EFFECT OF pH AND POLYVALENT CATIONS ON THE Y-SITE INCOMPATIBILITY OF CONTINUOUS INTRAVENOUS INFUSIONS OF SELECTED CRITICAL CARE DRUGS IN THE MEDICAL INTENSIVE CARE UNIT

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Certificate

This is to certify that the M.Pharm dissertation entitled "**Effect of pH and Polyvalent Cations on the Y-Site Incompatibility of Continuous Intravenous Infusions of Selected Critical Care Drugs in the Medical Intensive Care Unit"** was carried out by Reg.261440112 in the Department of Pharmacy Practice, College of Pharmacy, Sri Ramakrishna Institute Of Paramedical Sciences, Coimbatore ,which is affiliated to The Tamil Nadu Dr.MGR Medical University, Chennai, under my direct supervision and guidance to my fullest satisfaction.

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CONTENTS

ABBREVIATIONS

ADR	:	Adverse Drug Reactions
BPH	:	Benign Prostate Hyperplasia
CAD	:	Coronary Artery Disease
C	:	Compatibility
CHD	:	Congenital Heart Disease
CHF	:	Congestive Heart Failure
COPD	:	Chronic Obstructive Pulmonary Disease
CRF	:	Chronic Renal Failure
CVA	:	Cerebrovascular Accident
CVD	:	Cardiovascular Diseases
CVC	:	Central Venous Catheter
DA	:	Dopamine
DM	:	Diabetes Mellitus
DOA	:	Date of Admission
DOD	:	Date of Discharge
DU	:	Dobutamine
EID	:	Electronic Infusion Device
FDA	:	Food and Drug Administration
HTN	:	Hypertension
IC	:	Incompatible

IPA	:	Indian Pharmaceutical Abstract
IHD	:	Ischaemic Heart Disease
IV	:	Intra venous
IM	:	Intra Muscular
MI	:	Myocardial Infarction
MICU	:	Medical Intensive Care Unit
NE	:	Nor epinephrine
NICU	:	Neonatal Intensive Care Unit
NT	:	Not Tested
PICU	:	Paediatric Intensive Care Unit
PVC	:	Poly Vinyl Chloride
RTA	:	Road Traffic Accident
RD	:	Respiratory Disorders
SPC	:	Statistical Process Chart
SHT	:	Systemic Hypertension
SPSS	:	Statistical Packages for the Social Sciences
TPN	:	Total Parenteral Nutrition
T_2DM	:	Type 2 Diabetes Mellitus
UTI	:	Urinary Tract Infection
VAP	:	Vascular Ascess Point

ABSTRACT

BACKGROUND:

Critically ill patients in the Medical Intensive Care Unit (MICU) require multiple medications, often administered as continuous intravenous infusions. Two or more medications that are administered via Y-site connector mix in the lumen of the tubing prior to being infused into the patient. However, not all medications can be physically mixed together. The potential complications of co-administration of incompatible medications include precipitation, central venous catheter occlusion requiring additional venous access, reduced potency of medication, therapeutic failure and local and systemic inflammatory reactions. Various factors such as solvents, diluents, infusion fluids, pH of each drug, duration of stability and concentration of the selected critical care drugs play a major role in determining the compatibility of intravenous drug infusions at the Y-junction.

OBJECTIVES:

- To study the influence of polyvalent ions in the co-infused drug solutions and acid-base reactions between the continuously infused drug solution and Y-site administered drug on the physicochemical compatibility of various critical care drugs used in the Medical Intensive Care Unit.
- To identify the most frequent and clinically significant incompatibilities of continuous IV infusions of the selected critical care drugs with Y-site administered drugs in the MICU settings

STUDY DESIGN:

Prospective observational study

STUDY DURATION:

10 months (from November 2015 to August 2016).

SETTING:

Medical Intensive Care (MICU) unit of a 750 bedded multispecialty tertiary care teaching hospital.

PATIENTS:

Patients admitted to the Medical Intensive Care Unit, receiving Y-administration of drugs along with continuous intravenous infusions are included.

METHOD:

Compatibility of the selected critical care drugs when given as continuous intravenous infusions are analyzed against the Y-site administered drugs using the 2-dimensional compatibility chart. A 2-dimensional compatibility chart is prepared indicating the compatibility of selected critical care drug infusions with Y-site administered drugs commonly used in the Medical Intensive Care Unit is prepared

RESULTS

Five hundred and fifty four (81.23%) of the prescribed medications were administered intravenously, of these two hundred and sixty two (38.4%) drugs were given as continuous intravenous infusions while two hundred and ninety two drugs were given through Y-Site. Of the 600 drug-drug combinations or drug-diluent combinations evaluated, two hundred and two combinations (33.66%) were found to be compatible while 17 (2.83%) combinations were incompatible. The compatibility information of 354 (59%) combinations are not reported in the literature and 27 combinations were reported as caution (4.5%). Most of the incompatibilities were due to differing pH values of the drug pairs or drug and diluents. Ringer lactate and ceftriaxone is the only one drug –diluent combination and it is due to the presence of polyvalent cation (Ca^{++}) in the diluents. A 2-dimensional compatibility chart prepared and this

indicating the compatibility of selected continuous intravenous infusions with Y-site administered drugs commonly used in the MICU.

CONCLUSION:

The present study helps in the identification of the factors causing incompatibility of continuous intravenous infusions and Y-site administered drugs in the Medical Intensive Care Unit. The proposed study reviewed the compatibility of continuous intravenous infusions of certain selected critical care drugs against Y-site administered drugs with a view to improving the safety of multidrug therapy in the Medical Intensive Care Unit. The study also lead to the development of a two dimensional Y-site compatibility chart for commonly used critical care drugs in the Medical Intensive Care unit.

INTRODUCTION

INTRAVENOUS THERAPY

Intravenous (IV) delivery is extensively used for many reasons; it has rapid onset, high bioavailability, rapid clearance once stopped, and therefore is suitable for dose titration and maintenance of effect. Frequently the number of IV medication is more than number of venous access lumens for these patients. Consequently, co- administration of more than one medication in the same container, or same line, is inevitable. Evidence shows adding of additional lumens increases opportunities for infection, and multi lumen CVC's increase the risk of catheter related blood stream infection.. A larger number of medications will increase the incompatibility risk geometrically. However, this complex situation is poorly understood by health staff[1.] In modern medical practice, up to 80% of hospitalized patients receive intravenous therapy at some point during their admission. Medication, fluids, nutrition, and blood products can all be given via the intravenous route, which can be either peripheral or central. Although common, these practices are not devoid of complications, which may lead to mortality and morbidity, increased duration of hospital stay, and significant costs.

Peripheral Venous Cannulation: Peripheral venous cannulation is the commonest method used for intravenous therapy. There are numerous well recognised indications and contraindications for peripheral venous cannulation, but, despite these, there is no doubt that many intravenous lines are inserted unnecessarily. A French study also found that 28% of peripheral cannulae inserted in an emergency department were ''unjustified''. Indications for peripheral venous cannulation include intravenous fluids, limited parenteral nutrition, blood and blood products, drug administration (continuous or intermittent), prophylactic use before procedures, prophylactic use in unstable patients.

Central Venous Cannulation: Central venous cannulation is increasingly used not only in intensive care and high dependency units but also on general medical and surgical wards. Many problems can occur with the insertion of a central venous catheter, including arterial puncture, puncture of a lung leading to a pneumothorax, and perforation of the right atrium or pulmonary artery. Appropriate training and experience is essential in avoiding these complications, especially since the majority of central venous catheters are inserted by doctors in training. This has been recognised by the National Institute for Clinical Excellence in the UK, which has published guidelines that recommend two dimensional ultrasound guidance as the preferred method for cannulation of the internal jugular vein. The guidelines also stipulate that clinicians undertaking this procedure should receive appropriate training to achieve competence since the technique is operator dependent with a long learning curve.[2]

ADMINISTRATION TECHNIQUES IN INTRAVENOUS DRUG THERAPY

Drugs are also frequently administered by the intravenous route, either as bolus injections or by infusion. The indications for the intravenous administration of drugs can be summarised as follows:

- If the patient has a serious disease, the administration of a drug intravenously may have advantages over oral drug administration in terms of reducing mortality. This is perceived to be the case in patients with life threatening bacterial infections. Although the use of intravenous antibiotics may often be indicated in patients with serious infections, it is common practice in hospitals to start intravenous antibiotics irrespective of the severity of the infection. Oral antibiotics in most of the patients admitted to hospital with bacterial infections are just as effective as intravenous antibiotics and have the added advantages of ease of administration, reduce labour and administration costs, and reduced hospital stay.

- The drug may have limited oral bioavailability or only be available in an intravenous preparation; for example, amino glycoside antibiotics are polycations and highly polar and thus will not be absorbed via the gastrointestinal tract; therefore, they have to be administered parenterally

1. **Continous Intravenous Infusion:** High concentration drugs are used by continuous infusion because of facilitated monitoring (sampling time is not critical after the first loading dose, making interpretation of blood levels and pharmacokinetic calculations easier), potential decreased toxicity, easier nursing and the possibility of centralized preparation of ready-to-use solutions. To safely implement this mode of administration in a routine hospital setting it is, however, essential to ensure that drug remains stable over the whole process and that incompatibilities with other medications co-administered by the intravenous route are avoided[3]

2. **Intermittent Intravenous Infusion:** Intravenous intermittent infusion is an infusion of a volume of fluid/medication over a set period of time at prescribed intervals and then stopped until the next dose is required. An intermittent IV medication may be called a piggyback medication, a secondary medication, or a mini bag medication Intravenous medications may be given in small volumes of sterile IV solution (25 to 250 ml) and infused over a desired amount of time (given for 30 minutes every 4 hours) or as a single dose. Many medications must be given slowly to prevent harm to the patient, and this method of administration reduces the risk of rapid infusion. A piggyback medication is given through an established IV line that is kept patent by a continuous IV solution or by flushing a short venous access device (saline lock). Always check the *Parenteral Drug Therapy Manual* PDTM to ensure the correct guidelines are followed for each specific medication given in IV solution. The PDTM provides guidelines on how

to mix the IV medication, the amount and type of solution, and the rate of infusion[4]

An intermittent medication may be administered by gravity or on an electronic infusion device (EID), also known as an infusion (IV) pump. Many piggyback IV medications must be on an IV pump, which requires programming and specialized training to prevent medication errors. The IV infusion pumps provide hard- and soft-dose limits and safety practice guidelines to aid in safe medication administration[5]. IV medications may also be given by gravity infusion, in which case the health care provider must calculate the infusion rate for drops per minute. The best practice for piggyback infusions is to use an IV infusion pump.

Figure showing Secondary medication (upper IV mini bag) set up with primary infusion set (lower IV Bag)

3. **Bolus Injection:** The I.V. bolus injection method allows rapid drug administration. It can be used in an emergency to provide an immediate drug effect. It can also be used to administer drugs that can't be given I.M., to achieve peak drug levels in the bloodstream, and to deliver drugs that can't be diluted, such as diazepam, digoxin, and phenytoin. The term bolus usually refers to the concentration or amount of a drug. I.V. push is a technique for rapid I.V. injection. Bolus doses of medication may be

injected directly into a vein, through an existing I.V. line, or through an implanted vascular access port(VAP). The medication administered by these methods usually takes effect rapidly, so the patient must be monitored for an adverse reaction, such as cardiac arrhythmia and anaphylaxis. I.V. bolus injections are contraindicated when rapid drug administration could cause life-threatening complications. For certain drugs, the safe rate of injection is specified by the manufacturer. Some facilities permit only specially trained nurses (such as emergency department, critical care, and chemotherapy nurses) to give bolus injections.

Figure showing iv bolus administration of drug

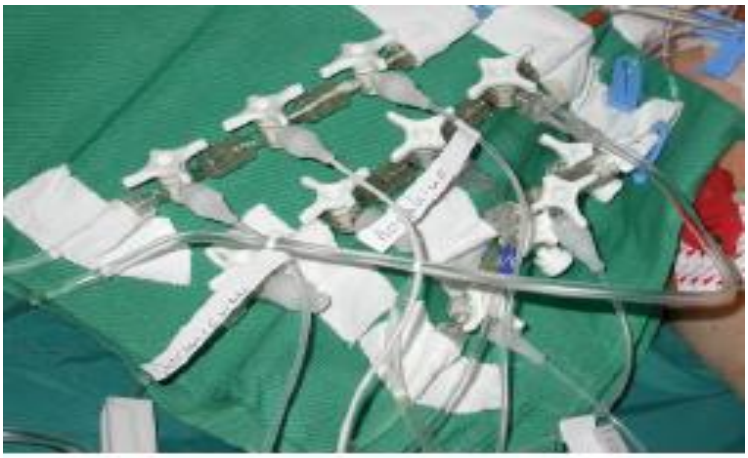

Figure showing Y-Site Administration of drugs

Critically ill hospitalized patients are often in need of many intravenous drugs, and a frequent problem is the lack of sufficient number of access sites or available lumen in multi-lumen catheters, to administer each product separately If a patient receives a continuous infusion of total parenteral nutrition (TPN), the infusion should be stopped and the line flushed before administration of other drugs in the same line However, frequent stops may lead to under-nutrition, and the repeated flushing may be problematic with regard to the patient's fluid balance . In this situation it might be beneficial to co-administer drugs and TPN through a Y-site connector.[6]

- **INTRAVENOUS ADMIXTURES**

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. 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. 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. The number of IV medications continues to expand and the need to administer different IV drug combinations are increasing day by day. 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[7].

INCOMPATIBILITIES IN INTENSIVE CARE UNIT

Incompatibility describes preventable or reversible precipitation or insolubility. An incompatibility reaction occurs inside a fluid container or infusion line and is usually visible. Visible precipitation (and all precipitation

that may be clinically significant is not visible) has been described as physical incompatibility. However, precipitates are physical products of intermolecular and interionic forces .[8]Mixing solutions of parenteral drugs is generally not recommended because of the potential for incompatibility and consequent loss of activity of one or both drugs. However, in some circumstances there may be compelling reasons for mixing two or more parenteral drug solutions in the same infusion bag, in the same syringe or at a Y-site junction where two or more intravenous lines meet. The decision to mix drugs should not be made without knowledge of their compatibility. If intravenous drugs are not mixed but are given consecutively, the infusion line should be flushed through with compatible fluid between each administration**.**[9]

Incompatibilities became an issue of concern, especially in intensive care units (ICUs), because of the large fraction of parenteral drug applications, the need for constant drug concentrations (e.g., vasoactive support), and the limited number of independent i.v. lines in critically ill patients.12-15 Compatibility is not certain for drug combinations in which the compatibility is unknown or ambiguous for up to 45% of coinfusions in an ICU[10]**.** Physicochemical incompatibilities between intravenous drugs are a recurrent problem in hospitals, mainly in intensive care units (ICUs). Critically ill patients often require multiple infusions of several drugs, which are administered simultaneously by the same intravenous line of a multi lumen catheter.[11]**.** Assessing their mutual physicochemical compatibility is therefore important to avoid precipitate formation or chemical inactivation of one or more drugs.[12]In the intensive care medicine, 25% of medication errors are highly significant clinical incompatibilities leading to loss of activity or increased microparticle load and posing severe risks for patients. Tissot et al stated that more than 63% of errors were significant and 26% even life threatening.[11] Mixing incompatible drugs is considered a serious medication error that could lead to therapeutic failure, microembolisms or even toxicity. Some authors found a high incidence of medication errors related to drug administration in intensive care units (ICUs). Taxis and Barber observed a

48% error rate in a German hospital, with 25% of these errors due to the co-administration of potentially incompatible drugs Carmen[13].Although this issue represents a major problem, information about drug incompatibilities under clinical conditions is still lacking. In ICU wards, it is usual practice to administer analgesics and sedatives to a patient via a single port of entry. It is thus important to know whether these drugs are physicochemically compatible or not.[11]

- **TYPES OF INCOMPATABILITIES**

1. Physical Incompatibilities: Physical reactions of drugs usually refer to either phase separation or precipitation (e.g. after the dilution of alcoholic solutions) due to a change of the relation between ionization and nonionization and solubility8. The alteration may result in synergism, antagonism or new effects.

The pH-value, Pka and the buffer capacity of the IV solutions and the drugs used are major factors responsible for physical interactions [8].The situation in an infusion regimen is specific to the combination of drugs and solution used. Usually, the drug has the greatest influence and therefore defines the pH-value of the solution infused. Many drugs are weak bases, present as the water soluble salts of the corresponding acids. Changes in pH-value in the infusion tubing, e.g. from simultaneous addition of another drug, may release the bases from their salts. Because of the low aqueous solubility of such bases, particles may precipitate. The process of precipitation is influenced by the relative quantity of the drugs added, as well as their buffering capacity. These pH-dependent precipitation reactions are usually very rapid and can be identified within a few centi meters in the infusion tubing system. They can visibly be observed as crystals, haziness or turbidity.[8]Precipitations based on drug incompatibilities are responsible for the most common particle formation seen in complex ICU infusion lines. Further invisible physical incompatibilities are reactions between drugs and plastic materials (adsorption effects). This leads to the drugs becoming immobilized at the inner surface of infusion

containers or infusion lines and so lowers the concentration and drastically decreases the quantity of the drug administered to a patient[14]

2. Chemical Incompatibility: A chemical incompatibility means that the drug is chemically degraded, due to oxidation, reduction, hydrolysis, or decomposition. Chemical reactions can manifest themselves through turbidity, precipitation and color changes.

3. Therapeutic Incompatibility: Therapeutic Incompatibility may be as a result of prescribing certain drugs to a patient with the intention to produce a specific degree of pharmacological action, but the nature or intensity of the action produced is different from that intended by the prescriber. This occurs either due to error in dosage form, wrong dose or dosage form, contra-indicated drugs or synergistic and antagonist drugs

- **MECHANISMS OF INCOMPATIBILITY**

Incompatibility problems are more likely to arise when small concentrated volumes are mixed in a syringe rather than in the larger volume of an infusion bag. This is because of higher mutual drug concentrations and potentially greater pH changes in the more concentrated solution. The absence of any visible change to a solution upon mixing does not automatically exclude degradation of either or both components.

Drugs that precipitate upon dilution: Precipitation of a drug from its concentrated injection solution when it is diluted with water or saline is counter-intuitive. However, a small number of injection solutions are formulated in non-aqueous solvents to allow dissolution of a poorly water soluble substance in a small volume. In these formulations, dilution of the non-aqueous injection vehicle with water or saline may precipitate the drug. The problem is frequently observed when diazepam injection is diluted. Diazepam is very poorly water soluble so it is formulated as an injection solution in a vehicle comprising 50% propylene glycol and 10% ethanol. At first, dilution produces a slight turbidity which clears upon mixing, but dilution

beyond fourfold produces an opaque white precipitate which does not clear until substantial further dilution.[9]

Precipitation of drugs due to pH change upon mixing: The water solubility of any drug is enhanced by ionisation of the molecule. For a drug molecule which acts as a proton acceptor (a Lowry-Bronsted base), ionisation is achieved by formulation in a low pH solution usually as a hydrochloride or hydrogen sulfate salt (for example, amiodarone hydrochloride or adrenaline acid tartrate). Conversely, for a drug molecule which can lose a proton or hydrogen ion (a Lowry-Bronsted acid – usually a weak organic acid), ionization is achieved by formulation in a high pH solution, usually as a sodium or potassium salt (for example, benzylpenicillin sodium). Any change in pH towards the other end of the pH scale will reduce the proportion of ionised to un-ionised drug in solution and will therefore reduce the water solubility of the drug. The most prominent example of a pH-related reduction insolubility is dilution of phenytoin sodium injection. The drug is formulated with non-aqueous solubilising agents and the solution is adjusted to a pH of 12. Dilution of injectable phenytoin by adding it to an infusion bag lowers its pH and therefore reduces its solubility resulting in precipitation of the drug.

Ionic reactions forming insoluble substances: The salts of monovalent cations, such as sodium and potassium, are generally more soluble than those of divalent cations, such as calcium and magnesium. Mixing solutions containing calcium or magnesium ions has a substantial risk of forming an insoluble calcium or magnesium salt. Mixing magnesium sulfate 50% and calcium chloride 10% results in precipitation of insoluble calcium sulfate. The mixing of drug salts of calcium, and to a lesser extent magnesium, with phosphates, carbonates, bicarbonates, tartrates or sulfates should also be avoided.

Evolution of gas: Addition of an acidic drug solution to a solution containing carbonate or bicarbonate may result in production of carbon

dioxide gas. However, the evolution of gas is a normal part of the reconstitution of some drugs, notably ceftazidime[9]

- **CAUSES OF INCOMPATABILITIES**

  - ❖ Incompatibilities of drugs can occur between drugs and inappropriate IV solutions as diluents.
  - ❖ Two drugs (drug-drug incompatibility) when they are:

    -mixed together, e.g. within the same infusion line (simultaneous infusion) and/or IV container.

    - administered one after the other, but within the same infusion line.
  - ❖ drugs and adjuvants (preservative, buffer, stabilizer, solvent)
  - ❖ drugs and materials of IV containers (e.g. PVC) or medical devices, which can concern the nature of the material used and/or reactions at the inner surface (e.g. adsorption) **.**

CONSEQUENCES OF INCOMPATIBILITY

- ❖ **Consequences for the patient**
  - damage from toxic products
  - particulate emboli from crystallization and separation
  - tissue irritation due to major pH changes
  - therapeutic failure
  - ❖ **Financial impact**

Adverse effects of drug incompatibilities extend periods of patients' hospitalization and the total costs for hospitals.

STRATEGIES TO PREVENT INCOMPATIBILITIES

❖ Dangerous incompatibilities can be prevented by:

- a plausibility check regarding the SPC and available sources on compatability information, also considering the material used for therapy (eg iv containers,IV line,diluents) and the infusion regimen
- Individual labeling for each drug preparation(including drug, concentration, patient name)
- Consistently checking alternative modes of administration and or using multi-lumen catheters.
- Separating the drug doses by time and place. This can include the rinsing of the infusion system with a neutral iv solution prior to the application of another drug[15]

Furthermore, inline filters can reduce influx of particles which results from incompatibilities. Morever they can used to monitor physical and chemical incompatibilities. Inline filters are able to retain solid particles of at least 0.2µm [17]As a consequence filter may be block. This is not a malfunction of the filter, but should initiate a check of the medication in order to eliminate any incompatibility.[16]

REVIEW OF LITERATURE

1) **Rodríguez *et al* (2016)[17]** conducted a study on Development of a Compatibility Chart for Intravenous Y-Site Drug Administration in a Paediatric Intensive Care Unit. The objective of study is to develop a chart showing drug compatibility in Y-site administration for the most common drugs in a paediatric intensive care unit. Paediatric patients admitted to intensive care units are likely candidates for intravenous drug administration. These patients may sometimes have limited vascular access, so availability of compatibility charts for intravenous Y-site administration may help daily clinical practice. The authors concluded that compatibility chart is a highly reliable quick reference for health professionals working in the PICU, and it may help to prevent the intravenous administration of incompatible drugs through the same line.

2)Staven *et al* (2016) [5]carried out a study development and evaluation of a test program for Y-site compatibility testing of total parenteral nutrition and intravenous drugs. The purpose of the study is to was to establish and evaluate a test program of methods suitable for detection of physical incompatibility in Y-site administration of total parenteral nutrition (TPN) and drugs. Dynamic light scattering, laser diffraction, light obscuration, turbidimetry, zeta potential, light microscopy, pH-measurements and visual examination methods were scrutinized to elucidate strengths and weaknesses for compatibility testing .Light obscuration together with turbidimetry, visual inspection and pH-measurements were able to capture signs of precipitations. The study concluded that testing of these complex blends should be based on a combination of several methods and accompanied by theoretical considerations.

3) Miranda *et al* (2016) [18]conducted a study on Compatibility: drugs and parenteral nutrition. The objective of study standardization and systematization of data to provide quick access to compatibility of leading

injectable drugs used in hospitals for parenteral nutrition. 55 injectable drugs analyzed individually with two types of parenteral nutrition: 2-in-1 and 3-in-1and variables like: active ingredient, compatibility of drugs with the parenteral nutrition with or without lipids, and maximum drug concentration after dilution for the drugs compatible with parenteral nutrition are considered. The authors concluded that systematization of compatibility data provided quick and easy access, and enabled standardizing pharmacists work.

4) Delaloye et al (2016)[19] carried out a study on Screening for physicochemical incompatibilities of intravenous drugs in intensive care units: the case of monobasic potassium phosphate and furosemide. The aim is to study the physicochemical incompatibilities between intravenous drugs are a recurrent problem in hospital setting and having observed a drug precipitation during Y-site administration in our intensive care units. The study concluded that monobasic potassium phosphate is not compatible with furosemide in the concentration range used in our intensive care unit and should not be administered together in the same intravenous line

5) Deepak *et al* (2015)[20] studied on the evaluation of intravenous admixtures in tertiary care teaching hospital. 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. Data for the study was collected by Patient interview and Chart Review Method and included all the hospitalized patients form general medicine departments. The 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 authors concluded that research work would certainly increase the safety in the use of IV admixtures by creating awareness among the nurses about the complications of iv incompatibility problems .The study also found that preparation and placing of IV medication admixtures

compatibility charts and drug information leaflet in wards can help to reduce IV incompatibilities especially when there is a need to mixing drugs together. A daily prescription review by pharmacist could possibly prevent compatibility errors found on the wards.

6)Wade *et al* (2015)[21]performed a study on Simulated Y-Site Compatibility of Vancomycin and Piperacillin-Tazobactam. The purpose of the study is to evaluate the physical compatibility of vancomycin with piperacillin-tazobactam during simulated Y-site administration. Vancomycin and piperacillin-tazobactam were tested using 2 different diluents: 0.9%sodium chloride and 5% dextrose for injection. The authors concluded that Y-site incompatibility was greater for the tested concentrations of piperacillintazobactam and vancomycin when 5% dextrose was used as the diluent versus 0.9% sodium chloride.

7) Cabezas *et al* (2015)[12] conducted a study on physicochemical compatibility of high concentration drugs usually Y-site administered in intensive care units. The objective is to study the physical compatibility of 63 binary mixtures of drugs usually Y-administered in intensive care units, and to evaluate the chemical stability of the most relevant binary mixtures. Binary mixtures were aseptically prepared in a 1:1 ratio. The study concluded by providing information about the physicochemical compatibility of ordinary mixtures, at high concentrations, commonly used in intensive care units and these results might help to improve drug safety management in the critically ill patient.

8) **Nagaraju *et al* (2015)**[7]6carried out a prospective observational study on the assessment of intravenous admixtures incompatibilities & the incidence of intravenous drug administration errors .The objective is to assess the potential incompatibilities associated with IV admixtures & the incidence of IV drug administration errors in a tertiary care teaching hospital and included all the hospitalized patients of general medicine. . The data for the present study was collected by chart review method. The study mainly focuses on compatibility of Drug-Solute and Drug-Drug combinations. The collected data

was analyzed for incompatibilities by using standard drug reference texts .The study concluded that research work would certainly increases the safety in the use of IV admixtures by creating awareness among the health care professionals about the incompatibility problems.

9)Sullivan *et al* (2015)[22] conducted a study on Compatibility of Cloxacillin Sodium with Selected Intravenous Drugs During Simulated Y-Site Administration. The objective of the study is to establish the compatibility of IV cloxacillin with 89 injectable drugs during simulated Y-site administration. Data regarding Y-site compatibility of intravenous (IV) cloxacillin sodium with other drugs are scarce and incomplete. The authors concluded that Sixty-four IV drugs were found to be compatible with cloxacillin via simulated Y-site, whereas 25 drugs were found to be incompatible with the antibiotic and the light obscuration particle count test should be used to complement visual evaluation when samples do not precipitate immediately

10) Machotka *et al* (2014)[23]carried out a prospective cross sectional study on the incidence of intravenous drug incompatibilities in intensive care units. The aim of the study was to identify the real incidence of drug incompatibilities in intravenous lines in critically ill patients in two intensive care units. The study was carried out in one medical and one surgical ICU and patients included were receiving at least two different intravenous drugs. The study showed that a significant number of drug incompatibilities occur in both medical and surgical ICUs. The authors concluded that the incidence of incompatibilities could be diminished by adhering to a few simple rules for medication administration following by recommendations for multiple lumen catheter use.

11) Hanifah *et al* (2014)[24]studied on the topic of mapping of incompatibility assay and bringing method to problem in critical care. The aim of the study is to identify the methodology of incompatibility assay. A search was conducted of incompatibility studies through International Pharmaceutical Abstract (IPA). The study used both in vivo and in vitro method .In vivo method compatibility

in the mixture of diluted product, and also in the blood were studied .In vitro method, study used static and dynamic method .The study concluded that a standardized procedure is meaningful for general judgement for incompatibility and particularly in critical care, setting up an evaluation procedure that mimics as closely as possible real practice within the clinical area should be undertaken to validate practice.

12)Raverdy *et al* (2013) [3]performed a study on Stability and compatibility of vancomycin for administration by continuous infusion. The background of the study is that vancomycin is increasingly used by continuous infusion, but few specific data are available about stability under practical conditions of preparation and use, and compatibility with other intravenous drugs commonly used in the routine hospital setting. The study concluded that centralized preparation of vancomycin and its use by continuous infusion in wards is safe concerning stability, but careful attention must be paid to incompatibilities.

13) Delaloye *et al* (2013)[25] performed a study on in vitro compatibility of various cardioactive drugs during simulated Y-site administration. The aim of the study to evaluate the physicochemical compatibility of five common associations of cardioactive drugs: dopamine (DA)–norepinephrine (NE); dobutamine (DU)–NE; amiodarone (AM)–DU–NE; DU–sodium nitroprusside (NI)±sodium thiosulfate (THIO); and. Their compatibility was verified by visual inspection of the different mixtures in glass tubes and by chemical assays and pH determination of the mixtures collected during in vitro simulated Y-site administration. The study concluded that when combined, the cardioactive amines were stable over 24 h. AM was compatible with DU and NE, but with a latency period owing to its adsorption on the heparin-coated Swan–Ganz catheter. Mixtures involving NI were compatible provided that NI was supplied in amber syringes or protected with aluminum foil.

14) Ramanath, Hymavath (2012)[26] performed a observational, prospective study on assessment of intravenous admixtures in hospitalized patients of a rural tertiary care teaching hospital. The present study mainly focused on

clinical pharmacist assessment in intravenous admixtures administration. 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. 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 ischemia, hypoxia and impairment in discharge of metabolic end products. 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.

15) Kanji *et al* (2010)[27] conducted a study on systematic review of physical and chemical compatibility of commonly used medications administered by continuous infusion in intensive care units . The aim of the study is to quantify the physical and chemical stability data published for commonly used continuously infused medications in the intensive care unit and to evaluate the quality of the studies providing these data. The study concluded that physical compatibility studies that provide the basis for y-site compatibility are lacking for commonly used medications in intensive care unit patients and may contribute to unsafe medication practices and also the heterogeneity in the methodology of these studies likely contributes to the common finding of conflicting data for specific combinations of drugs.

16) Kalikstad *et al* (2010)[28] performed a study on Compatibility of drug infusions in the NICU. The majority of drugs used in sick newborns receiving intensive care are unlicensed and off-label, exposing infants to greater risk of adverse drug reactions. Our aim was to study the compatibility of co-infusions for a selected group of drugs and nutrition solutions as part of our quality assurance programme in the neonatal intensive care unit. The authors reviewed drug studies in the literature and t he results of searches were reviewed against predetermined criteria for co-infusion of 13 intensive care

drugs with 66 other drugs and two nutrition solutions and albumin. Study concluded that here is a lack of data on compatibility for the majority of drugs used for co-infusions in neonates and therefore caregivers therefore need to pay special attention to infusion lines when drugs are co-administer.Their results also suggest that further studies on drug compatibility are needed to reduce possible ADRs and toxicity, and avoid precipitation and occlusion of infusion lines in critically ill neonates.

17) De Giorgi et al (2010)[29] studied on the Evaluation of tools to prevent drug incompatibilities in paediatric and neonatal intensive care units. Intravenous drug administration in neonatal (NICU) and paediatric intensive care units (PICU) is critical because of poor venous access, polymedication, fluid restriction and low infusion rate. Risk is further increased by inadequate information on the physicochemical compatibility of drugs. Eight decision-supporting tools were hence evaluated to improve the detection of drug incompatibilities in paediatric wards. The percentage of non-compliant answers was calculated for both the performing pharmacists and the tools .Study concluded that large ranges of pharmacists' non complaint answers shows that such an assessment is subject to different interpretations. Standard operating procedures for drug-incompatibility assessment should be implemented in drug-information centres.

18) Knudsen *et al* (2010)[30] conducted a study on Physicochemical compatibility of commonly used analgesics and sedatives in the intensive care medicine. To minimise the risk of incompatibilities in parenteral drugs in a cardiovascular intensive care unit by analysing the physical and chemical compatibility of seven commonly used analgesics and sedatives and to determine whether these drugs can be administered by the same intravenous line. Clonidine hydrochloride, 4-hydroxybutyricacid, (S)-ketamine hydrochloride, lormetazepam, midazolam hydrochloride, piritramide and sufentanil citrate were diluted with sodium chloride 0.9% to standardised concentrations and mixed in different ways and combinations and stored for 7

days.During storage physical incompatibility was verified by visually and the chemicalcompatibility of two multiple drug mixtures and 10 drugpairs was determined by high-performance liquid chromatography examination. The study found that 4-Hydroxybutyric acid was physically incompatible with (S)-ketamine hydrochloride, midazolamhydrochloride and piritramide .Also the combination of clonidine hydrochloride and sufentanil citrate showed instabilities within the first hours after mixing. The auhtors concluded that 4-Hydroxybutyric acid carries a major risk for incompatibilities when mixed with other drugs and therefore has to be administered separately. Mixtures of clonidine hydrochloride and sufentanil citrate should only be used with great caution, and a dose adjustment should be considered.

19) Newton David (2009)[7] performed study on Drug incompatibility chemistry. The purpose of the study is to know the chemical interactions that cause drug incompatibility in solutions, with emphasis on the acid–base and ionized–nonionized forms of organic, weak, electrolyte drugs. When the dilution or mixing of the salt or ionized forms of organic drugs results in precipitation. Acid–base reactions are the most common causes of drug incompatibility as precipitation of nonionized drug forms. The authors concluded that incompatibility of drug and nutrient injections is clinically hazardous and precipitation in injectable drug solutions should be suspected, particularly when oppositely charged drug salts are mixed in relatively strong concentrations and when pH values of dilutions create more than 1% of nonionized drug forms.

20) Bertsche *et al* (2008)[31] conducted a study on the Prevention of Intravenous Drug Incompatibilities in an intensive care unit. The authors discussed the frequency of drug administration errors and incompatibilities between intravenous drugs before and after an intervention in an intensive care unit. They included the most frequent brands of I.V medications used in the ICU of a gastroenterological department in retrospective analysis. They found out the all possible combinations and resulting incompatibilities. Study

stated that administration of incompatible I.V drugs in critically ill patients was frequent but can significantly reduced by following procedural interventions with SOP.

21) Walker *et al* (2004)[32]performed a study on Physical Compatibility of Pantoprazole with Selected Medications during Simulated Y-Site Administration. Patients receiving IV pantoprazole often require concomitant IV drugs and solutions. The objective of the study is to complete a visual compatibility study of IV pantoprazole with 17 other IV medications, as well as with a mixture of 3.3% dextrose and 0.3% sodium chloride for injection, during simulated Y-site injection. Seventeen drugs, each at 3 different concentrations, as well as a mixture of 3.3% dextrose and 0.3% sodium chloride forinjection, were selected for physical compatibility testing with 3 concentrations (0.16 mg/mL, 0.40 mg/mL, and 0.80 mg/mL) of pantoprazole in 0.9% sodium chloride for injection (NS).The authors concluded that admixtures prepared in the clinical setting are subject to greater error than in the laboratory, and it is therefore recommended that practitioners avoid Y-site administration of pantoprazole with incompatible drugs.

22) Trissel, Christopher (**2001)**[33] studied on the topic Incompatibility of Lansoprazole Injection with other drugs during stimulated Y site Administration. The purpose of the study was to evaluate the physical compatibility of lansoprazole injection during stimulated Y site injection with 112 other drugs by visual observation, turbidity measurement and particle content assessment. Of the drugs tested ,92 incompatible with lansoprazole 0.55mg/ml in 0.9% NaCl injection during the fourth hour observational period. The authors concluded that only twenty drugs were found to be physical compatible with lansoprazole and ninety two drugs exhibited physical incompatibility within 4hours

23)Gikic *et al* (2000)[14] performed a open prospective study on evaluation of physiochemical incompatibilities during parenteral drug administration in a pediatric intensive care unit. The objective of the study is to identify

prospectively the combinations of injectable drugs administered in the paediatric intensive care unit and to analyze them according to the information found in literature. The authors concluded that in vitro compatibility tests on standard drug combinations as well as a training program for nurses on drug incompatibility problems would sensitively increase the security of parenteral drug administration

SCOPE OF STUDY

Critically ill patients in the Intensive Care Unit (ICU) require multiple medications, often administered as continuous intravenous infusions. Since IV access is usually limited, they need to be administered at the same time through the same port of a central venous catheter or peripheral venous catheter. This is facilitated by a “Y-site” connector that can be joined to a port on any catheter. Two or more medications that are administered via Y-site connector mix in the lumen of the tubing prior to being infused into the patient. However, not all medications can be physically mixed together. The accepted standard for medications deemed to be compatible for Y-site co-administration is that they must be physically compatible, which typically means that when mixed, there is no gross evidence of incompatibility at clinically relevant concentrations over a period of time. In contrast, when two or more medications are intended to be prepared as a mixture and infused from the same bag or bottle, they are required to demonstrate chemical stability whereby the molecular integrity of all components of the mixture are maintained for the duration of mixing. The main difference between the two is the duration of mixing that warrants different standards. Medications that are combined via Y-site typically mix for less than one minute prior to being infused into the patient. Medications that are pre-mixed in the same bag or bottle will mix for much longer. When there is a challenge of administering more medication infusions than there are ports available, they are forced to consider co-administering multiple medications through the same port/catheter using a Y-site connector.

The potential complications of co-administration of incompatible medications include precipitation, central venous catheter occlusion requiring additional venous access, reduced potency of medication, therapeutic failure and local and systemic inflammatory reactions. The prevalence and outcomes of these types of complications are not well documented. Previous studies found incompatibility problems in upto 18.6% of critical care patients and

18.7% of continuously infused medications. Few studies have reported co-infusion of incompatible medications leading to negative outcomes in humans such as pulmonary embolism of medication precipitates. In September of 2007 the FDA issued an alert related to the co-administration of calcium-containing products and ceftriaxone due to potential end-organ damage associated with calcium-ceftriaxone precipitates leading to lung and kidney damage. A subsequent report suggested that the majority of these negative outcomes were due to a Y-site incompatibility between ceftriaxone and calcium infusions administered simultaneously through the same intravenous catheter. Various factors such as solvents, diluents, infusion fluids, pH of each drug, duration of stability and concentration of the selected critical care drugs play a major role in determining the compatibility of intravenous drug infusions at the Y-junction. More than 90% of the drugs are organic, weak electrolytes, especially those compounded, manufactured or reconstituted as injections in predominantly ionized or salt forms. Acid-base reactions are most common causes of drug incompatibility as precipitation of nonionized drug forms. Precipitation is likely when oppositely charged, organic drug ions that contain aromatic rings are combined in relatively strong concentrations. Salts of polyvalent anions and cations are generally less soluble than salts in which both ions are monovalent or in which one ion is monovalent and its opposite ion is polyvalent. The proposed study I tests the hypothesis that polyvalent ions in the co-infused drug solutions or acid-base reactions between the continuously infused drug solution and Y-site administered drug would cause a significant number of physicochemical incompatibilities in the Medical Intensive Care Unit.

OBJECTIVE OF THE STUDY

- To study the influence of polyvalent ions in the co-infused drug solutions and acid-base reactions between the continuously infused drug solution and Y-site administered drug on the physicochemical compatibility of various critical care drugs used in the Medical Intensive Care Unit.
- To identify the most frequent and clinically significant incompatibilities of continuous IV infusions of the selected critical care drugs with Y-site administered drugs in the MICU settings.
- To prepare a two dimensional compatibility chart for the most commonly used continuous intravenous infusions and Y-site administered drugs in MICU.

PLAN OF THE STUDY

The proposed study entitled “Effect of pH and polyvalent cations on the Y-site incompatibility of continuous intravenous infusions of selected critical care drugs in the Medical Intensive Care Unit” was planned and carried out as given below.

Phase 1

- Identification of research problem and scope of the study
- Preparation of study protocol
- Obtaining permission from the hospital ethical committee
- Literature survey

Phase II

- Design of structured proforma.
- Patient selection, inclusion /exclusion criteria.
- Data retrieval from intensive care unit department.
- Identication, evaluation and resolving of incompatibilities in intensive care unit.
- Documentation and concurrent feedback to doctor and nurses.

Phase III

- Data Analysis
- Report Submission

METHODOLOGY

Study Site: Medical Intensive Care Unit (MICU) of a 750 bedded multispecialty tertiary care teaching hospital.

Study Design: Prospective observational study.

Study Duration: 8 months (from February 2015 to September 2016).

Inclusion Criteria: Patients admitted to the Medical Intensive Care Unit, receiving co-infusions of at least two IV drugs or one drugs are included.

Exclusion Criteria: Patients who receives continuous intravenous infusion of drugs but no Y-site drug administration will be excluded.

Major Outcome measures: The major outcome measure is the compatibility between drugs administerd by continuous intravenous infusion and Y-site administerd drugs. Secondary outcome measures include the factors influencing compatibility of the drugs such as pH or presence of polyvalent cations in the drug or diluents.

Method:. The medication charts of 80 consecutive patients admitted to the Intensive Care Unit and treated with continuous intravenous infusions and Y – Site administered drugs are analyzed. The diluents, infusion fluid, pH, duration of stability, the nature and drug concentrations of the selected critical care drugs such as vasoactive agents, other cardiovascular drugs, analgesics, other drugs and nutrition solutions are recorded and carefully evaluated. Drugs given as continuous intravenous infusions are chosen because they have longer infusion time and therefore pose the majority of compatibility problems when a second drug is administered at the Y-junction.

Compatibility of the selected critical care drugs when given as continuous intravenous infusions are then analyzed against the Y-site administered drugs using the 2-dimensional compatibility chart. On observing any incompatibility, the possible mechanism such as acid-base reactions due

to pH variations of the co-infused drug solutions/ drug and nutrient solutions or drug precipitation due to the presence of polyvalent cations such as Ca^{2+}, Mg^{3+} will be identified. The pH, drug, concentration and other physiochemical properties of both drug and infusion fluids were also recorded.

A 2-dimensional compatibility chart was developed indicating the compatibility of selected critical care drug infusions with Y-site administered drugs commonly used in the Medical Intensive Care Unit is prepared. *Trissel's Handbook of Injectable Drugs, Micromedex Healthcare Series,MEDLINE* databases and manufacturer's product information are used as the primary source of information. Other sources like AHFS drug information or the *Stabilis* Website are also referred

Outcome of the study: The primary outcome of the study is the identification of the factors causing incompatibility of continuous intravenous infusions and Y-site administered drugs in the Medical Intensive Care Unit. The proposed study will review the compatibility of continuous intravenous infusions of certain selected critical care drugs and nutrition solutions against Y-site administered drugs with a view to improving the safety of multidrug therapy in the Medical Intensive Care Unit. The study will also lead to the development of a two dimensional Y-site compatibility for commonly used critical care drugs in the intensive care unit.

The study will also estimate the prevalence of inappropriate co-administration of continuously infused IV medications, and also identify the gaps in the medication compatibility literature that can be addressed by the physical incompatibility studies in future. The compatibility chart prepared in the study will help as a tool to reduce the incidence of medication errors in critically ill patients when exposed to multiple co-infusions. In other words, the proposed study will improve the safety of multidrug therapy in the Medical Intensive Care Unit.

RESULTS

Data were obtained from 80 consecutive admissions in Medical Intensive Care Unit, of which 55 were male patients. The mean age of the study population was 54.0625±19.739 (range: 17 to 87). Their mean duration of hospitalization was 1.6330±3.0625 (range: 1 to 7days). Table 1 shows the demographic details of these patients.

Major diagnosis include Diabetes Mellitus (12.5%), Road Traffic Accident/Head Injury(12.5%), Chronic Renal Failure(10%), Systemic Hypertension (8.75%), Cerebrovascular Accident(7.5%), Chronic Obstructive Pulmonary Disorder (5%), Respiratory Disorders (5%), Cancer (5%), Poisoning (5%), Subarachnoid haemorrhage (3.75%), Ischaemic Heart Disease (3.75%) and others as shown in Table 2.

Total number of drugs prescribed in the study subjects was 682 with a mean of 8.743±3.680 (range: 2 to 15). The details are presented in table 3. Five hundred and fifty four (81.23%) of the prescribed medications were administered intravenously (table 4). Of these, 262 (38.4%) were administered as continuous Intravenous infusions (table 5) while 292 (42.81%) were administered using Y-connector (table 6). Most frequently prescribed continuous intravenous infusions were Levetiracetam (9.54%), Citicoline (9.16%), Midazolam (6.48%), Methyl Prednisolon (6.10%) and Fentanyl (5.34%) while drugs such as Ondansetron (18.83%), Pantoprazole (17.80%), Piperacillin Sodium+Tazobactum Sodium (10.60%) and Ceftriaxone (9.58%) were most commonly administered using Y-connector.

Table 7 illustrates the compatibility of continuous intravenous infusions with Y-site administered drugs. Of the 600 drug-drug combinations or drug-diluent combinations evaluated, two hundred and two combinations (33.66%) were found to be compatible while 17 (2.83%) combinations were incompatible. The compatibility information of 354 (59%) combinations are not reported in the literature and 27 combinations were reported as caution

(4.5%) Table 8 and 9 shows the details of compatibility particulars of the continuous intravenous infusions with the Y-site administered drugs. Fentanyl+ Pantoprazole (1.44%), Metronidazole + Pantoprazole (1.44%), Levofloxacin+ Piperacillin Na, Tazobactum Na (0.90%), Ringer Lactate+ Ceftriaxone (0.72%) and Fluconazole + Pantoprazole (0.72%) constituted the maximum number of incompatibility.

Details such as the diluents used, rate of infusion, duration of administration, concentration of reconstituted solution, presence of monovalent or polyvalent ions and pH of the drug solutions are given in table 11. Only one incompatibility was due to the presence of polyvalent cation (Ca^{++}) in the combination while most of the drug pairs were found to have differing pH values ranging from 2.5 pH (acidic) to 11(basic). A majority of the continuous intravenous infusions had a pH value in the acidic range (except ondansetron) while that of Y-site administered drugs were found to be in the alkaline range.

The 2-dimensional compatibility chart prepared is shown table 12. This chart indicates the compatibility of selected continuous intravenous infusions with Y-site administered drugs commonly used in the MICU.

TABLE 1: DEMOGRAPHIC DETAILS (n=80)

Characteristics of patients	No of patients
Total number of patients	80
Age (years) ➢ 17 – 37 ➢ 38 – 58 ➢ 39 – 79 ➢ 80 and above	54.0625±19.739 10 23 25 22
Gender ➢ Male ➢ Female	 55 25
Duration of hospitalization	1.6330±3.0625

TABLE 2: CLINICAL CONDITIONS (n=80)

Sl No	Diagnosis	No.of Patients	Percentage (%)
1	Diabetes Mellitus (DM)	10	12.5
2	Road Traffic Accident/Head Injury(RTA)	10	12.5
3	Others	9	11.25
4	Chronic Renal Failure(CRF)	8	10
5	Systemic Hypertension (SHT)	7	8.75
6	Cerebro vascular Accident	6	7.5
7	Chronic Obstructive Pulmonary Disorder (COPD)	4	5
8	Respiratory Disorders(RD)	4	5
9	Myocardial Infarction (MI)	4	5
10	Cancer	4	5
11	Poisoning	4	5
12	Subarachnoid hemorrhage(SAH)	3	3.75
13	Ischaemic Heart Disease (IHD)	3	3.75
14	Stroke	2	2.5
15	Urinary Tract Infection(UTI)	2	2.5

TABLE: 3 DRUGS PRESCRIBED (n=682)

Sl No	Drugs Prescribed	Number	Percentage (%)
1	Ondansetron	55	68.75
2	Pantoprazole	52	65
3	Piperacillin Tazobactum	31	38.75
4	Ceftriaxone	28	35
5	Levetiracetam	25	31.25
6	Citicoline	24	30
7	Esomeprazole	17	21.25
8	Midazolam	17	21.25
9	Methyl Prednisolone	16	64
10	Fosphenytoin	15	18.75
11	Clopidogrel Aspirin	14	17.50
12	Fentanyl	14	17.50
13	Frusemide	13	16.25
14	NorAdrenaline	13	16.25
15	Paracetamol	12	15
16	Ethohylline Theophylline	12	15
17	Levofloxacin	11	13.75
18	Meropenem	10	12.50
19	Atorvastatin	9	11.25
20	Piracetam	9	11.25
21	Nimodipine	9	11.25
22	Vitamin k	9	11.25
23	Cerebroprotein hydrosylate	8	10
24	Mannitol	8	10

25	Amikacin	8	10
26	Linezolid	8	10
27	Clindamycin	7	10
28	Ornidazole	7	10
29	Hydrocortisone	7	10
30	Dexamethasone	7	10
31	Sucralfate	6	7.50
32	Fluconazole	6	7.50
33	Edaravone	6	7.50
34	Clinidipine	6	7.50
35	ImipenemCilastin	6	7.50
36	Metronidazole	6	7.50
37	Dopamine	6	7.50
38	Calcitrol	6	7.50
39	Ursodeoxycholic acid	6	7.50
40	Atracurim	6	7.50
41	Amlodipine	5	6.25
42	Telmisartan	5	6.25
43	Insulin	4	5
44	Rifaxcimin	4	5
45	Levothyroxine	4	5
46	Ramosetron	3	3.75
47	Potassium Chloride	3	3.75
48	Febuxstat	3	3.75
49	Ferrous Fumarate	3	3.75
50	Vasopressin	3	3.75
51	Torsemide	3	3.75
52	Enoxparin Sodium	3	3.75
53	Lacosamide	3	3.75

54	Ketorolac	3	3.75
55	Cefoperazone Sulbactum	3	3.75
56	Alphacalcidol	3	3.75
57	Nevivolol	3	3.75
58	Folic Acid	3	3.75
59	Hydroxychloroquinine	3	3.75
60	Prednisolone	3	3.75
61	Calcium	3	3.75
62	Aspirin	3	3.75
63	Methyl Cobalamine	2	2.50
64	Amiodarime	2	2.50
65	Isosorbide Mononitrate	2	2.50
66	Vancomycin	2	2.50
67	Dobutamine	2	2.50
68	Clonazepam	2	2.50
69	CalciumCarbonate	2	2.50
70	Amphotericin B	2	2.50
71	Tranexmic Acid	2	2.50
72	Chymotrypsin ,trypsin	2	2.50
73	Trimethoprine,sulphamethoxazole	2	2.50
74	Tramadol	2	2.50
75	Pralidoxime	1	1.25
76	Glycopyrolate	1	1.25
77	Amoxcillin Clavunate	1	1.25
78	Acetyl Cysteine	1	1.25
79	Vitamin B	1	1.25
80	Colisthimate	1	1.25
81	Digitoxin	1	1.25
82	Levodopa Carbidopa	1	1.25

83	Ascorbic Acid	1	1.25
84	L Ornthine L Aspartate	1	1.25
85	Pazofloxacin	1	1.25
86	Modafinil	1	1.25
87	Bethanechol Chloride	1	1.25
88	Oxcarbamazepine	1	1.25
89	Calcium Gluconate	1	1.25
90	Azathioprine	1	1.25
91	Glimipride	1	1.25
92	Acetazolamide	1	1.25
93	Hysocyamine	1	1.25
94	Prazosin	1	1.25
95	Moxonidine	1	1.25
96	Sevelamer	1	1.25
97	Isolazine	1	1.25
98	Eplerenone	1	1.25
99	Cilostazol	1	1.25
100	Clarithromycin	1	1.25
101	Sodium Bicarbonate	1	1.25
102	Lactobacillus acidophillus	1	1.25
103	Pyrazinamide	1	1.25
104	Isoniazid	1	1.25
105	Human Isophane	1	1.25
106	Mycophenolate	1	1.25
107	Spiranolactone	1	1.25
108	Atenalol	1	1.25
109	Rabiprazole	1	1.25
110	Sorafinib	1	1.25
111	Trazadone Hcl	1	1.25

112	Cobalamine+Pyridoxine+Thiamine	1	1.25
113	Doxycycline	1	1.25
114	Oxfloxacin	1	1.25
115	Acyclovir	1	1.25
116	Ceftazidime+Tazobactum	1	1.25
117	Tazobactum+Sulbactum	1	1.25
118	Human Insulin	1	1.25
119	Metformin	1	1.25
120	Ethambutol	1	1.25
121	Thyroxine	1	1.25
122	Cefixime,Oxfloxacin	1	1.25
123	Amantidime	1	1.25
124	Magesium Sulphate	1	1.25

TABLE 4 : INTRAVENOUS DRUGS PRESCRIBED

(n=554)

Sl No	Drugs Prescribed	Dose	No.	Percentage (%)
1	Ondansetron	4 mg	55	9.92
2	Pantoprazole	40mg	52	9.3
3	Piperacillin +Tazobactum	4.5g	31	5.59
4	Ceftriaxone	1g	28	5.05
5	Levetericetam	500mg	25	4.5
6	Citicoline	4ml	24	4.33
7	Esomeprazole	40mg	17	3.06
8	Midazolam	0.5mcg	17	3.06
9	Methyl Prednisolone	40mg	16	2.88
10	Fosphenytoin	150mg	15	2.70
11	Fentanyl	0.5mcg	14	2.52
12	Frusemide	20mg	13	2.34
13	Noradrenaline	0.2mg	13	2.34
14	Etophylline Theophylline	25.3mg+84.7mg	12	2.166
15	Levofloxacin	500mg	11	1.98
16	Vancomycin	500mg	11	1.98
17	Meropenem	500mg	10	1.80
18	VitamimK	1 amp	9	1.62
19	Piracetam	60ml	9	1.62
20	Nimodipine	30mg	9	1.62
21	Cerebroprotein Hydrosylate	60mg	8	1.44
22	Mannitol	2.5mg	8	1.44
23	Amikacin	500mg	8	1.44
24	Linezolid	600mg	8	1.44
25	Ornidazole	500mg	7	1.26

26	Clindamycin	600mg	7	1.26
27	Hydrocortisone	100mg	7	1.26
28	Dexamethasone	20mg	7	1.26
29	Fluconazole	200mg	6	1.08
30	Edaravone	30mg	6	1.08
31	Imipenem Cilastin	500mg	6	1.08
32	Metronidazole	500mg	6	1.08
33	Dopamine	5mcg	6	1.08
34	Atracuirum	10mg	6	1.08
35	Insulin	10units	4	0.72
36	Ramosetron	300mcg	3	0.54
37	Potassium Chloride	2meq/ml	3	0.54
38	Vasopressin	300mcg	3	0.54
39	Torsemide	5mg	3	0.54
40	Enoxparin Sodium	40mg	3	0.54
41	Lacosamide	100mg	3	0.54
42	Sulbactum+Cefoperazone	1g	3	0.54
43	Prednisolone	300mcg	3	0.54
44	Dobutamine	2.5mcg	2	0.36
45	Amphotericin B	2mg	2	0.36
46	Tranexemic Acid	100mg	2	0.36
47	Tramadol	50mg	2	0.36
48	Methylcobalamine		2	0.36
49	Pralidoxime	1g	1	0.18
50	Omeprazole	20mg	1	0.18
51	Amoxcillin Clavunate	500mg	1	0.18
52	Vitamim B		1	0.18
53	Pazofloxacin	500mg	1	0.18
54	Clarithromycin	250mg	1	0.18

55	Sodium Bicarbonate	2g	1	0.18
56	Glycopyrolate	2.5mg	1	0.18
57	Oxfloxacin	400mg	1	0.18
58	Acyclovir	200mg	1	0.18
59	Ceftazidime+Tazoactum	2g	1	0.18
60	Tazobactum+Sulbactum	2g	1	0.18
61	Cefixime+Oxfloxacin	10mg	1	0.18
62	L-ornithine,LAspartate		1	0.18
63	Magnesium Sulphate	1g	1	0.18
64	Calcium Gluconate	3g	1	0.18
65	Folic Acid	1mg	1	0.18
66	Cobalamine+Pyrodoxime+Thyroxine		1	0.18
67	Colisthimate	2.5mg	1	0.18
68	Thiamine		1	0.18

TABLE 5 : CONTINOUS INTRAVENOUS INFUSIONS PRESCRIBED (n=262)

Sl.No	Drug	Dose	Number	Percentage (%)
1	Levetiracetam	500mg	25	9.54
2	Citicoline	4ml	24	9.16
3	Midazolam	0.5mcg	17	6.48
4	Methyl Prednisoline	40mg	16	6.10
5	Fentanyl	0.5mcg	14	5.34
6	Noradrenaline	0.2mg	13	4.96
7	Levofloxacin	500mg	11	4.19
8	Vancomycin		11	4.19
9	Meropenem	500mg	10	3.81
10	Piracetam		9	3.43
11	Nimodipine	30mg	9	3.43
12	Cerebroprotein hydrosylate	60mg	8	3.05
13	Mannitol	2.5mg	8	3.05
14	Amikacin	500mg	8	3.05
15	Linezolid	600mg	8	3.05
16	Ornidazole	500mg	7	2.67
17	Clindamycin	600mg	7	2.67
18	Fluconazole	200mg	6	2.29
19	Edaravone	30mg	6	2.29
20	Imipenem+Cilastin	500mg	6	2.29
21	Metronidazole	500mg	6	2.29
22	Dopamine	5mcg	6	2.29

23	Atracurium	10mg	6	2.29
24	Insulin	40 units	4	1.52
25	Potassium Chloride	2meq/ml	3	1.14
26	Vasopressin		3	1.14
27	Lacosamide	100mg	3	1.14
28	Dobutamine	2.5mcg	2	0.76
29	Amphotericin B	2mg	2	0.76
30	Pazufloxacin	500mg	1	0.38
31	Clarithromycin	250mg	1	0.38
32	Oxfloxacin	400mg	1	0.38
33	Lornithine Aspartate		1	0.38

TABLE 6: Y SITE ADMINISTERED DRUGS IN INTENSIVE CARE UNIT (n=292)

Sl.No	Y Site Administered Drugs	Dose	Number	Percentage (%)
1	Ondansetron	4mg	55	18.83
2	Pantoprazole	40mg	52	17.80
3	Piperacillin Sodium+Tazobactum Sodium	4.5mg	31	10.60
4	Ceftriaxone	1g	28	9.58
5	Esomeprazole	40mg	17	5.82
6	Fosphenytoin	150mg	15	5.13
7	Frusemide	20mg	13	4.45
8	Etophylline+Theophylline		12	4.10
9	VitaminK		9	3.08
10	Amikacin	500mg	8	2.73
11	Hydrocortisone	100mg	7	2.39
12	Dexamethasone	20mg	7	2.39
13	Ramosetron	300mcg	3	1.02
14	Torsemide	5mg	3	1.02
15	Esomeprazole Sodium	40mg	3	1.02
16	Sulbactum+Cefoperazone		3	1.02
17	Prednisolone	300mg	3	1.02
18	Folic Acid	1mg	3	1.02
19	Tranexmic acid	100mg	2	0.68
20	Tramadol	50mg	2	0.68
21	Methyl cobalamine		2	0.68
22	Pralidoxime	1g	1	0.34
23	Omeprazole	20mg	1	0.34
24	Amoxcillin Clavunate	500mg	1	0.34

25	Vitamin B		1	0.34
26	Glycopyrolate	2.5mg	1	0.34
27	Acyclovir	200mg	1	0.34
28	Ceftazidime+Tazobactum	2g	1	0.34
29	Tazobactum+Sulbactum	2g	1	0.34
30	Cefexime+Oxfloxacin	10mg	1	0.34
31	Magnesium Sulphate	1g	1	0.34
32	Calcium Gluconate	3g	1	0.34
33	Cobalamine,Pyridoxime		1	0.34
34	Thiamine	5mg	1	0.34
35	Colistimethate sodium	2.5mg	1	0.34

TABLE 7: **COMPATIBILITY OF CONTINOUS INTRAVENOUS DRUGS WITH Y SITE ADMINISTERED DRUGS (n=600)**

S.No	Drug combinations	Number	Percentage (%)
1	Compatible (C)	202	33.66
2	Incompatible (IC)	17	2.83
3	Caution	27	4.5
4	Not tested (NT)	354	59

TABLE 8: DETAILS **OF COMPATIBILITY OF CONTINOUS INTRAVENOUS INFUSIONS DRUGS WITH Y- SITE ADMINISTERED DRUGS (n=552)**

Sl No	Continouss Intravenous Infusion	Y-Site Drugs	Compatibility	No	Percentage (%)
1	Normal Saline	Ondansetron	NT	13	2.35
2	Normal Saline	Pantoprazole	NT	13	2.35
3	Levetiracetam	Pantoprazole	NT	12	2.17
4	Levetiracetam	Ondansetron	NT	11	1.99
5	Midazolam	Ondansetron	C	10	1.81
6	Midazolam	Pantoprazole	Caution	10	1.81
7	Fentanyl	Pantoprazole	IC	8	1.44
8	Normal Saline	Ceftriaxone	NT	8	1.44
9	Levetiracetam	Fosphenytopin	NT	8	1.44
10	Metronidazole	Piperacillin Na+ Tazobactum Na	C	8	1.44
11	Metronidazole	Torsemide	C	8	1.44
12	Midazolam	Esomeprazole	IC	8	1.44
13	Normal Saline	Piperacillin Na+ Tazobactum Na	NT	7	1.26
14	Nor adrenaline	Ondansetron	NT	7	1.26
15	Methyl Prednisolone	Pantoprazole	NT	7	1.26
16	Meropenem	Pantoprazole	IC	7	1.26
17	Fentanyl	Ondansetron	C	7	1.26
18	Nor adrenaline	Pantoprazole	NT	6	1.08
19	Midazolam	Piperacillin Sodium+tazobactum Sodium	NT	6	1.08
20	Levofloxacin	Pantoprazole	IC	6	1.08
21	Normal Saline	Furosemide	NT	6	1.08

22	Dopamine	Pantoprazole	Caution	6	1.08
23	Levetiracetam	Ceftriaxone	NT	6	1.08
24	Metronidazole	Hydrocortisone	C	6	1.08
25	Insulin	Ondansetron	C	5	
26	Nor adrenaline	Piperacillin Sodium+tazobactum Sodium	NT	5	0.90
27	Meropenem	Ondansetron Hcl	IC	5	0.90
28	Normal Saline	Esomeprazole	NT	5	0.90
29	Levofloxacin	Piperacillin Na+Tazobactum Na	IC	5	0.90
30	Ringer Lactate	Ondansetron	NT	5	0.90
31	Dopamine	Ceftriaxone	C	5	0.90
32	Levetiracetam	Furosemide	NT	5	0.90
33	Metronidazole	Ondansetron	C	5	0.90
34	Fluconazole	Piperacillin Na + Tazobactum Na	C	5	0.90
35	Fentanyl Citrate	Dexamethasone	C	5	
36	Imipenem+Cilastin	Ondansetron	C	4	0.72
37	Imipenem+Cilastin	Pantoprazole	C	4	0.72
38	Fentanyl	Piperacillin Sodium+tazobactum Sodium	C	4	0.72
39	Ringer Lactate	Ceftriaxone	IC	4	0.72
40	Ringer Lactate	Pantoprazole	C	4	0.72
41	Fentanyl	Ceftriaxone	C	4	0.72
42	Dopamine	Piperacillin Na+ Tazobactum Na	C	4	0.72
43	Potassium Chloride	Ceftriaxone	C	4	0.72
44	Potassium Chloride	Pantoprazole	C	4	0.72
45	Thiamine	Ceftriaxone	NT	4	0.72

46	Thiamine	Pantoprazole Sodium	NT	4	0.72
47	Fluconazole	Frusemide	IC	4	0.72
48	Midazolam	Amikacin SO4	NT	4	0.72
49	Ornidazole	Pipercillin Na + Tazobactum Na	NT	4	0.72
50	Levofloxacin	Ethophylline+Theophylline	NT	3	0.5
51	Levofloxacin	Ondansetron Hcl	C	3	0.54
52	Normal Saline	Ethophylline+Theophylline	NT	3	0.54
53	Levetiracetam	Esomeprazole	NT	3	0.54
54	Midazolam	Ceftriaxone	C	3	0.54
55	Levetiracetam	Piperacillin Na+Tazobactum Na	NT	3	0.54
56	Levetiracetam	Vitamin K	NT	3	0.54
57	NorAdenaline	Calcium Gluconate	NT	3	0.54
58	Levetericetam	Dexamethasone	NT	3	0.54
59	Linezolid	Fosphenytoin	NT	3	0.54
60	Linezolid	Furosemide	C	3	0.54
61	Meropenem	Ethophylline +Theophylline	NA	3	0.54
62	Insulin	Ceftriaxone	Caution	3	0.54
63	Insulin	Pantoprazole	C	3	0.54
64	Atracurium	Pantoprazole	IC	3	0.54
65	Insulin	Esomeprazole	C	2	0.36
66	Clindamycin	Pantoprazole	IC	2	0.36
67	Clindamycin	Deriphylline	NT	2	0.36
68	Fentanyl	Ethophylline+Theophylline	C	2	0.36
69	Meropenem	Esomeprazole	NT	2	0.36

70	Meropenem	Furosemide	C	2	0.36
71	Levofloxacin	Esomeprazole	NT	2	0.36
72	Dobutamine	Furosemide	IC	2	0.36
73	Normal Saline	Hydrocortisone	NT	2	0.36
74	Levofloxacin	Torsemide	NT	2	0.36
75	Methyl Prednisolone	Piperacillin Na+Tazobactum Na	C	2	0.36
76	Dopamine	Ondansetron	C	2	0.36
77	Levetiracetam	Ketorolac	NT	2	0.36
78	Normal Saline	Vitamin K	NT	2	0.36
79	Linezolid	Ceftriaxone	C	2	0.36
80	Linezolid	Pantoprazole	IC	2	0.36
81	Sodium Bibarbonate	Htdrocortisone	C	2	0.36
82	Sodium Bibarbonate	Ondansetron	IC	2	0.36
83	Sodium Bibarbonate	Pantoprazole	Caution	2	0.36
84	Levofloxacin	Hydrocortisone	C	2	0.36
85	Normal Saline	Dexamethasone	NT	2	0.36
86	Normal Saline	Fosphenytoin	NT	2	0.36
87	Dopamine	Torsemide	NT	2	0.36
88	Methyl Prednisolone	Ceftriaxone	C	2	0.36
89	Linezolid	Fosphenytoin	NT	2	0.36
90	Fentanyl Citrate	Fosphenytoin	NT	2	0.36
91	Midazolam	Fosphenytoin	IC	2	0.36
92	Potassium Chloride	Ondansetron	C	2	0.36
93	Imipenem + Cilastin	Amikacin Sulphate	C	2	0.36
94	Midazolam	Omeprazole	IC	2	0.36
95	Paracetamol	Ondansetron	C	2	0.36

96	Normal Saline	Cefuperazone + Sulbactum	NT	2	0.36
97	Amoxcillin Clavunate	Ondansetron Hcl	NT	2	0.36
98	Amoxcillin Clavunate	Pantoprazole Na	NT	2	0.36
99	Methyl Prednisolone	Amikacin Sulphate	C	2	0.36
100	Methyl Prednisolone	Ondansetron	Caution	2	0.36
101	Thiamine	Amikacin sulphate	NT	2	0.36
102	Thiamine	Ondansetron	NT	2	0.36
103	Mannitol	Pantoprazole	IC	2	0.36
104	Mannitol	Amikacin SO4	C	2	0.36
105	Mannitol	Ondansetron	C	2	0.36
106	Fluconazole	Paracetamol	NT	2	0.36
107	Fluconazole	Fosphenytoin	NT	2	0.36
108	Dopamine	Enoxparin Na	NT	2	0.36
109	Potassium Chloride	Enoxparin Na	NT	2	0.36
110	Metronidazole	Ceftazidime	C	2	0.36
111	Levofloxacin	Ceftriaxone	C	2	0.36
112	Levetiracetam	Dexamethasone	C	2	0.36
113	Atracurium	Amikacin SO4	C	2	0.36
114	Atracurium	Ondansetron	C	2	0.36
115	Atracurium	Pipercillin Na + Tazobactum Na	NT	2	0.36
116	Potassium Chloride	Esomeprazole	NT	2	0.36
117	Potassium Chloride	Dexamethasone	NT	2	0.36%
118	Imipenem+Cilastin	Piperacillin Na+Tazobactum Na	NT	1	0.18%
119	Clindamycin	Ondansetron	C	1	0.18%

120	Clindamycin	Piperacillin Sodium+tazobactum Sodium	C	1	0.18%
121	Midazolam	Ethophylline+Theophylline	C	1	0.18%
122	Imipenem+Cilastin	Deriphylline	NT	1	0.18%
123	Nor Adrenaline	Esomeprazole	NT	1	0.18%
124	Aminophylline	Ceftriaxone	IN	1	0.18%
125	Aminophylline	Enoxparin Sodium	NT	1	0.18%
126	Aminophylline	Hydrocortisone	NT	1	0.18%
127	Aminophylline	Pantoprazole	C	1	0.18%
128	Aminophylline	Ethophylline +Theophylline	NT	1	0.18%
129	Metronidazole	Torsemide	C	1	0.18%
130	Linezolid	Ondansetron	C	1	0.18%
131	Linezolid	Vitamin K	NT	1	0.18%
132	Normal Saline	Calcium Gluconate	NT	1	0.18%
133	Dopamine	Calcium Gluconate	NT	1	0.18%
134	Dopamine	Esomeprazole	IN	1	0.18%
135	NorAdenaline	Esomeprazole	NT	1	0.18%
136	Sodium Bibarbonate	Piperacillin Na+ Tazobactum Na	C	1	0.18%
137	Metronidazole	Esomeprazole	NT	1	0.18%
138	Dopamine	Folic Acid	NT	1	0.18%
139	Dopamine	Vitamin K	NT	1	0.18%
140	Nor Adrenaline	Folic Acid	NT	1	0.18%
141	Nor Adrenaline	Vitamin K	NT	1	0.18%
142	Nor Adrenaline	Oxfloxacin	NT	1	0.18%
143	Dopamine	Oxfloxacin	NT	1	0.18%

144	Methyl Prednisolone	Fosphenytoin	NT	1	0.18%
145	Paracetamol	Amikacin Sulphate	NT	1	0.18%
146	Paracetamol	Ceftriaxone	C	1	0.18%
147	Methyl Prednisolone	Enoxparin Na	NT	1	0.18%
148	Normal Saline	Enoxparin Na	NT	1	0.18%
149	Metronidazole	Vitamin K	NT	1	0.18%
150	Metronidazole	Theophylline + Ethophylline	NT	1	0.18%
151	Clarithromycin	Hydrocortisone	C	1	0.18%
152	Clarithromycin	Ondansetron	NT	1	0.18%
153	Clarithromycin	Pantoprazole	NT	1	0.18%
154	Clarithromycin	Theophylline + Ethophylline	NT	1	0.18%
155	Sodium Bicarbonate	Esomeprazole	NT	1	0.18%
156	Sodium Bicarbonate	Ceftriaxone	C	1	0.18%
157	Clindamycin	Ceftriaxone	IC	1	0.18%
158	Clindamycin	Esomeprazole	NT	1	0.18%
159	Dobutamine	Pantoprazole	IC	1	0.18%
160	Levetiracetam	Glycopyrolate	NT	1	0.18%
161	Levetiracetam	Pralidoxime	NT	1	0.18%
162	Mannitol	Ceftriaxone	C	1	0.18%
163	Fluconazole	Amikacin So4	C	1	0.18%
164	Normal Saline	Colisthimate	NT	1	0.18%
165	Imipenem + Cilastin	Esomeprazole	NT	1	0.18%
166	Paracetamol	Esomeprazole	NT	1	0.18%
167	Paracetamol	Piperacillin Na + Tazobactum Na	C	1	0.18%

168	Paracetamol	Tramadol	NT	1	0.18%
169	Clindamycin	Furosemide	C	1	0.18%
170	Methyl Prednisolone	Furosemide	C	1	0.18%
171	Normal Saline	Ramosetron	NT	1	0.18%
172	Fluconazole	Acyclovir	C	1	0.18%
173	Fluconazole	Ondansetron	C	1	0.18%
174	Normal Saline	Acyclovir	NT	1	0.18%
175	Amphotericin B	Acyclovir	NT	1	0.18%
176	Amphotericin B	Ondansetron	IC	1	0.18%
177	Amphotericin B	Pantoprazole	IC	1	0.18%
178	Nor Adrenaline	Dexamethasone	NT	1	0.18%
179	Nor Adrenaline	Ethophylline+ Theophylline	NT	1	0.18%
180	Nor Adrenaline	Ceftriaxone	NT	1	0.18%
181	Vasopressin	Pantoprazole	C	1	0.18%
182	Vasopressin	Piperacillin Na + Tazobactum Na	C	1	0.18%
183	Normal Saline	Amikacin SO4	NT	1	0.18%
184	Atracurium	Ketorolac	NT	1	0.18%
185	Midazolam	Ketorolac	NT	1	0.18%
186	Fentanyl	Ketorolac	C	1	0.18%
187	Mannitol	Pipercillin Na + Tazobactum Na	C	1	0.18%
188	Vancomycin	Ondansetron	C	1	0.18%
189	Vancomycin	Pantoprazole	Caution	1	0.18%
190	Vancomycin	Pipercillin Na + Tazobactum Na	Caution	1	0.18%
191	Meropenem	Paracetamol	Caution	1	0.18%
192	Levofloxacin	Oxfloxacin	C	1	0.18%
193	Ringer Lactate	Esomeprazole	C	1	0.18%

194	Ringer Lactate	Thiamine,Cobalamine,Pyridoxine	C	1	0.18%
195	Ringer Lactate	Tranexmic Acid	C	1	0.18%
196	Lacosamide	Ceftriaxone	NT	1	0.18%
197	Lacosamide	Ondansetron	NT	1	0.18%
198	Lacosamide	Pantoprazole	NT	1	0.18%
199	Ringer Lactate	Hydrocortisone	C	1	0.18%
200	Ringer Lactate	Pipercillin Na + Tazobactum Na	Caution	1	0.18%
201	DNS	Pantoprazole	C	1	0.18%
202	DNS	Ceftriaxone	NT	1	0.18%
203	DNS	Pipercillin Na + Tazobactum Na	NT	1	0.18%
204	Insulin	Piperacillin Sodium+ Tazobactum Sodium	C	1	0.18%

TABLE 9: COMPATIBILITY OF CONTINOUS INTRAVENOUS INFUSIONS WITH SYRINGE PUMP ADMINISTERED DRUGS AT Y-SITE (n=48)

Sl No	Continouss Intravenous Infusion	Syringe Pump Administerd Drugs	Compatibility	No.	Percentage (%)
1	Methyl Prednisolone	Midazolam	C	3	6.25
2	Levetiracetam	Midazolam	NT	3	6.25
3	NS	Fentanyl Citrate	NT	3	6.25
4	Levetiracetam	Fentanyl citrate	NT	2	4.16
5	NS	Noradrenaline	NT	2	4.16
6	Thiamine	Fentanyl citrate	NT	2	4.16
7	Thiamine	Midazolam	NT	2	4.16
8	Metronidazole	Noradrenaline	NT	2	4.16
9	Ornidazole	Dobutamine	NT	2	4.16
10	Ornidazole	Dopamine	NT	2	4.16
11	Methyl Prednisolone	Atracurium	C	1	2.08
12	Methyl Prednisolone	Fentanyl citrate	C	1	2.08
13	Linezolid	Atracurium	C	1	2.08
14	Linezolid	Fentanyl Citrate	C	1	2.08
15	Linezolid	Noradrenaline	NA	1	2.08
16	Linezolid	Midazolam	C	1	2.08
17	Levetiracetam	Atracurium	NT	1	2.08
18	Insulin	Noradrenaline	NT	1	2.08
19	Levofloxacin	Noradrenaline	NT	1	2.08
20	Insulin	Dopamine	C	1	2.08
21	Levofloxacin	Dopamine	C	1	2.08
22	Mannitol	Fentanyl citrate	C	1	2.08
23	Mannitol	Midazolam	C	1	2.08
24	Meropenam	Dobutamine	C	1	2.08

25	Methyl Prednisolone	Dobutamine	C	1	2.08
26	Meropenam	Fentanyl citrate	NT	1	2.08
27	Meropenam	Midazolam	NT	1	2.08
28	Metronidazole	Fentanyl citrate	C	1	2.08
29	Metronidazole	Midazolam	C	1	2.08
30	Metronidazole	Dopamine	C	1	2.08
31	Clindamycin Phosphate	Fentanyl citrate	C	1	2.08
32	Clindamycin Phosphate	Midazolam	C	1	2.08
33	Imipenam+ Cilastin	Midazolam	IC	1	2.08
34	Imipenam+ Cilastin	Dopamine	C	1	2.08
35	Mannitol	Fentanyl citrate	C	1	2.08

TABLE 10: COMPATIBILITY OF CO – INFUSIONS ADMINISTERED THROUGH Y-SITE (n=65)

Sl No	Infusion 1	Infusion 2	Compatibility	No.	Percentage (%)
1	Midazolam	Fentanyl Citrate	C	10	15.38
2	Nor Adrenaline	Dopamine	NT	6	9.20
3	Atracurium	Fentanyl Citrate	C	5	7.69
4	Normal Saline	Ornidazole	NT	5	7.69
5	Normal Saline	Levetiracetam	NT	4	6.15
6	Nor Adrenaline	Fentanyl Citrate	NT	4	6.15
7	Nor Adrenaline	Midazolam	NT	3	4.61
8	Normal Saline	Levofloxacin	C	2	3.07
9	Atracurium	Midazolam	C	2	3.07
10	Potassium Chloride	Levetiracetam	NT	2	3.07
11	Levetiracetam	Fentanyl Citrate	NT	2	3.07
12	Levofloxacin	Insulin	IC	2	3.07
13	Normal Saline	Midazolam	NT	2	3.07
14	Potassium Chloride	Insulin	C	2	3.07
15	Normal Saline	Dopamine	NT	2	3.07
16	Normal Saline	Noradrenaline	NT	2	3.07
17	Normal Saline	Vancomycin	NT	1	1.53
18	Normal Saline	Fluconazole	NT	1	1.53
19	Normal Saline	Amphotericin B	NT	1	1.53
20	Potassium Chloride	Dopamine	C	1	1.53
21	Normal Saline	Linezolid	NT	1	1.53
2	Dobutamine	Fentanyl Citrate	C	1	1.53
23	Dobutamine	Midazolam	C	1	1.53

234	Normal Saline	Sodium Bicarbonate	NT	1	1.53
25	Levofloxacin	Sodium Bicarbonate	C	1	1.53
26	Dopamine	Fentanyl	C	1	1.53
27	Dopamine	Midazolam	C	1	1.53
28	Normal Saline	Imipenem+Cilastinq	NT	1	1.53
29	Nor Adrenaline	Sodium Bicaronate	NT	1	1.53
30	Dopamine	Sodium Bicaronate	IC	1	1.53
31	Normal Saline	Atracurium	NT	1	1.53
32	Mannitol	Midazolam	C	1	1.53
33	Levetiracetam	Nimodipine	NT	1	1.53
34	Normal Saline	Meropenem	NT	1	1.53

TABLE 11: DETAILS OF INCOMPATIBLE DRUGS

Drugs given by continuous intravenus infusion	Ysite administered drug & dose	Dil: of Infusion	Rate of infusion	Duration ion of infusion	Conc: of reconstituted soln	Diluent of Y-site administered drug	Presence of Polyvalent or monovalent ions	pH of continuous intravenous infusion	pH of Ysite administered drugs
Dobutamine	Frusemide 20 mg	-	1.8ml/hr	24hrs	-	2ml direct	-	2.5-5.5	8-9.3
Linezolid (600mg	Pantoprazole (40mg)	-	100ml/hr	1hr	4mg/ml	10 ml NS	-	2.5-5.5	9-10
NaHCO3	Ondansetron (4mg)	-	50ml/hr	1 hr	-	2ml direct	Na^+	8.4	3.3-4
Midazolam (15mg)	Fosphenytoin	NS	5ml/hr	24hrs	1.5mg/ml	10ml NS	Cl^-	2.5-3.5	8.3 to 9.3
Midazolam (15mg	Omeprazole (20mg)	-	100ml/hr	24hrs	2mg/ml	10ml NS	Na^+	2.5-3.5	
Midazolam (15mg	Esomeprazole	NS	5ml/hr	24hrs	4mg/ml	10ml NS	Cl^-	2.5-3.5	9-11
Dobutamine 500mg	Pantoprazole	NS	1.8ml/hr	24hrs	10mg/ml	10 ml NS	-	2.5-5.5	9-10
Fluconazole	Furosemide(20 mg)	-	100ml/hr	1hr	2mg/ml	10 ml NS	SO_2^-	4 to 8	8-9.3
RL	Ceftriaxone	-	50ml/hr	2hr	100mg/ml	10ml SWI	Ca^{++}	6.5	6.6

TABLE 12: TWO DIMENSIONAL COMPACTABILITY CHART

	Ceftriaxone	Esomeprazole	Levofloxacin	Midazolam	Ondansetron	Pantoprazole	Piperacillin-Tazobactum	Ringer Lactate	Sodium Bicarbonate	Atracurium	Linezolid	Fentanyl	Metronidazole	Flucanazole
Ceftriaxone	-	NT	C	C	Caution	C	NT	IC	C	C	C	C	C	Caution
Esomeprazole	NT	-	NT	IC	NT	NT	NT	C	NT	NT	NT	C	NT	NT
Levofloxacin	C	NT	-	C	C	IC	IC	NI	C	C	C	C	C	C
Midazolam	C	IC	C	-	C	NT	IC	C	IC	C	C	C	C	C
Ondansetron	C	NT	C	IC	-	Caution	C	C	IC	C	C	C	C	C
Pantoprazole	NT	NT	C	C	IC	-	C	C	IC	IC	I	I	I	I
Piperacillin-Tazobactum	C	NT	IC	Caution	IC	Caution	-	C	NT	NT	C	C	C	C
Ringer Lactate	NT	NT	IC	IC	C	Caution	Uncertain	-	C	IC	C	NI	C	C
Sodium Bicarbonate	IC	C	NI	C	C	C	NI	Caution -	-	IC	C	C	C	C
Atracurium	C	NT	C	C	C	IC	NT	IC	IC	-	C	C	C	C
Linezolid	C	NT	C	C	C	IC	C	C	C	C	-	C	C	C
Fentanyl	C	C	C	C	C	IC	C	NI	C	C	C	-	C	C
Metronidazole	C	NT	C	C	C	IC	C	C	C	C	C	C	-	C
Flucanazole	Caution	NT	C	C	C	IC	C	C	C	C	C	C	C	-

NT-Not Tested,C-Compatible,IC-

DISCUSSION

The current study showed that 2.83(%) combinations were incompatible. The incompatibility between ceftriaxone and Ringer Lactate was due to the presence of polyvalent cation (Ca^{++}) in the diluents. This result is supported by the previous work done by Sumeet *et al* who reported that mixing calcium-containing solutions, including Hartmann's solution or Ringer's lactate, with ceftriaxone causing the formation of the insoluble ceftriaxone calcium salt. Most of the incompatibilities were due to differing pH values of the drug pairs or drug and diluents. A majority of the continuous intravenous infusions had a pH value in the acidic range (except ondansetron) while that of Y-site administered drugs were found to be in the alkaline range. The water solubility of any drug is enhanced by ionisation of the molecule. For a drug molecule which acts as a proton acceptor (a Lowry-Bronsted base), ionisation is achieved by formulation in a low pH solution usually as a hydrochloride or hydrogen sulfate salt (for example, amiodarone hydrochloride or adrenaline acid tartrate). Conversely, for a drug molecule which can lose a proton or hydrogen ion (a Lowry-Bronsted acid – usually a weak organic acid), ionization is achieved by formulation in a high pH solution, usually as a sodium or potassium salt (for example, benzylpenicillin sodium). Any change in pH towards the other end of the pH scale will reduce the proportion of ionised to un-ionised drug in solution and will therefore reduce the water solubility of the drug.

Dobutamine + pantoprazole constitutes 0.18 % usage among the continuous intravenous drug along with Y site drugs. This incompatible drug combinations was also reported by a study carried out by Walker *et al* [34] who also reported that mixtures of pantoprazole with dobutamine, esmolol, or midazolam were physically incompatible over clinically useful concentration ranges. Precipitation occurred with mixtures containing pantoprazole and dobutamine.

Linezolid + Pantoprazole (0.36%) was found to be a incompatible combinations used in the ICU. This incompatibility results is supported by Cayo Lisa (2013)[35].

The combination of sodium bicarbonate + ondansetron prescribed in the MICU was found to be incompatible and similar reports are observed in a work carried out by Jarosinski *et al*[36] A faint appearance of a cloudy precipitate in the intravenous tubing was reported.

Midazolam + Fosphenytoin (0.36%) is another incompatible combination used in MICU. A work carried out Riggs [37] reported that midazolam free base was precipitated upon admixture of midazolam hydrochloride and fosphenytoin solutions. Therefore, midazolam hydrochloride and fosphenytoin should not be given via the same IV line.

Dobutamine + Furosemide (0.36%) were found to be incompatible in our study. This incompatibility results was consistent with the work carried out by Cabezas *et al* (2015)[12]. A possible explanation for this instability could be related to the fact that furosemide solutions are mildly alkaline and so should be stable when mixed with neutral or weakly basic solutions. However, combination with dobutamine resulted in an acidic solution of pH 4.8-5 which might destabilize furosemide leading to instability to the final mixture.

Midazolam+esomeprazole combination used in the study site was found to be incompatible. This incompatibility results is supported by the work carried out by Cabezas et al who reported that Esomeprazole in the mixture with midazolam 4 mg/mL and dopamine 8 mg/mL was undetectable, with degradation product peaks present on the chromatogram. Other incompatible combinations observed in the study such as Midazolam + Omeprazole, frusemide + fluconazole are also reported by Machotka et al (2014).

CONCLUSION

The present study demonstrated that the critically ill patients in the Medical Intensive Care Unit are receiving 2.83 % of incompatible combination of drugs or drugs and diluents. The 2-dimensional compatibility chart prepared in the study will be helpful to avoid incompatibility problems arising due to the concurrent administration of these drugs as continuous intravenous infusions and Y-site administration. 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 for commonly used medications in the Medical Intensive Care unit patients for safe usage. Routine drug administration review to identify those incompatible drug combination used in Medical Intensive Care Unit is strongly recommended to improve the treatment outcome of patients in the ICU.

FUTURE OUT LOOK

Further studies to estimate the incidence of incompatibility problems in critically ill patients are needed and also assess the impact of pharmacist in order to avoid incompatibility related problems. Due to increased availability of number of drug combinations, the knowledge regarding the incompatibilities of intravenous drugs should be improved. It is not possible to predict all incompatibilities that may arise, hoping that their occurrence can be minimized by active participation of 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. Much more studies are needed to get informations about undocumented combinations.

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Ethics Committee Registration No. ECR/690/Inst/TN/2014

SRH/EC.5-6/2016-17 26th February 2016

ETHICAL CLEARANCE CERTIFICATE

Project title: "Effect of ph And Polyvalent Cations On The Y-site Incompatibility of Continuous Intravenous Infusions of selected Critical Care Drugs in the Medical Intensive Care Unit".

Researcher: **Ms. Heleena Moncy Thomas**
M.Pharmacy II year,
Department of pharmacy Practice,
College of Pharmacy,
Sri Ramakrishna Institute of Paramedical Sciences,
Coimbatore – 641 044

The following members of the ethics committee were present at the meeting held on 20.02.2016 at 3.00pm at New Auditorium, Sri Ramakrishna Hospital Campus, Coimbatore.

SI NO	Members Name	Qualification	Designation	Address	Affiliation To the Institution Yes/NO
1.	Dr.P.Murali	M.Sc.,Ph.D., D.Sc	Scientist Mg. Director & CEO	Mg.Director & CEO Evolve Biotech Pvt.Ltd., 401 – 405, 4th floor Ticel Bio park Ltd, Taramani, Chennai - 13	No
2.	Dr.P.Sukumaran	MS., M.Ch., FIACS	Scientific / EC Member Secretary Dean	Dean Sri Ramakrishna Hospital, 395, Sarojini Naidu Road, Sidhapudur, Coimbatore	Yes
3.	Dr.T.Mohan Kumar	MD.,D.Sc., AB.,DPPR., FCCP.,	Clinician	Sr.Consultant Pulmonologist Sri Ramakrishna Hospital, 395, Sarojini naidu Road, Sidhapudur, Coimbatore.	Yes
4.	Dr.S.Rajagopal	M.Ch.,	Clinician	Sr. Consultant Neuro Surgeon Sri Ramakrishna Hospital, 395, Sarojini naidu Road, Sidhapudur, Coimbatore.	Yes

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5.	Dr.R.Lalitha	DGO.,(OG)	Clinician	Sr.Consultant Gynecologist & HOD Sri Ramakrishna Hospital, 395, Sarojini naidu Road, Sidhapudur, Coimbatore.	Yes
6.	Dr.T.K.Ravi	M.Pharm Ph.D	Scientific Member	Principal Sri Ramakrishna College of pharmacy 395, Sarojini naidu Road, Sidhapudur, Coimbatore.	Yes
7.	Dr.N.Paramasivan	MBBS.,MD	Basic Medical Scientist	Prof.of pharmacology and HOD Sri Ramakrishna Dental College and Hospital, Coimbatore.	Yes
8.	Dr.M.Rangasamy	B.E., M.Sc., Ph.D.,	Lay Person	Former Professor Government College of Technology, Coimbatore.	No

This is to certify that the research work entitled "Effect of ph And Polyvalent Cations On The Y-site Incompatibility of Continuous Intravenous Infusions of selected Critical Care Drugs in the Medical Intensive Care Unit", placed before the Institutional Ethical Committee has been approved as there is no objection to do this research work.

This ethics committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report.

The Ethics Committee wishes her well in her research.

Yours Truly,

Member Secretary,

Institutional Human Ethics Committee,

Dr. P. SUKUMARAN, M.S.,M.Ch.,FIACS.,
Dean
SRI RAMAKRISHNA HOSPITAL,
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PATIENT INFORMATION FORM

Project Title: Effect of pH and Polyvalent Cations on the Y-Site Incompatibility of Continuous Intravenous Infusions of Selected Critical Care Drugs in Medical Intensive Care Unit

I, **Heleena Moncy Thomas,** II year M. Pharm., (Pharmacy Practice) student of College of Pharmacy, SRIPMS, Coimbatore which is attached to Sri Ramakrishna Hospital Coimbatore, pursuing a dissertation work, entitled "**Effect of pH and Polyvalent Cations on the Y-Site Incompatibility of Continuous Intravenous Infusions of Selected Critical Care Drugs in Medical Intensive Care Unit"** which has to be submitted to the Tamil Nadu Dr. M.G.R. Medical University, Chennai for partial fulfillment for the award of degree of Master of Pharmacy. The details about the patient and the treatment are required by the investigator for carrying out the dissertation. It is here by assured that the details collected are only for the purpose of research and it will helpful to the patient and care giver. It is also assured that the information obtained from the patient will be maintained confidentially. We hope you will provide us the necessary co-operation for the above mentioned work by providing a written consent.

Thanking you

Signature of the Investigator

Ms.Heleena Moncy Thomas,
II- M. Pharm, Pharmacy Practice,
College of Pharmacy, SRIPMS,
Coimbatore-44

COLLEGE OF PHARMACY

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PATIENT CONSENT FORM

Project Title: Effect of pH and Polyvalent Cations on the Y-Site Incompatibility of Continuous Intravenous Infusions of Selected Critical Care Drugs in the Medical Intensive Care Unit

I G. ராதாமணி

have been made understood the necessity of the work entitled **"Effect of pH and Polyvalent Cations on the Y-Site Incompatibility of Continuous Intravenous Infusions of Selected Critical Care Drugs in the Medical Intensive Care Unit"** that is being carried out by **Heleena Moncy Thomas,** II year M. Pharm, (Pharmacy Practice) in College of Pharmacy, SRIPMS, Coimbatore. I voluntarily here by agree by giving my consent to participate in this study and provide the necessary co-operation for the same.

Place: Coimbatore

Signature of the Patient/By- stander:

Date: 10/2/16

Name of the Patient:

Name of the ~~Patient~~/ By-stander: G. ராதாமணி

Signature of the Investigators:

Ms.Heleena Moncy Thomas,
II M. Pharm, Pharmacy Practice,
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Thanking you

Signature of the Investigator

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DEPARTMENT OF PHARMACY PRACTICE
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Case No.:

Effect of pH andPolyvalent Cations on the Y-site Incompatibility of Continuous Intravenous infusions of Selected Critical Care Drugs in the Medical Intensive Care Unit

DATA ENTRY FORM

PATIENT DETAILS

Name	Age	Sex	Wt.	Ht.	BMI	IP No.	Dept.	DOA	DOD
Mr Balasubramanian	54	M				2016/32909	ICU		

REASONS FOR ADMISSION c/o giddiness c fall c H/o vomiting

PAST MEDICAL HISTORY —

PAST MEDICATION HISTORY —

SOCIAL HISTORY Known allergies :

Smoker:Y/N Alcoholic:Y/N Marital status:

None:

Tobacco in any form:Y/N

Vital Signs												Blood sugar (mg %)										
Date	1	2										Day										
Temp.	97	98										F.B.S (60-90)										
BP	130/90	120/80										P.P.S (80-150)										
Pulse	81											R.B.S (90-110)										

BLOOD COUNTS

Haemoglobin (g/dl)	TLC (cells/cumm) (5000-10000)	ESR (mm/hr) (M<10; F<20)	Differential Leukocyte Count (%)

Effect of pH and polyvalent cations on the Y-site incompatibility of continuous intravenous infusions of selected critical care drugs in the Medical Intensive Care Unit.

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Case No.:

(11-17g/dl)					
13.9	19867	08	Polymorphs (10-75%)	94.6	
			Lymphocytes(20-50%)	3.4	
Platelets (1-4 lakhs)	Clotting Time(1-10min)	Bleeding Time(2-5min)	Basophils (0-1%)	0.0	
2,74,000			Eosinophils (1-6%)	0.0	
			Monocytes (8-10%)	1.9	

LIVER FUNCTION TESTS								RENAL FUNCTION TESTS				
Total bilirubin (<1mg %)	2.7			Alk. Phosphatase (84-306 U/L)				Urea (mg %) (20-40)	31			
								Uric acid (mg %) F-2-5, M-2-7				
P.T Time (14 sec) 17sec				SGPT (5-37 U/L)	26			Sr.Creatinine (mg %) (0.6-1.4)	1.4			

ELECTROLYTES (mEq/l)						URINE EXAMINATION			
Sodium (130-150)						Colour	Pale yellow	Sugar	9.
Potassium (3.5 – 5.8)						Bile salts	2-4	WBC	
Chloride (98-100)						Bile pigment		RBC	
Bicarbonate (22-36)						Albumin	+	Casts	Nil
						Pus cells	6-8	Epithelial cells	2-4

C/S: Y/N
Organism Isolated:

No. of organisms isolated:
Sensitive to:

Other Investigations:

DIAGNOSIS : Diffuse SAH

Effect of pH and polyvalent cations on the Y-site incompatibility of continuous intravenous infusions of selected critical care drugs in the Medical Intensive Care Unit.

DEPARTMENT OF PHARMACY PRACTICE
College of Pharmacy, SRIPMS, Coimbatore - 44.
Email: pharmacy_practice@rediffmail.com Phone: 0422-4500297

Case No.:

DRUG PRESCRIBED

S.No.	Drugs		Dose	Administration technique	DATE OF TREATMENT										
	T. Name	G.Name			1	2	3	4	5	6	7	8	9	10	11
01	Inj Hcpred	Methyl Pred Sodium	500mg BD	IV	✓	✓									
02	Inj Stacid	Cimetidine	400mg OD	IV	✓	✓									
03	Inj Taxim	Cefotaxime Na	1g	IV	✓	✓									
04	Inj Pesdeni	Phosphenytoin	150mg OD	IV	✓	✓									
05	Inj Pan	Pantoprazole	40mg BD	IV	✓	✓									
06	Inj Emset	Ondansetron	4mg BD	IV	✓	✓									
07	Inj Nemodip	Nimodipine	1mg/hr	IV	✓										
08	Inj Atracurium	atracurium	20mg												
09	Inj fentanyl	fentanyl													
10	Inj midaz	midazolam	15mg	IV	✓										
11															
12															
13															

Effect of pH and polyvalent cations on the Y-site incompatibility of continuous intravenous infusions of selected critical care drugs in the Medical Intensive Care Unit.

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Case No.:

DRUG INTERACTIONS/ ADVERSE DRUG REACTIONS

DRUGS	EFFECTS	INFERENCE

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Case No.:

IV Infusion : Inj Noradrenaline Rate: 5ml/hr Duration: 24 hr. pH
Inj Midaz + fentanyl " 24 hr
Inj Sterone (Celestan) 1/2 5ml/hr. 1 hr.

DRUG			Preparation technique	Admin. technique	Rate of admin.	Conc.of admin	Storage of reconstdsoln	Ph of medication
B.Name	G.Name							
Inj Taxcef	Ceftriaxone Na	OBSERVED	1 amp NS + 1 mg	Y site	—	100 mg/ml		
Inj fosclin	Phosphenytoin		2 ml 50 mg + 10 ml NS	"	—	15 mg/ml		
Inj Pan	Pantoprazole		1 amp NS + 40 mg, 10 ml tab		—	4 mg/ml		
Inj Emend	Ondansetron		2 ml 4 ml		—			
Inj Taxcef	Ceftriaxone Na	RECOMMENDE	NS + 1 mg					
Inj fosclin	Phosphenytoin		SW 1 / NS + 1 mg					
Inj Pan	Pantoprazole		NS + 40 mg					
Inj Emend	Ondansetron							

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Case No.:

IV Infusion : 4mg Nicardipine Rate: 5ml/hr. Duration: 1hr pH
4mg fentanyl + midazolam
RL
"
RS ml/hr.
fentanyl
midazolam - 2-5-3-5

DRUG			Preparation technique	Admin. technique	Rate of admin.	Conc.of admin	Storage of reconstdsoln	Ph of medication
B.Name	G.Name							
Inj Taxif	Ceftriaxone	OBSERVED	1 amp NS + 5mg	Ysli	—	100mg/ml	—	
4mg fosolen	Phosphenytoin		2 vial + 5mg + 1 amp NS	"	—	1.5mg/ml	—	
Inj Pantop	Pantoprazole		1 amp NS + 5mg, 1 amp later	"	—	4mg/ml	-	
4mg Emset	Ondansetron		2 amp dil	"	—			
Inj Taxif	Ceftriaxone	RECOMMENDED	NS + 5mg	"	—			
Inj fosolen	Phosphenytoin		5ml/NS + 5mg	"	—			
3mg Pantop	Pantoprazole		1 amp NS + 5mg	"	—			
Inj Emset	Ondansetron		dil					

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Case No.:

COMMENTS: fentanyl + Ceftriaxone - CR X2 , midazolam + Ceftriaxone - CR X2
fentanyl + fosphenytoin - NA X2 " + fosphenytoin - Incom X2
fentanyl + noradd - NA X1 " + Noradrenaline - NA X2
" + midazolam - com : X2 " + Ondansetron - com X2
" + ondansetron - com X2 " + Pantoprazole - CR X2
" + pantoprazole - CR X2
Rt Ceftriaxone - I X1

MECHANISM OF ACTION:
Rt + ceftriaxone - Incompatibility due to presence of polyvalent calcium Ca^{2+} ion Rt
midazolam + Ceftriaxone - Incompatibility due to pH difference in both drug.

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