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Evaluation of Intravenous Admixtures in MICU & General Medicine Department of South Indian Tertiary Care Teaching Hospital

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Abstract: *Intravenous drug administration is used when we want to give a large amount of fluid or when we need to dilute a medication in a lot of fluid to make it the correct strength or prevent it from causing irritation. There are different products formulated for Intravenous administration like IV Admixtures, IV fluids and Electrolyte preparations, parenteral antibiotic preparations. 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. This was a prospective observational study which was conducted with the total of 125 cases for 6 months among intravenous admixtures drugs prescribed for inpatients of MICU & General Medicine Department. The present 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 important to make nurses aware of compatibility problems. Some incompatibilities are eminently predictable from simple chemical knowledge, but most compatibilities and incompatibilities are not easily predicted.*

Keywords: *Admixtures, compatibility, Drug-drug interactions, Intravenous, MICU.*

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I. Introduction

Intravenous (IV) Route of Drug Administration:

When compared with other routes of drug administration like subcutaneous or intramuscular injections, we have a limit of 3 mL of fluid for adults when giving them because more than that will cause problems in the tissue surrounding the injection site, but because an IV injection goes directly into a patient's vein, the only limit on the amount of fluid that can be administered via an IV is the limit on the amount of a fluid a person's body can consume without receiving more liquid than the body can absorb or excrete. Because of this, IV administration is used when we want to give a large amount of fluid or when we need to dilute a medication in a lot of fluid to make it the correct strength or prevent it from causing irritation. Apart from this the onset of drug action is rapid when compared with other routes of drug administration [1].The vascular system also called as circulatory system, is made up of the vessels that carry blood and lymph through the body. In using IV therapy, we will mainly be utilizing veins and occasionally the arteries.

Status of IV Therapy Today:

IV therapy is a very therapeutic treatment today. Indeed, it is estimated that over 90 % of all hospitalized in - patients in the United States are recipients of IV therapy. Moreover, IV therapies are not restricted to the in - patient hospital environment. IV therapies are prescribed and used commonly on the same - day of surgeries, long-term care facilities, out - patient clinics and home health settings [2].

Intravenous Preparations:

There are different products formulated for Intravenous administration and some of them are as follows;

A. IV admixtures: These 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.

B. IV fluids;

Fluids are used in the preparation and administration of parenteral products includes sterile water and sodium chloride, dextrose and Ringer's solution, all of which have multiple uses. These fluids serve as vehicles in IV admixtures, providing a means for reconstituting sterile powders. They serve as the basis for correcting body fluid and electrolyte disturbances and provide a caloric source in parenteral nutrition [3].

C. Electrolyte Preparations;

Ions present in both intracellular and extracellular fluid, electrolytes are crucial for various biological processes. Surgical and medical patients who cannot take food by mouth or who need nutritional supplementation require the addition of electrolytes in hydrating solutions or parenteral nutrition solutions.

D. Parenteral antibiotic preparations

They are available as sterile un reconstituted powders, which must be reconstituted with sterile water, normal saline or D5W or as a sterile, ready-to-use liquid parenteral.

IV INCOMPATIBILITIES:

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 [4]. A patient who receives a preparation in which an incompatibility has occurred could experience toxicity or an incomplete therapeutic effect [1]. These are also known as reactions of IV drugs resulting in solutions that are no longer safer for the patient [5].

Types of Incompatibilities: There are 3 – types if incompatibilities Physical, Chemical and Therapeutic incompatibilities [6].

1. Physical Incompatibility: A physical incompatibility occurs when a drug combination produces a visible change in the appearance of a solution.**2** It is also known as **"**Pharmaceutical Incompatibility or Visual Incompatibility**" [7].**

2. Chemical Incompatibility**:** A chemical incompatibility reflects the chemical degradation of one or more of the admixed drugs, resulting in toxicity or therapeutic inactivity [3]. 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. Chemical incompatibilities occur in several ways like complexation, oxidation, reduction and photolysis.

3. Therapeutic Incompatibility: A therapeutic incompatibility occurs when two or more drugs, IV fluids or both are combined and the result is a response other than that intended. This occurs within the body of the patient [8].

II. Research Methodology

Place of Study: The study **"***Assessment of Intravenous Admixtures in MICU & General Medicine Department of Teaching Hospital"**,* which was carried out in the **„**MICU & Department of General Medicine" IP at Rajiv Gandhi Institute of Medical Sciences (RIMS), Kadapa**,** a 750 bedded multi-disciplinary tertiary care teaching hospital

Period of Study: 6 – months.

Type of Study: A Prospective observational study.

Study Population: A total of 142 cases.

Patient Enrollment: Patients are enrolled in the study based on inclusion and exclusion criteria,

(a) Inclusion Criteria:

1. Patients receiving one or more drugs through IV by directly dripping in IV solutions or infusion bags.
2. Patients receiving two or more drugs by directly mixing in same Syringe.
3. Patients receiving two or more drugs simultaneously through Y-Site.
4. Patients receiving Single IV drugs as bolus either with or without cannula.
5. Patients receiving intravenous drugs which are incorrectly formulated or manipulated before administration.
6. Patients receiving intravenous drugs with inappropriate rate if administration.
7. Patient who failed to receive the prescribed dose.

b) Exclusion Criteria:

Doses that had to be administered continuously over 24 hours and medication that had to be given as required were excluded from the observation as these were given outside peak times of drug administration.

1. Patient receiving only IV fluids.

2. Patients taking Intramuscular and Subcutaneous injections were excluded

III. Results

The Prospective Observational Study was conducted for 6 months in South Indian Teaching Hospital Inpatient MICU and General Medicine Department (Both MMW & FMW) at RIMS (Rajiv Gandhi Institute of Medical Sciences), Kadapa. A total of 145 Patients were observed under inclusion criteria and were followed for the present study. All collected & documented, intravenous admixtures drugs {Inpatient MICU and General Medicine Department (Both MMW & FMW)} data are analyzed based upon the following parameters;

1. Gender wise distribution of study population.
2. Age wise distribution of study population.
3. Details on Compatibility of IV drugs administered during the study period.

4. Details on Compatibility of Drugs with Combination of Medication and IVsolution.

A. Details on frequency of usage of Compatible Drug & IV solution combinations.
B. Details on frequency of usage of Incompatible Drug & IV solution combinations.
C. Details on frequency of usage of Variable Drug & IV solution combinations.
D. Details on frequency of usage of Undocumented Drug & IV solution combinations.

5. Details on Compatibility of Drug - Drug Combinations.

A. Details on frequency of usage of Compatible Drug - Drug Combinations.
B. Details on frequency of usage of Incompatible Drug - Drug Combinations.
C. Details on frequency of usage of Variable Drug - Drug Combinations.
D. Details on frequency of usage of Undocumented Drug - Drug Combinations.

Tables

Table 1: Gender wise distribution of study population

Total No. Of Patients	No. Of Female Patients (%)	No. Of Male Patients (%)
145 (100%)	76 (52.41%)	69 (47.58%)

Table 2: 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)**

Table 3: Details on Compatibility of Drugs with Combination of Medication and IV solution:

COMPATIBILITY	NO. OF DRUG – IV SOLUTION COMBINATION (N= 15)	PERCENTAGE (%)
COMPATIBLE	7	46.66%
INCOMPATIBLE	2	13.33%
VARIABLE	1	6.66%
UNDOCUMENTED	5	33.33%
TOTAL	**15**	**100%**

Table 3(A): 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 ATROPINE + NORMAL SALINE	1	7.69 %

Table 3(B): Details on frequency of usage of Incompatible Drug & IV solution combinations

INCOMPATIBLE DRUG & IV SOLUTION COMBINATIONS	FREQUENCY	FREQUENCY %

	N = 3	
PHENYTOIN + NORMAL SALINE	2	66.66%
CEFTRIAXONE + RINGER LACTATE	1	33.33%

Table 3(C): Details on frequency of usage of Variable Drug & IV solution combination.

DRUG – SOLUTION COMBINATION	FREQUENCY (N= 1)	FREQUENCY (%)
PHENYTOIN + DEXTROSE NORMAL SALINE	1	100%

Table 3(D): 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 N- ACETYLCYSTINE + NORMAL SALINE	1	14.28%

Table 4: Details on Compatibility of Drug - Drug Combinations (at different site/contact site)

COMPATIBLE	NO. OF DRUG – DRUG COMBINATIONS		TOTAL (%)
	Y –SITE	MIXTURE	
COMPATIBLE	12	1	13 (14.60%)
INCOMPATIBLE	21	1	22 (24.71%)
VARIABLE	4	0	4 (4.49%)
UNDOCUMENTED	48	2	50 (56.17%)
TOTAL	**85 (95.50%)**	**4 (4.49%)**	**89 (100%)**

Table 4(A): Details on frequency of usage of Compatible Drug - Drug Combinations

S. No.	COMPATIBLE DRUG COMBINATIONS (N = 13)	FREQUENCY	FREQUENCY (%)
1.	CEFTRIAXONE + PANTOPRAZOLE	46	41.81%
2.	CEFTRIAXONE + FUROSEMIDE	17	15.45%
3.	DERIPHYLLINE + PANTOPRAZOLE	6	5.45%
4.	FUROSEMIDE + DERIPHYLLINE	5	4.54%
5.	CIPROFLOXACIN+ METRONIDAZOLE CEFTRIAXONE + METRONIDAZOLE	4	3.63%
6.	DEXAMETHASONE + ONDANSETRON FUROSEMIDE + RANITIDINE	2	1.81%
7.	RANITIDINE + FUROSEMIDE PIPERCILINTAZOBACTUM + ONDANSETRON DERIPHYLLINE + HYDROCORTISONE	1	0.90%
TOTAL	**13**	**149**	**100%**

Table 4(B): Details on Frequency of Usage of Incompatible Drug - Drug Combinations

S. No.	INCOMPATIBLE DRUG – DRUG COMBINATIONS (N = 22)	FREQUENCY	FREQUENCY (%)
1.	FUROSEMIDE + PANTOPRAZOLE	24	22.22%
2.	ONDANSETRON + PANTOPRAZOLE	13	12.03%
3.	HYDROCORTISONE + PANTOPRAZOLE	11	10.18%
4.	PIPERCILINTAZOBACTUM + PANTOPRAZOLE	7	6.48%
	CIPROFLOXACIN + PANTOPRAZOLE	5	4.62%

5.	DIAZEPAM + PANTOPRAZOLE		
6.	PHENYTOIN + PANTOPRAZOLE DEXAMETHASONE + PANTOPRAZOLE CEFTRIAXONE + DERIPHYLLINE CEFOTAXIME + PANTOPRAZOLE CIPROFLOXACIN + CEFTRIAXONE FUROSEMIDE + ONDANSETRON	4	3.70%
7.	METRONIDAZOLE + PANTOPRAZOLE PHENYTOIN + DIAZEPAM	3	2.77%
8.	FUROSEMIDE + CIPROFLOXACIN ATROPINE + PANTOPRAZOLE PANTOPRAZOLE + AMIKACIN DIAZEPAM + CEFTRIAXONE PHENYTOIN + CEFTRIAXONE	2	1.85%
9.	DERIPHYLLINE + ONDANSETRON PANTOPRAZOLE + RANITIDINE HYDROCORTISONE + AMPICILLIN	1 1	0.92% 0.92%
TOTAL	**22**	**108**	**100%**

Table 4(C): Details on Frequency of Usage Of Variable Drug - Drug Combinations

S. No.	VARIABLE DRUG – DRUG COMBINATIONS (N = 4)	FREQUENCY	FREQUENCY (%)
1.	FUROSEMIDE + HYDROCORTISONE	5	45.45%
2.	PERCILINTAZOBACTUM + AMIKACIN	3	27.27%
3.	MANNITOL + PANTOPRAZOLE	2	18.18%
4.	AMPICILLIN + RANITIDINE	1	9.09%
TOTAL	**4**	**11**	**100%**

Table 4(D): Details on Frequency of Usage of Undocumented Drug – Drug Combinations

S. No.	UNDOCUMENTED DRUG – DRUG COMBINATION (N = 50)	FREQUENCY	FREQUENCY (%)
1.	AUGMENTIN + PANTOPRAZOLE	11	9.09%
2.	CEFTRIAXONE + RANITIDINE CEFTRIAXONE + ONDANSETRON	9	7.43%
3.	PANTOPRAZOLE + PIRACETAM	8	6.61%
4.	AUGMENTIN + DERIPHYLLINE HYDROCORTISONE + CHLORPHENERAMINE MALEATE	7	5.78%
5.	AUGMENTIN + FUROSEMIDE	6	4.95%
6.	HYDROCORTISONE + CEFTRIAXONE	5	4.13%
7.	CHLORPHENERAMINE MALEATE + PANTOPRAZOLE PIRACETAM + CEFTRIAXONE	4	3.30%
8.	AUGMENTIN + DEXAMETHASONE MANNITOL + PIRACETAM	3	2.47%
9.	CHLORPHENERAMINE MALEATE + FUROSEMIDE		

	PIRACETAM + FUROSEMIDE AUGMENTIN + HYDROCORTISONE AUGMENTIN + ONDANSETRON FUROSEMIDE + CEFOTAXIME DEXAMETHASONE + CEFTRIAXONE METRONIDAZOLE + ONDANSETRON	2	1.65%
10.	AUGMENTIN + RANITIDINE HYDROCORTISONE + DEXAMETHASONE EDVERAN + PIRACETAM 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 MULTI VITAMIN + HYDROCORTISONE HYDROCORTISONE + PIRACETAM PIPERCILINTAZOBACTUM + PIRACETAM MULTI VITAMIN+ NEUTROPHIL 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 CIPROFLOXACIN + ONDANSETRON	1	0.82%
TOTAL	**50**	**112%**	**100%**

IV. Discussion

The preparation and administration of intravenous admixtures are associated with considerable risks and one of the risks is physicochemical incompatibilities. In general, nurses prepare and administer intravenous admixtures prescribed by doctors. Nursing staff doesn't have enough knowledge regarding the compatibilities of intravenous drugs in infusions, leading to Physical or Chemical or Therapeutic Incompatibility of drugs.

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.,*** [09] and ***Celine Serrurier et al.,*** [10] in which undocumented combinations were more when compared to compatible and incompatible combinations. This result is contrast to the studies conducted by ***M. Gikic et al.,***[11] ***Humbert - Delaloye Valia et al.,*****[**12] in which compatible combinations were more when compared to incompatible and undocumented combinations. The incompatibility problem should be considered seriously for better therapeutic outcomes.

Out of 15 Drug-Solute combinations 7 (46.66%) are found to be compatible, 2 (13.33%) incompatible, 1(6.66%) are found to be variable and 5 (33.33%) are undocumented combinations. This is similar to the study conducted by ***K.V. Ramanath et al.,*** [9] in which undocumented combinations are more when compared to compatible, variable and incompatible combinations. The 2 - incompatible combinations found were Phenytoin + Normal Saline and Ceftriaxone + Lactated Ringer's solutions. When phenytoin is mixed with normal saline solution or dilution of injectable phenytoin by adding to an infusion bag containing normal saline lowers it PH and therefore, it reduces its solubility resulting in precipitation of the drug [13].

Out of 13 compatible Drug-Drug combinations Ceftriaxone + Pantoprazole and Ceftriaxone + Furosemide are most frequently used combinations i.e., in 46 (41.81%) and 17 (15.45%) patients respectively. Compatibility data has already been established for these Drug-Drug combinations.

Out of 22 (24.71%) incompatible Drug-Drug combinations Furosemide + Pantoprazole and Ondansetron + Pantoprazole are the most frequently used combinations i.e. in 24 (22.22%) and 13 (12.03%) patient's respectively. The PH 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 (3.3-4), Ciprofloxacin (3.3-3.9) are incompatible when mixed with Furosemide. A study conducted by ***K.V. Ramanath et al***.,[9]found Amikacin + Ceftriaxone and Amikacin + Pantoprazole as most frequently given combinations and another study conducted by ***M. Gikic et al***.,[11].

Out of 50 undocumented Drug-Drug combinations Amoxicillin/clavulanic acid + Pantoprazole were most frequently given combinations i.e. in 11 (9.09%) patients respectively. Ceftriaxone + Ondansetron were 2nd most frequent given combinations i.e. in 9 (7.43%) patients respectively. These undocumented combinations don't have any evidence of data regarding their compatibility. Similarly a study conducted by ***K.V. Ramanath et al.,*** [9]

V. Conclusion

This study showed that physical compatibility provide basis for Y-site compatibility which are lacking for commonly used medications in ICU and General Medicine Wards and this may lead to unsafe medication practices.

When compatibility between drugs are unknown and if circumstances are so compelling as to warrant mixing of two or more drugs and solutions to gather then there is another way to approach this problem i.e.,

1. With appropriate course of medical decision suppress a non-essential drug.

2. To administer the drug by another route when possible.

3. Rinsing the IV line with the compatible solutions of two drugs given through the same IV line.

4. To always consider the PH values of different drugs and to group those similar values and administer them based on PH.

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

This study mainly helps to avoid incompatibilities among IV drugs in ICU and GM departments. It is very important to make aware of health care professionals regarding incompatibility problems. This study concluded that such type of research work would certainly increase the safety in the use of intravenous admixtures.

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