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Evaluation of Intravenous Admixtures in Tertiary Care Teaching Hospital

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ABSTRACT

Intravenous medication continues to expand and there is an increase in number of mediations administered to the each patient. There are no specific studies to identify the incompatibilities the commonly occur in hospitalized patients while administering these intravenous admixtures. The main objective of the study was to assess the potential incompatibilities associated with Intravenous admixtures in tertiary care teaching hospital. The data for the present study was collected by Patient interview and Chart Review Method for a period of 6 months. This study included all the hospitalized patients form General Medicine Departments. The Collected data was analyzed for incompatibilities using standard drug reference books. This prospective study found out 104 combinations (both Drug-Solute and Drug-Drug combinations) among them 20 (19.23%) were compatible, 24 (23.07%) incompatible, 5 (4.80%) were variable and 55 (52.88%) were undocumented combinations. This study concluded that such type of research work would certainly increase the safety in the use of intravenous admixtures. It is important to make health care professionals aware of compatibility problems, daily prescription review by clinical pharmacist and providing unbiased information from reliable references could possibly prevent compatibility errors found on the wards.

Keywords: Intravenous admixtures, Physical Incompatibility, Y-site, Compatibility chart, Clinical Pharmacist.

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INTRODUCTION

Intravenous admixtures are the preparations consist of one or more sterile drug products added to an IV fluid, generally Sodium Chloride Solution (0.9% Nacl) or Dextrose alone or in combination. IV admixtures are used for drugs intended for continuous infusion. Drugs that may cause irritation or toxicity when given as a rapid direct IV injection are also prepared as IV admixtures[1]. These parental drug solutions are commonly mixed in the same infusion bag, at the Y-site junction where two or more IV lines meet and in the same syringe[2]. Intravenous Incompatibilities occur when two are more drugs are administered through a single intravenous line or given in a single solution, resulting in an undesirable reaction[3]. They arise during preparation and administration of drugs[4]. A patient who receives a preparation in which an incompatibility has occurred could experience toxicity or an incomplete therapeutic effect.These are also known as reactions of IV drugs resulting in solutions that are no longer safer for the patient[5]. There are three types of incompatibilities physical, chemical and therapeutic incompatibilities[6]. A physical incompatibility occurs when a drug combination produces a visible change in the appearance of a solution.[1]It is also known as "Pharmaceutical Incompatibility or Visual Incompatibility" [7]. Physical incompatibilities are observed most easily and can be detected by changes in the appearance of admixture such as change in color, formation of precipitate or evolution of gas. This renders the solution unsafe for administration[5]. A chemical incompatibility reflects the chemical degradation of one or more of the admixed drugs, resulting in toxicity or therapeutic inactivity[2]. The degradation is not always visible but the reaction of drug or drugs in solutions which results in alterations in either integrity or potency of the drug[8]. Non-visible chemical incompatibility may be detected only by analytical methods[5]. Large amount of particulate matter in injections is considered as a potential life threatening health hazard[9]. Drug incompatibility reactions may not only generate particles in the infustae, but also transform drug into an inactive form and deleterious effects on the patients prescribed drug regimen. Clinical effects of incompatibilities are hypoxia, impairment in discharge of metabolic products and finally tissue ischemia. These incompatibilities may therefore have most detrimental effects in patients who suffer from preexisting microcirculatory disorders due to trauma, major surgery, sepsis etc. In these patients incompatibilities may lead to a further and serious reduction in microcirculation[10]. It is prudent not to mix the solutions of parenteral drugs without knowledge of their compatibility[2]. Information regarding drug incompatibilities are well documented in computer databases, American reference books[11,12] and information leaf lets

published by pharmaceutical laboratories[4]. The number of IV medications continues to expand and the need to administer different IV drug combinations are increasing day by day.[13]In general nursing staff prepare and administer intravenous drugs prescribed by Doctors. Due to increased number of drug combinations, the knowledge regarding intravenous drugs is limited. It is not possible to predict all incompatibilities but the presence of clinical pharmacist in ward, clinical review of possible incompatibilities may minimize the occurrence and ultimately it increases the patient safety. Hence the main objective of the study was to identify parenteral drug combinations and to categorize them into compatible, incompatible and undocumented drug combinations based on literature.

MATERIALS AND METHOD

The study was conducted in Department of General Medicine at Rajiv Gandhi Institute of Medical Sciences (RIMS), Kadapa,a 750 bedded multi-disciplinary tertiary care teaching hospital for a period of 6 months (December 2013 to May 2014). This is anprospective observational study and the total number of cases included were 145.

Ethical Considerations:

The study was done after obtaining approval from Institutional Ethics and Research Committee of Rajiv Gandhi Institute of Medical Sciences, Kadapa(RC. No.3349/Acad./2013-14/Dated 19-11-2013).

Data Collection

The data for the present study was collected by "Patient interview" and "Chart Review Method", which is well suited to identify the prescribed drugs for the individual patients. A suitable data collection form was prepared and utilized to collect the study details. This form mainly contains details likepatients demographics, reasons for hospitalization, drugs and solutes and method of drug administration. Drug administration data was collected basing on 2 criteria

a) When a single drug delivered by infusion, the compatibility of drug in solution will be noted.
b) When two or more drugs are used in the same infusion line then drug-drug and drug-solute compatibilities will be noted.

This obtained data will be compared with the information available in the literature, i.e., from Incompatibility Charts and by referring Standard Text Books on Intravenous Admixtures.

The following are the literature used to analyze the collected data;

Drugdex-Drug evaluation monographs in Micromedex 2.0 (Computer drug database), AHFS Drug Information 2010,2011.s[11, 12], British National Formulary 57thEdition. [13], Trissel's

Handbook on Inject able drugs.[14]

Published leaflets of Pharmaceutical companies.

Incompatibility charts are made available on the wards and the usage of them was taught to the nursing staff by us to prevent unsafe medication administration practices.

RESULTS AND DISCUSSION

The study population is of 145 cases with respect to age group that majority of patients were found in between the age group of 46 - 60 years were 73 (50.34%), followed by 45 (31%) were in between the age group of 20 - 40 years and 27 (18.62%) were at above 60 years. The demographic details are mentioned in Table 1

Table 1: Age wise distribution of study population

Age groups (yrs.)	No. of male (%)	No. of female (%)	Total (%)
20- 40	17 (24.63%)	28 (36.84%)	45 (31.03%)
40- 60	33 (47.82%)	40 (52.63%)	73 (50.34%)
>60	19 (27.53%)	8 (10.52%)	27 (18.62%)
Total	69 (47.58%)	76 (52.41%)	145 (100)

Details on Compatibility of IV drugs administered during the study period: Out of 145 study population we found a total of 104 Intravenous drug admixtures combinations, among that

i) Drug – IV solution Combinations were 15 (14.42%) which includes, based on contact site (Y – site) 7 (6.73%) were compatible, 2 (1.92%) were incompatible, 1 (0.96%) were variable and 5 (4.80%) were undocumented.

ii) Drug – Drug Combinations were 89 (85.57%) which includes, based on contact site (Y – site) 85 (81.73%), i.e., 12 (11.53%) were compatible, 21 (20.19%) were incompatible, 4 (3.84%) were variable, 48 (46.15%) were undocumented and based on Mixture site (i.e., when two parenteral drugs are mixed in same syringe) 4 (3.84%)among those 1 (0.96%) were compatible, 1(0.96%) were incompatible and 2 (1.92%) were undocumented. Details of IV drugs administered are mentioned in Table 2

Table 2: Details Compatibility of IV drugs administered during study period (Separately)

Compatibility	No. of Drug – IV solution Combinations		No. of Drug – Drug Combination		Total (%)
	Y - site	Mixture	Y-site	Mixture	
Compatible	7 (6.73%)	0	12 (11.53%)	1 (0.96%)	20 (19.23%)
Incompatible	2 (1.92%)	0	21 (20.19%)	1 (0.96%)	24 (23.07%)
Variable	1 (0.96%)	0	4 (3.84%)	0	5 (4.80%)
Undocumented	5 (4.80%)	0	48 (46.15%)	2 (1.92%)	55 (52.88%)
Total	15(14.42%)	0	85 (81.73%)	4 (3.84%)	104 (100%)

Compatible Drug & IV solution combinations:

Out of 15 Drug – IV solution combinations, 7 (46.66%) were found to be Compatible Combinations they are Streptokinase + Normal saline, Multivitamin + Normal saline 3 (23.07%) times followed by Theophylline + Normal saline, Iron sucrose + Normal saline i.e., 2 (18.18%) times.

Table 3: Details on frequency of usage of Compatible Drug & IV solution combinations

Compatible Drug & IV solution combinations	Frequency (N= 13)	Frequency (%)
Streptokinase + Normal saline		
Multivitamin + Normal saline	3	23.07 %
Theophylline + Normal saline		
Iron sucrose + Normal saline	2	15.38 %
Calcium + Normal saline		
Dopamine + Normal saline	1	7.69 %
Atropine + Normal saline		

Incompatible Drug & IV solution combinations:

Out of 15 Drug – IV solution combinations, 2 (13.33%) were found to be Incompatible drug – IV solution combinations i.e., Phenytoin + Normal saline is the frequently used combination 2 (66.66%) & Ceftriaxone + Ringer lactate 1 (33.33%). Details are mentioned in Table 4 when Phenytoin is mixed with normal saline solution or dilution of injectable Phenytoin by adding to an infusion bag containing normal saline lowers it P^H and therefore, it reduces its solubility resulting in precipitation of the drug. This is because Phenytoin is formulated with non-aqueous solubilizing agents and the solution P^H is adjusted to 12. Indeed Phenytoin injection is so incompatible that it should not generally be mixed with any other solutions[2]. Ceftriaxone is incompatible with Lactated Ringer's solution as the calcium present in this solution form precipitate with ceftriaxone. So, ceftriaxone should not be diluted with Lactated Ringer's solution and Hartmann's solution[15].

Table 4: Details on frequency of usage of Incompatible Drug & IV solution combinations

Incompatible Drug & IV solution combinations	Frequency N = 3	Frequency %
Phenytoin + Normal saline	2	66.66%
Ceftriaxone + Ringer lactate	1	33.33%

Variable Drug & IV solution combinations:

Out of 15 Drug – IV solution combinations, 1 (6.66%) were found to be variable combination (Phenytoin + DNS). The literature data was found to be conflicting regarding this combination.

Undocumented Drug & IV solution combinations:

Out of 15 Drug – IV solution combinations, 5 (33.33%) were found to be undocumented drug – IV solution combinations, Diclofenac + NS, Hepamerz + DNS is the frequently used combination 2 (28.57%), followed by use of Diclofenac + RL, Edveran + NS, and N-Acetylcystine + NS 1 (14.28%). Details are mentioned in Table 5

Table 5: Details on frequency of usage of Undocumented Drug & IV solution combinations

Drug – solution combination	Frequency (N= 7)	Frequency (%)
Diclofenac + Normal saline Hepamerz + Dextrose normal saline	2	28.57%
Diclofenac + Ringer lactate Edveran + Normal saline	1	14.28%
N- Acetylcystine + Normal saline		

Compatible Drug - Drug Combinations:

Out of 13 Compatible Drug – Drug combinations, Ceftriaxone + Pantoprazole is the most frequently used combination 46 (48.1%), followed by Ceftriaxone + Furosemide 17 (15.45%) and Deriphylline + Pantoprazole 6 (5.45%) etc. Details are mentioned in Table 6 compatibility data has already been established for these Drug-Drug combinations.

Table 6: Details on frequency of usage of Compatible Drug - Drug Combinations

Compatible drug combinations (n = 13)	Frequency	Frequency (%)
Ceftriaxone + Pantoprazole	46	41.81%
Ceftriaxone + Furosemide	17	15.45%
Deriphylline + Pantoprazole	6	5.45%
Furosemide + Deriphylline	5	4.54%
Ciprofloxacin+ Metronidazole	4	
Ceftriaxone + Metronidazole		3.63%
Dexamethasone + Ondansetron	2	1.81%
Furosemide + Ranitidine Ceftriaxone + Mannitol	2	1.81%
Hydrocortisone + Pipercilintazobactum Ranitidine + Furosemide Pipercilintazobactum + Ondansetron	1	0.90%
Deriphylline + Hydrocortisone 13	149	100%

Incompatible Drug - Drug Combinations:

Out of 22 Incompatible Drug – Drug combinations, Furosemide + Pantoprazole is the most frequently used combination i.e., 24 (22.22%), followed by Ondansetron + Pantoprazole 13 (12.03%) and Hydrocortisone + Pantoprazole 11 (10.18%) etc. The P^H of Furosemide solution is 8.0-9.3 and it is unstable in acidic media. So, the most of the acidic drugs such as Ondansetron with P^H 3.3-4and Ciprofloxacin with P^H 3.3-3.9 are incompatible when mixed with Furosemide.

So, avoid use of these drugs together. However, in emergency conditions when concomitant administration is required the manufacturers recommend maintaining time gap between administrations and flushing of IV line with their respective compatible solutions is necessary[12,16]. Details are mentioned in Table 7.

Table 7: Details on frequency of usage of Incompatible Drug - Drug Combinations

Incompatible Drug – Drug combinations (n = 22)	Frequency	Frequency (%)
Furosemide + Pantoprazole	24	22.22%
Ondansetron + Pantoprazole	13	12.03%
Hydrocortisone + Pantoprazole	11	10.18%
Pipercilintazobactum + Pantoprazole	7	6.48%
Ciprofloxacin + Pantoprazole	5	4.62%
Diazepam + Pantoprazole Phenytoin + Pantoprazole Dexamethasone + Pantoprazole Ceftriaxone + Deriphylline Cefotaxime + Pantoprazole	4	3.70%
Ciprofloxacin + Ceftriaxone Furosemide + Ondansetron Metronidazole + Pantoprazole Phenytoin + Diazepam	3	2.77%
Furosemide + Ciprofloxacin Atropine + Pantoprazole Pantoprazole + Amikacin Diazepam + Ceftriaxone Phenytoin + Ceftriaxone	2	1.85%
Deriphylline + Ondansetron	1	0.92%
Pantoprazole + Ranitidine	1	0.92%
Hydrocortisone + Ampicillin		
22	108	100%

Variable Drug - Drug Combinations:

Out of 4 Variable Drug – Drug combinations among that, Furosemide + Hydrocortisone is the most frequently used combination i.e., 5 (45.45%), followed by Pipercillin - tazobactum + Amikacin i.e., 3 (27.27%), Mannitol + Pantoprazole 2 (18.18%) etc. Though the variable combinations have conflicting data regarding their incompatibility so, it is better to avoid the use of such combinations to minimize the incompatibilities. Details regarding these combinations are mentioned in Table 8.

Table 8: Details on frequency of usage of Variable Drug - Drug Combinations

Variable Drug – Drug combinations (n = 4)	Frequency	Frequency (%)
Furosemide + Hydrocortisone	5	45.45%
Pipercilintazobactum + Amikacin	3	27.27%
Mannitol + Pantoprazole	2	18.18%

Ampicillin + Ranitidine	1	9.09%
4	11	100%

Undocumented Drug - Drug Combinations:

Out of 50 Undocumented Drug – Drug combinations, Augmentin + Pantoprazole is the most frequently used combination i.e., 11 (9.09%) followed by Ceftriaxone + Ranitidine, Ceftriaxone + Ondansetron 9 (7.43%), Pantoprazole + Piracetam 8 (6.61%) etc. These undocumented combinations don't have any evidence of data regarding their compatibility. Details are mentioned in Table 9.

Table 9: Details on frequency of usage of Undocumented Drug – Drug Combinations

Undocumented Drug – Drug combination (n = 50)	Frequency	Frequency (%)
Augmentin + Pantoprazole	11	9.09%
Ceftriaxone + Ranitidine, Ceftriaxone + Ondansetron	9	7.43%
Pantoprazole + Piracetam	8	6.61%
Augmentin + Deriphylline, Hydrocortisone + Chlorpheneramine maleate	7	5.78%
Augmentin + Furosemide	6	4.95%
Hydrocortisone + Ceftriaxone	5	4.13%
Chlorpheneramine maleate + Pantoprazole Piracetam + Ceftriaxone	4	3.30%
Augmentin + Dexamethasone, Mannitol + Piracetam	3	2.47%
Chlorpheneramine maleate + Furosemide Piracetam + Furosemide, Augmentin + Hydrocortisone Augmentin + Ondansetron, Furosemide + Cefotaxime Dexamethasone + Ceftriaxone Metronidazole + Ondansetron Augmentin + Ranitidine, Edveran + Piracetam Hydrocortisone + Dexamethasone, Dicyclomine + Ranitidine,Dicyclomine + Pantoprazole Dicyclomine + Ceftriaxone,Vitamin K +Ceftriaxone Vitamin K + Ranitidine,Vitamin K + Furosemide Hydrocortisone + Ranitidine, Piracetam + Ranitidine Augmentin + Ethamsylate, Deriphylline + Ethamsylate Multi vitamin + Pantoprazole, Ciprofloxacin + Ondansetron Multi vitamin + Hydrocortisone	2	1.65%
Hydrocortisone + Piracetam Pipercilintazobactum + Piracetam Multi vitamin + Pipercilintazobactum Phenytoin + Artesunate, Ceftriaxone + Artesunate Chlorpheneramine malate + Ceftriaxone Augmentin + Paridaxamine, Pantoprazole + Paridaxamine Pipercilintazobactum + Ceftriaxone Phenytoin + Cefotaxime, Piracetam + Diazepam Piracetam + Phenytoin, Furosemide + Pipercilintazobactum Ciprofloxacin + Pipercilintazobactum	1	0.82%
50	**112%**	**100%**

Explaining to the nurses about clinical consequences of a wrong injection rate can potentially reduce wrong rate errors.Clinical Pharmacist can have potential role in teaching about preparation and administration of IV medication to the nurses and other health care professionals. The preparation and administration of intravenous admixtures are associated with considerable risks and one of the risks is physicochemical incompatibilities. Nursing staff doesn't have enough knowledge regarding the compatibilities of the drugs and so, clinical pharmacist can may not prevent but minimize the incidence of such type of reactions."Rajeev Gandhi Institute of Medical Sciences" (RIMS), is a 750 bedded tertiary care teaching hospital situated in Kadapa, there was no studies conducted previously in this rural hospital regarding assessment of intravenous admixtures in hospitalized patients. Such a study could provide valuable information to the physicians and nursing staff regarding to the safe usage of intravenous admixtures. 145 in-patients who are on intravenous admixtures were included in the study. The study mainly focuses on compatibility of Drug-Solute 15 (14.42%) and Drug-Drug combinations 89 (85.57%). This study showed that out of 104 combinations (both Drug-Solute and Drug-Drug combinations), 20 (19.23%) were compatible, 24 (23.07%) incompatible 5 (4.80%) were variable and 55 (52.88%) were undocumented combinations. This is similar to the study conducted by K.V. Ramanath et al., [10] and Celine Serrurier et al.,[17] in which undocumented combinations were more when compared to compatible and incompatible combinations. This result is contrast to the studies conducted by M. Gikicet al., [4]Humbert – Delaloye Valiaet al.,[18]in which compatible combinations were more when compared to incompatible and undocumented combinations. The incompatibility problem should be considered seriously for better therapeutic outcomes. This showed that undocumented combinations are more in number, more information is needed for these types of drug combinations in order to clarify whether they can be infused through the same line or not. When compatibility between drugs are unknown and if circumstances are so demanding as to warrant mixing of two or more drugs and solutions together then there are some steps to approach this problem i.e.,

- With appropriate course of medical decision suppress a non-essential drug.
- To administer the drug by another route when possible.
- Rinsing the IV line with the compatible solutions of two drugs given through the same IV line.
- To always consider the P^H values of different drugs and to group those similar values and administer them based on P^H.

- In vitro testing of combination by the pharmacist and observe it for particle formation and color change (Physical compatibility).

Given the importance of compatibility of IV medication admixtures a compatibility chart and drug information leaflet for frequently used drugs was prepared and placed in wards which mainly help to reduce IV incompatibilities especially when there is a need to mixing drugs together.

Limitations of the Study

There are two major limitations for the present study. Firstly, data collection was done only during day time. It was thus not possible to report every drug injected. Secondly, the duration of the study was small and most frequently used drugs in General Medicine were included. But rare drugs such as Amrinone which has high potential for incompatibilities were not included in the study.

CONCLUSION

The present observation based prospective study found that out of 104 combinations (both Drug-Solute and Drug-Drug combinations), 20 (19.23%) were compatible, 24 (23.07%) incompatible, 5 (4.80%) were variable and 55 (52.88%) were undocumented combinations. This study concluded that such type of research work would certainly increase the safety in the use of intravenous admixtures. It is very imperative to make physicians and nurses aware of compatibility problems, daily prescription review by clinical pharmacist and providing unbiased information from reliable references could possibly prevent compatibility errors found on the wards.

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