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Assessment of Intravenous Admixtures in Hospitalized Patients of a Rural Tertiary Care Teaching Hospital

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ABSTRACT

Intravenous Incompatibilities are 'undesirable reactions which occur when two are more drugs are administered through a single intravenous line or given in a single solution', will leads to experience toxicity or an incomplete therapeutic effect in the patient. Hence the present study mainly focused on clinical pharmacist assessment in intravenous admixtures administration.This study was an observational, prospective study method. When a single (drug solution) two or more drug (drug-drug solution compatibilities) administered directly into the infusion or in the same infusion line, the compatibility of the drug will be checked by using primary, secondary or tertiary resources. A one day workshop was conducted for the nursing professionals about intravenous incompatibilities for increasing the awareness and for providing of standardized nursing care services while administering of intravenous drugs. The results of this study showed that out of 145 combinations; 25 (17.24%) are compatible, 41 (28.28%) incompatible, 10 (6.9%) variable and 69 (47.58%) undocumented. Comparative evaluation of pre and post test score percentage of 78 participants showed that, ≤ 40 percentage score was observed in 37.18% in pre-evaluation test whereas only 5.13% was observed in the post-evaluation test, and interestingly >80 percentage score was not found in the pre-evaluation test, whereas 7.69% participants scored in the post-evaluation test . This study showed that Clinical Pharmacist assessment in intravenous admixture will helps in minimizing of incompatibilities , unidentified area research gaps , and also make the nurses to aware about nursing care /precautions in intravenous administration.

Key words: Intravenous admixtures, Incompatibilities, Clinical Pharmacist.

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INTRODUCTION

Intravenous Admixtures are the preparations consisting of one or more sterile drug products added to an intravenous fluid and are used / intended for continuous infusion. Drugs that cause irritation or toxicity when administered as rapid direct IV injection are prepared as intravenous admixtures.[1]

Intravenous Incompatibilities are the undesirable reactions that occur when two are more drugs are administered through a single intravenous line or given in a single solution. Because of this incompatibility, the patient could experience toxicity or an incomplete therapeutic effect.[2]

There are three types of incompatibilities. Physical, chemical and therapeutic incompatibilities.[3]

Potential incompatibilities should be identified by using various types of available resources from drug information centers / help lines and pharmacy (hospital/community).[4]

Compatibility differences were observed and reported for different brands of same drug. So recognizing the compatibility is not just a function of the drugs themselves, but it also depends on a variety of factors, including concentration, temperature, storage vehicle, infusion solution, order of mixing, and administration technique.[5]

Drug incompatibility reactions may not only generate a many particles in the infusate, but also transform the drug into an inactive form and deleterious effects on the patient's prescribed drug regimen. A recently published study showed that drug incompatibility reactions are the one of the most common errors in infusion therapy.

The various clinical effects caused due to incompatibilities ultimately cause tissue ischaemia, hypoxia and impairment in discharge of metabolic end products. Due to reduction in the microcirculation, the major organs like lungs and liver functions are reduced and ultimately progress to multi-organ failure, leading to an extremely high mortality.[6]

Intravenous therapy is a complex health care technology. In general; nursing staff prepare and administer intravenous drugs prescribed by doctors. Due to increased availability of number of drug combinations, the knowledge regarding the incompatibilities of intravenous drugs is limited. Sometimes this will result in severe adverse drug reactions in patients.[7] It is not possible to predict all incompatibilities that may arise, hoping that their occurrence can be minimized by presence/alertness of a clinical pharmacist in the ward rounds, clinical review about the possible incompatibilities & by making the nurses aware of the incompatibility problems will enhance the patient safety to a substantial degree.[5, 8, 9]

Hence the main objective of this study was focused on assessing the intravenous admixtures and to educate the nursing professions regarding intravenous incompatibilities.

MATERIALS AND METHODS:

Compatibility Charts.

Patient Data Collection Form.

Pre and post-evaluation questionnaire Forms.

This was an observational based prospective study carried out after obtaining ethical approval from Institutional Ethics Committee (AHRC, Ref:No.AIMS/EC/753/2011-12). This study was conducted among the intravenous admixtures inpatients, after obtained their consent. The intravenous drug admixtures patients' data were collected in the Patient Data Collection Form. The data form mainly consists of information like patient details (name, age, reason for hospitalization), drugs and solutes (brand name, dose, and type of administration), type of compatibility. When a single drug was administered/delivered by infusion, the compatibility of the drug in the infusion solution will be checked and when two or more drugs were used in the same infusion line then drug-drug compatibilities were also checked.

The obtained data was assessed for any type of incompatibilities by using the available literature, i.e., from Compatibility Charts (helps for assessing the most commonly used intravenous drug admixtures and also to outline the most potential incompatibilities when these drugs are infused concurrently) and reference of various primary, secondary, tertiary sources (e.g.: standard text books on Intravenous Admixtures, Micromedix software).

Incompatibility charts on intravenous drug incompatibilities were made available on each ward as a reference for nursing staff to increase the security/better service in the use of intravenous drugs.

Assistance was given to the nursing staff about intravenous admixtures preparation (i.e. by providing information) for their queries or for observed/noticed incompatibilities. A one day workshop (Training Programme) was conducted for the Nursing Professionals about intravenous incompatibilities for increasing the awareness & for providing good nursing services. The Pre-evaluation and Post-evaluation questionnaire forms were made (Each questionnaire consisting of 10 questions and correct answer carry one mark each) and administered to the nursing professionals before and after the workshop respectively. The obtained data was subjected for descriptive statistical analysis(The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.)**

RESULTS AND DISCUSSION

About 150 in-patients who are on intravenous admixtures were approached and informed about the study; only 130 patients gave the consent to participate.

Out of 145 total combinations Drug-Solute were 19 and Drug-Drug combinations were 125 respectively, In 19 Drug-Solute combinations, 7 (36.84%) are found to be compatible, 2 (10.53%) are incompatible, 1 (5.26%) is variable (i.e. conflicting information) and 9 (47.37%) are undocumented combinations. In 126 Drug-Drug combinations, 18 (14.29%) are compatible, 39 (30.95%) are incompatible, 9 (7.14%) are variable and 60 (47.62%) are undocumented drug-drug combinations. The two incompatible Drug-Solute combinations found are Insulin + DNS (Dextrose Normal Saline) and Phenytoin + DNS (Normal Saline). When Insulin is given along with DNS, Insulin gets adsorbed to the surface of intravenous infusion solution containers (both glass and plastic), tubing and filters. This leads to the potency loss range up to about 80%, leading to chemical incompatibility. When Phenytoin is mixed with DNS, physical incompatibility like Phenytoin crystals/precipitation will get formed within 10 – 15 minutes, this ultimately leading to problems like blocking of intravenous line. This study mainly focused on to know the compatibility of Drug-Solute and Drug-Drug combinations and also for creating awareness among nursing professional about the incompatibilities.. This study results are similar to the study conducted by Salmaan.[10] This study also showed undocumented combinations were observed more when compare to compatible and undocumented combinations. Other similar type of studies conducted by Gikic M et.al.[11], Valia HD et.al.[12] and Serruier C et.al.[13]**,** also showed compatible combinations were more when compared to incompatible and undocumented combinations. This type of study showed incompatibility problems must be considered very seriously for better therapeutic management & outcomes **(Table 1)**

Table 1: Details on Compatibility of Intravenous drugs administered during the study period:

Compatibility	No. of Drug-Drug combinations		No. of Drug-Solute combinations		Total (%)
	Y site	Mixture	Y site	Mixture	
Compatible	16 (13.33)	02 (33.33)	00 (00)	07 (36.84)	25 (17.24)
Incompatible	37 (30.83)	02 (33.33)	00(00)	02 (10.53)	41 (28.28)
Variable	09 (07.50)	00 (00.00)	00(00)	01 (5.26)	10 (06.90)
Undocumented	58 (48.34)	02 (33.33)	00(00)	09 (47.37)	69 (47.58)
Total	120	06	00	19	145 (100)

Y site (same IV line) -A site where the syringe is connected to IV line polythene tube which is Y shape, **Mixture (same bottle/syringe)** – the drug which can be directly injected into the large volume/in the syringe

Table 2 showed Out of 18 compatible Drug-Drug combinations, Ceftriaxone + Pantoprazole is the most frequently used combination i.e., 41 (54.66%) times, followed by Amikacin + Ranitidine i.e., 10 (13.33%) times and Ceftriaxone + Mannitol i.e., 6 (8%) times.

Table 2: Details on frequency of usage of compatible Drug - Drug combinations:

Drug code	Compatible Drug - Drug combinations(n = 18)	Frequency	Frequency (%)
1	Ceftriaxone + Pantoprazole	41	54.66
2	Amikacin + Ranitidine	10	13.33
3	Ceftriaxone + Mannitol	06	08.00
4	Ranitidine + Metoclopramide Amikacin + Metronidazole Atropine + Ondansetron	02	02.67
5	Amikacin + Ondansetron Cefoperazone + Furosemide Mannitol + Ondansetron Gentamycin + Metronidazole Linezolid + Piperacillin - Tazobactum Hydrocortisone + Ondansetron Furosemide + Nitroglycerine Ondansetron + Ranitidine Furosemide + Ranitidine Enoxaparin + Ondansetron Hydrocortisone + Theophylline Metronidazole + Piperacillin – Tazobactum	01	01.33

Table 3 showed Out of 39 incompatible Drug-Drug combinations, Amikacin + Ceftriaxone is the most frequently used combination i.e., 25 (24.04%) times, followed by Amikacin + Pantoprazole i.e., 14 (13.46%) times and Metronidazole + Ranitidine i.e., 5 (4.81%) times. Amino glycosides, such as Amikacin sulfate and Ceftriaxone sodium are physically incompatible in intravenous admixtures (during Y site administration). So avoid use of these drugs together. However, in emergency conditions, when concomitant administration is required, the manufacturer recommends sequential drug administration and thorough intravenous line flushing (with a compatible fluid) between administrations. Amikacin when mixed with Pantoprazole, there will be formation of precipitate, leading to physical incompatibility.

When Calcium gluconate or calcium containing preparation [Total parental Nutrition(TPN)] should not be mixed/administered concurrently with Ceftriaxone sodium, because there will be formation of Ceftriaxone-Calcium precipitate, leading to physical incompatibility. Due to this risk concurrent use of this combination is contraindicated (either as a mixture / Y site) in neonates (28 days old or less). Because the neonates blood vessels are very narrow/ in developing stage.

Table 3: Details on frequency of usage of incompatible Drug - Drug combinations:

Drugs code	Incompatible Drug - Drug combinations (n = 39)	Frequency	Frequency (%)
1	Amikacin + Ceftriaxone	25	24.04
2	Amikacin + Pantoprazole	14	13.46
3	Metronidazole + Ranitidine	05	4.81
4	Atropine + Pantoprazole Furosemide + Ondansetron Hydrocortisone + Pantoprazole	04	3.85
5	Amikacin + Tramadol Amikacin + Rabeprazole Metronidazole + Pantoprazole	03	2.88
6	Amikacin + Ofloxacin Diclofenac + Metronidazole Metronidazole + Metoclopramide Metronidazole + Rabeprazole Ciprofloxacin + Ondansetron Mannitol + Pantoprazole Pantoprazole + Piperacillin – Tazobactum Pantoprazole + Phenytoin Amikacin + Diclofenac	02	1.92
7	Ofloxacin + Ranitidine, Metronidazole + Ondansetron Cefoperazone + Ondansetron Ciprofloxacin + Furosemide Cefotaxim + Pantoprazole Calcium gluconate + Ceftriaxone Amoxicillin + Gentamycin Amoxicillin + Metronidazole Gentamycin + Hydrocortisone Furosemide + Gentamycin Metronidazole + Phenytoin Ciprofloxacin + Hydrocortisone Ciprofloxacin + Rabeprazole Phenytoin + Theophylline Amikacin + Amoxicillin,Nabuphine + Ofloxacin Amikacin + Nabuphine Ofloxacin + Pantoprazole Enoxaparin + Pantoprazole Amikacin + Ornidazole Ceftriaxone + Ciprofloxacin	01	0.96

Other than neonates patients, Ceftriaxone and Calcium-containing solutions may be administered with certain precautions like infusion lines are sequentially & thoroughly flushed between infusions with a compatible fluid.

When Amoxicillin is mixed with Gentamycin, there is chemical inactivation of both compounds in in-vitro. Manufacturers recommend mixing of Gentamycin with other drugs should be avoided.

When Furosemide and Ondansetron are mixed, white turbidity followed by chalky precipitate will appear. When Furosemide and Ciprofloxacin are mixed together immediate precipitation occurs. When Furosemide and Gentamycin, Cefoperazone and Ondansetron are mixed are mixed, Flocculant precipitate gets formed. This clearly showed that the health care professional must be alert about these types of frequent incompatibilities

The study also showed that Amino glycosides (Amikacin, Gentamycin), Phenytoin, Metronidazole, Ofloxacin, Mannitol and Theophylline derivatives should not be mixed with any other drugs. The Drugs like Dopamine and Nitroglycerine have limited compatibility, So, while administering with other drug combination check for compatibility

Table 4 showed Out of 50 undocumented Drug-Drug combinations, Ceftriaxone + Ranitidine is the most frequently used combination i.e., 26 (18.05%) times, followed by Ceftriaxone + Furosemide and Ceftriaxone + Ondansetron i.e., 8(5.55%) times. There is no clear evidence /information about these combinations.

Table. 4: **Details on frequency of usage of undocumented Drug - Drug combinations:**

Drugs code	Undocumented Drug - Drug combinations(n = 50)	Frequency	Frequency (%)
1	Ceftriaxone + Ranitidine	26	18.05
2	Ceftriaxone + Furosemide , Ceftriaxone + Ondansetron	08	5.55
3	Ceftriaxone + Diclofenac, Ondansetron + Pantoprazole Cefotaxime + Ranitidine	07	4.86
4	Ceftriaxone + Rabeprazole ,Ceftriaxone + Hydrocortisone	05	3.47
5	Diclofenac + Ranitidine, Atropine + Ceftriaxone Hydrocortisone + Pheniramine	04	2.78
6	Ceftriaxone + Tramadol, Pantoprazole + Tramadol Ceftriaxone + Phenytoin	03	2.08
7	Ceftriaxone + Metoclopramide, Ceftriaxone + Pralidoxime Ondansetron + Rabeprazole, Diclofenac + Pantoprazole	02	1.39
8	Diclofenac + Ondansetron, Ondansetron + Tramadol Cefoperazone + Ciprofloxacin, Furosemide + Rabeprazole Cefotaxime + Furosemide, Amoxicillin + Hydrocortisone Linezolid + Pantoprazole, Hydrocortisone + Rabeprazole Cefoperazone + Ranitidine, Cefoperazone + Ceftriaxone Ceftriaxone + Nitroglycerine, Hydrocortisone + Nitroglycerine Mannitol + Rabeprazole Glycopyrrolate + Piperacillin – Tazobactum Glycopyrrolate + Rabeprazole		0.69

Piperacillin – Tazobactum + Rabeprazole	
Ondansetron + Phenytoin,Ceftriaxone + Chloroquine	
Chloroquine + Mannitol, Chloroquine + Theophylline	
Chloroquine + Phenytoin, Mannitol + Theophylline	
Mannitol + Phenytoin, Furosemide + Vit K	
Amoxicillin + Pantoprazole, Rabeprazole + Torsemide	01
Ondansetron + Torsemide,Nabuphine + Pantoprazole	
Cefoperazone + Pantoprazole, Artesunate + Cefoperazone	
Artesunate + Pantoprazole , Pheniramine + Ranitidine	
Hydrocortisone + Ranitidine, Ondansetron +Pantoprazole	
Pralidoxime + Pantoprazole ,Ornidazole + Pantoprazole	
Ornidazole + Tramadol, Ceftriaxone + Ondansetron	
Ceftriaxone + Pheniramine, Pantoprazole + Pheniramine	
Insulin + Piperacillin – Tazobactum , Dexamethasone + Mannitol	

Table 5 showed Out of 9 variable Drug-Drug combinations (i.e. contradictory information regarding compatibility), Ceftriaxone + Metronidazole is the most frequently used combination i.e., 11 (37.93%) times, followed by Furosemide + Pantoprazole i.e., 5 (17.24%) times. .

Table 5: Details on frequency of usage of variable Drug - Drug combinations:

Drugs code	Variable drug drug combinations (n = 9)	Frequency	Frequency (%)
1	Ceftriaxone + Metronidazole	11	37.93
2	Furosemide + Pantoprazole	05	17.24
3	Ciprofloxacin + Pantoprazole Amikacin + Cefotaxime	03	10.34
4	Ceftriaxone + Theophylline Amikacin + Furosemide	02	6.89
5	Ciprofloxacin + Metronidazole Hydrocortisone + Metronidazole Amikacin + Piperacillin – Tazobactum	01	3.45

In order to minimize/reduce the intravenous incompatibilities, the Nursing professionals were provided with training program/workshop. Both final years BSC, GNM nursing students and Practicing Nurses took part in the workshop. The work shop pre evaluation test scores of total 78 participant Nursing professionals results showed, 29 (37.18%) participants [17 (54.84%) are GNM students, 11 (28.94%) are B.Sc students and 01 (11.11%) is staff] had score percentage was ≤40, 38 (48.72%) participants [14(45.16%) are GNM students, 16 (42.11%) are B.Sc students and 08 (88.89%) are staff] are in the score percentage of 41 - 60, 11 (14.1%) participants [11 (28.94%) are B.Sc students] are in the score percentage of 61 – 80 and none have >80 percentage score. (Table 6)

The post test scores of 78 participant Nursing professionals showed that 4 (5.13%) participants [2 (6.45%) are GNM students, 1 (2.63%) participant is B.Sc student and 01 (11.11%) is staff] had score percentage of ≤40, 34 (43.59%) participants had [15 (48.39%) are GNM students, 14

(36.84%) are B.Sc students and 5 (55.56%) are staff] 41-60 scores percentage, 34 participants (43.59%) [14 (45.16%) are GNM students, 18 (47.37%) are B.Sc students and 2 (22.22%) are staff] had score percentage of 61 – 80 and 6 (7.69%) participants [5 (13.16%) are B.Sc students and 1 participant (11.11%) is staff] are in the score percentage of >80**. (Table 6)**

Table 6: Comparative evaluation of score ranges of the participants based on percentage:

Score %	No. of students				No. of staff		Total (%)	
	GNM (%)		BSC (%)		GNM (%)			
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
≤40	17 (54.84)	02 (6.45)	11(28.94)	01 (2.63)	01(11.11)	01(11.11)	29(37.18)	04 (5.13)
41-60	14(45.16)	15(48.39)	16(42.12)	14(36.84)	08(88.89)	05(55.56)	38(48.72)	34(43.59)
61-80	00(00)	14(45.16)	11(28.94)	18(47.37)	00(00)	02(22.22)	11 (14.1)	34(43.59)
>80	00(00)	00 (00)	00 (00)	05(13.16)	00(00)	01(11.11)	00 (00)	06(7.69)
Total	31	31	38	38	09	09	78	78

GNM- general nursing management, BSC nursing –bachelor of science in nursing, pre test – test before the training program starts, post test – Test after the training program .

The comparative evaluation of pre and post test scores results showed , in pre-evaluation test, 29 participants (37.18%) are in the score percentage of ≤ 40, where as in post-evaluation test, only 04 participants (5.13%) are in the score percentage of ≤ 40; in pre-evaluation test, 38 participants (48.72%) are in the score percentage of 41 -60, where as in post-evaluation test, 34 participants (43.59%) are in the score percentage of 41-60; in pre-evaluation test, 11 participants (14.1%) are in the score percentage of 61-80, whereas in post-evaluation test, 34 participants (43.59%) are in the score percentage of 61-80 and in pre-evaluation test, zero are in the score percentage of >80, whereas in post-evaluation test, 06 participants (7.69%) are in the score percentage of >80. (**Table 6).** This clearly showed that workshop/continuing education program results in bringing awareness to a maximum level in B.Sc students when compared to GNM students and staff. This might be because of syllabus updating and advancement in technology and more exposure about new practical concepts in B.Sc students.

The compatibility charts displayed in the wards was very useful for the Nursing staff to check the compatibility of Drug-Drug combinations prior to mixing of a drugs with other drugs and nurses also expressed this type of continuing education program required even in future for better service .The limitation of this study showed that practicing/working nursing professional participation was less because of their tight schedules.

The future direction of this study showed that, there is an need of this type of continuous educational programs and clinical pharmacist involvement/support in an intravenous administration & preparation.

CONCLUSION

The undocumented combinations are more when compared to incompatible, compatible and variable combinations. This study showed that physical compatibility studies provide the basis for Y-site compatibility (commonly used medications administration in intensive care unit patients) for safe usage. This study also helps to avoid incompatibilities among intravenous drugs in intensive care/general & other wards settings. The workshop conducted for nurses showed that Clinical Pharmacist plays a key role in providing unbiased information about intravenous incompatibilities. The participants (Nursing Professionals) also expressed that the training program (workshop) is useful in their daily practice & further need of these types of training/research work in rural hospitals and continuous training programs for increasing the safety use of medications.

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