 is banned for human use.[9]

This study was conducted for 14 months, that is throughout the year to minimize the bias due to seasonal influence on use of FDCs. In 1131 legible prescriptions 2038 FDCs were prescribed that is on an average 1.8 FDCs were prescribed per prescription. Of the total 3959formulation prescribed , FDCs accounts for the 51.46%(2038) in contrast to a study by Raj Goel, Sanjay Khanna, Anoop Verma, Pratap Shankar, Vipender Singh Chopra, Rakesh Kumar Dixit in OPD of pediatrics, Ghaziabad, Uttar Pradesh showing FDC accounted for 18.1% of drugs out of total number of drugs prescribed,[10] suggestting moderate use of FDCs in this hospital but similar study by J.D. Balat from Ahmedabad showed shown that 80% of the prescription contained one or more than one FDCs.[7] Akhil Dahiya from MAMC had shown in a study that 7.45% of the prescription had FDC.[8] Ratnakar UP et al in a study from Karnataka showed the use of 63.8% FDCs from Kasturba Medical College hospital.[11] Since this is a pediatric OPD, where multivitamins and nutritional supplements which accounts for 22.62% of the total FDC followed by anticold medications and cough syrup. That is 24.1%, moderate use of FDC i.e., 51.46% is justified. This study shows that out of the total formulations, 1428(36.07%) were prescribed in generic name in contrast to 63.93% were prescribed in brand name. The main reason to prescribe in the brand name is that most of the time OPD is overloaded, where time is precious, writing the prescription in generic name, for example CLAVAM, instead of Amoxycillin + Clavaunic acid, SEPTRAN instead of Sulfamethaxole + Trimethoprim, lumerax instead of Artemether+ Lumefantrene is less time consuming. This study results shows similarity with Akhil Dahiya et al from MAMC, New Delhi which in a study has shown that drug prescribed by generic name in New Delhi is 31.1%.[8] A similar study by Sanjay Sankhala and Suchitra Gaur have concluded that only 13.09% were by official or generic name and rest 86.91% were by brand names.[12]

Of these FDCs prescribed, maximum number of FDCs were prescribed in the age group 1 year to<6 yrs i.e. 917(52.37%), followed by 6 to <12yrs i.e. 557 (27.33%). These results are not consistent with the study of Balat et al in Gujarat and another study in Uttaranchal, as this study was conducted in pediatric age group[7,13]

Majority of the FDCs in our study shows 96.08% were prescribed for oral use and 3.92 % are prescribed for topical use.Table 7 shows there was statistically significant difference between oral and topical route. This is at par with the study of Balat et al which showed that FDCs by oral route in 92 % suggesting that oral route is the most common and preferred route for prescribing the FDCs.

It was observed that out of 2038 FDCs prescribed only 417 (20.46%) were included in Essential Drug List of WHO /National/Odisha. This result is also similar to another study by Akhil Dahiya from MAMC, which showed that 19.7% of the prescribed FDCs were present in WHO EML 2011 and 18.9% FDCs are present in NEML, India 2011,[8] This study has similar findings with the study conducted by Jain N.K et.al in which 20% FDCs were from the W.H.O Essential Drug List. S. P Londhee et al from Gujarat in a tertiary care teaching ospital showed that 1.4% of the prescribed FDCs were in the W.H.O Essential Drug List.

This study shows highest percentage of FDCs with 2 constituents (39.15%) in contrast to study by Akhil Dahiya et al from MAMC, New Delhi where FDCs with 5 &>5 constituents were prescribed in 45.9%.[13] A study done by Nimbagiri Swammy Thiruthopu, Uday Venkat Mateti, Raju Bairi, Divya Sivva and Srinivas Martha showed 4.5 number of drugs per average prescription.[14] FDCs with three constituents were present in 32.33% of total FDCs prescribed in this study in contrast to study by A. Dahiya et al where only 5.3% of FDCs prescribed with three constituents.[8] In our set up FDCs with two drug constituents are more frequently prescribed. The cost analysis revealed that cost of all the prescribed FDCs wherever feasible for analysis were cheaper as compared to the sum of cost of their individual cost as shown in Table 9. This study shows cost difference of 8 FDCs was Rs. 159.87with a mean of Rs19.98. Ratnakar UP et al from Kasturaba Medical College, Karnataka in a similar study has shown that mean cost of FDC per prescription per day was Rs 9.03.[11] However this aspect requires further evaluation in case of other FDCs.

5. Conclusion

The study revealed that more than 50% of the prescriptions contain fixed dose combinations of drugs. Out of this about only one third formulations are prescribed in generic name and rest are in brand name. Out of the total number of FDC prescribed, majority were used by oral route. Most of the drug combinations prescribed was not included in National Essential medicine list. Most common drug categories are antimicrobials. However, cost analysis of the FDCs revealed that the FDCs were much cheaper compared to individual drug combinations.

6. Source of Funding

No financial support was received for the work within this manuscript.

7. Conflict of Interest

The authors declare they have no conflict of interest.

References

1. Kumar V, Gupta N, Kumar KA. A comparision between old and latest systems in DPCO. *Int J Pharm Pharm Sci*. 2014;6(2):19–20.
2. Nigam M, Fernandes V, Rataboli P. Fixed dose combinations-to prescribe or not to prescribe: a dilemma of medical profession. *Int J Basic Clin Pharmacol*. 2014;3(1):105–13. doi:10.5455/2319-2003.ijbcp20140212.
3. National Essential Medicine list(NEML)- World Health Organisation. Available from: https://apps.who.int/medicinedocs/en/cl/CL6.4.1.1.15.16/clmd.
4. Mirza NY, Desai S, Ganguly B. Prescribing pattern in a pediatric out-patient department in Gujarat. *Bangladesh J Pharmacol*. 2008;4(1):39–42. doi:10.3329/bjp.v4i1.1062.
5. Londhe SP, Basavanagowda GM, Gowraw NS, Roopashree PM, Baishnab S. Study of Prescribing Pattern of Fixed Dose Combinations in the Medicine Department of a South Indian Tertiary Care Teaching Hospital. *Int J Pharm Res Sch*;(4):168–77.
6. Dimri S, Tiwari P, Basu S, Parmar VR. Drug use pattern in children at a teaching hospital. *Indian Pediatr*. 2009;46(2):165–7.
7. Balat JD, Gandhi AM, Patel PP, Dikshit RK. A study of use of fixed dose combinations in Ahmedabad, India. *Indian J Pharmacol*. 2014;46(5):503–9. doi:10.4103/0253-7613.140581.
8. *The Journal of MacroTrends in Health and Medicine*;.
9. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/list-banned-drugs.html.
10. Goel RK, Khanna S, Verma A, Shankar P, Chopra VS. Drug prescribing pattern in the outpatient department of pediatrics in Ghaziabad. *Int J Pharma Sci Res*. 2013;4(4):78–80.
11. Kardas P.
12. Sankhla S, Gaur S. A retrospective study of drug utilization pattern in the outpatient department of pediatrics in a tertiary care teaching hospital of Rajasthan, India. *Int J Basic Clin Pharmacol*. 2016;p. 2025–31. doi:10.18203/2319-2003.ijbcp20163231.
13. Sharma T, Dutta S, Dhasmana DC. Prescribing pattern of NSAIDs in orthopaedic OPD of a tertiary care teaching hospital in Uttaranchal. *JK Sci*. 2006;8:160–2.
14. Martha S, Thiruthopu NS, Mateti UV, Bairi R, Sivva D. Drug utilization pattern in South Indian pediatric population: A prospective study. *Perspect Clin Res*. 2014;5(4):178. doi:10.4103/2229-3485.140558.

Author biography

Aparajita Mohapatra, Assistant Professor

Rajlaxmi Upadhyay, Assistant Professor

Rajendra Kumar Panda, Ex- Associate Professor

Manas Ranjan Upadhyay, Associate Professor

Trupti Rekha Swain, Professor and HOD

Cite this article: Mohapatra A, Upadhyay R, Panda RK, Upadhyay MR, Swain TR. Study of utilisation pattern of fixed dose drug combinations used in pediatric patients at a tertiary care teaching hospital of Eastern India. *Panacea J Med Sci* 2020;10(3):337-342.