International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 8, Issue 1, 2016

Case Study

A CASE REPORT: DRUG INTERACTION BETWEEN LINEZOLID AND DOPAMINE

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Received: 01 Oct 2015 Revised and Accepted: 25 Nov 2015

ABSTRACT

Linezolid is a weak, non-selective inhibitor of monoamine oxidase (MAO). It can inhibit the breakdown of the tyramine by MAO in the gut and can also potentiate the effect of tyramine at nerve endings, thereby causing an increase in blood pressure. We encountered a neonate who developed acute hypertensive episode after simultaneous administration of dopamine and linezolid. A 25 w preterm neonate was admitted in NICU (Neonatal Intensive Care Unit) with complaints of Patent Ductus Arteriosus and respiratory infection. Linezolid infusion 6.5 mg every 8 h over 30 min (7 am, 3pm, 11 pm) was added after confirmation of gram-positive cocci (Staphylococcus epidermis) growth. Inj. Dopamine 20 mcg/kg/min was started for derangement in blood pressure 52/28 mm Hg (Mean blood pressure 43) at 5 pm. The baby developed acute hypertensive episode at 5.30 pm for which dopamine was withdrawn immediately. The half-life of Linezolid is 5.6 h in preterm baby, and that of Dopamine is 2 min. Since the probability of peak concentration for both the administered drugs was around the same time period, the baby developed acute hypertensive episode. So the combination of Linezolid with Dopamine should be avoided if possible or the dosage interval has to be extended to minimize the adverse reaction.

Keywords: Linezolid, Acute hypertension, Neonatal Intensive Care Unit

INTRODUCTION

A drug interaction is defined as the "pharmacologic or clinical response to the administration of a drug combination different from that anticipated from the known effects of the two agents". The interaction may result in a change in the nature or type of response to a drug (i.e., pharmacodynamic interaction), or a change in the magnitude or duration of response to a drug (i.e., pharmacokinetic interaction) [1].

Linezolid is an oxazolidinone antibacterial agent that has a unique mechanism of inhibition of bacterial protein synthesis [2]. It is also a weak, reversible non-selective monoamine oxidase inhibitor (MAOI) [3-12]. It can inhibit the breakdown of the tyramine by MAO in the gut and can also potentiate the effect of tyramine at nerve endings, thereby causing an increase in blood pressure [6-13]. Studies in adults recommended that it should not be taken while administering another MAOI or within 2 w of stopping another MAOI, unless close observation and blood pressure monitoring are possible. It should be avoided in those receiving Selective Serotonin Reuptake Inhibitors (SSRIs), $5HT_1$ (Serotonin) agonist, Tricyclic Anti-depressant (TCA), sympathomimetics, dopaminergic, buspirone, pethidine and possibly other opioid analgesics [5]. The usual dose and administration for Neonate is 10 mg/kg per dose every 8 h by IV infusion over 30 min to 120 min and for preterm newborns less than 1 w of age: 10 mg/kg per dose every 12 h. Oral dosing is the same as IV [2, 14-15].

CASE REPORT

A male preterm baby of 25 w gestational age, weighing 800 gm was born to a cervical incompetence mother after two successive spontaneous abortion/miscarriage. The baby was on a ventilator for 2 w and later Ibuprofen was given after extubation. The baby was diagnosed to have Patent Ductus Arteriosus and respiratory infection and was on ampicillin, amikacin, meropenem and vancomycin from outside hospital. Due to persistent lung congestion, the baby was reintubated and later came here for further management.

The baby was admitted in the Neonatal Intensive Care Unit (NICU) of Neonatology Department, Amrita Institute of Medical Sciences. Empirically the baby was started on Inj. Meropenem 25 mg every 8 hourly, Inj. Cefoperazone+Salbactum 25 mg 8 hourly, Inj. Amphotericin 1 mg every 24 hourly and later Inj. Caffeine 3.5 mg every 24 hourly was added for apnea at 6 pm. The culture from Endotracheal Suction tube was found to have Burkholderia Cepacia, which was resistant to Piperacillin and sensitive to Ceftazidime, Meropenem, and Trimethoprim+Sulfamethoxazole. Arterial blood culture detected Staphylococcus epidermidis (Coagulase-negative) and was resistant to Penicillin G, Cloxacillin/Oxacillin, Rifampicin and Ofloxacin but sensitive to Vancomycin, Cotrimoxazole, Teicoplanin, and Linezolid. Salbutamol Nebulisation was given on eighth day every 6 hourly and inj. Fluconazole was also added on next day.

From the 5th day of admission Inj. Linezolid 6.5 mg every 8 h (7 am, 3 pm and 11 pm) was infused over 30 min. On 11th day of admission (39th day of life) the baby developed deranging heart rate of 16 beats/min and blood pressure of 52/28 mm Hg, (Mean Blood Pressure-43) for which Inj. Dopamine 20 mcg/kg/min was started at 5 pm. The baby developed acute hypertensive episode (99/59 mm Hg and Mean Blood Pressure 78) at 5.30 pm. Subsequently Dopamine was withdrawn and blood pressure monitored. For a low birth weight infant, the normal systolic range is 50-62 mmHg, and the diastolic range is 26-36 mmHg. It was advised that combination of Linezolid with Dopamine should be avoided if possible.

DISCUSSION

Linezolid interacts with Dopamine to cause acute hypertensive episodes. The half-life of dopamine is 2 min and that of Linezolid is 5.6 h for preterm. For linezolid, the time to reach peak concentration was after 1-2 h [14]. So after the completion of Linezolid infusion at 3.30 pm its peak concentration will be reached around 5.30 pm during which the interaction has been encountered."Linezolid is a reversible non-selective MAOI. Administration of MAOI causes accumulation of Norepinephrine within adrenergic neurons including sympathetic neurons that innervate arterial blood vessels. Under such circumstances, the administration of a sympathomimetic agent can cause the release of the stored excess NE and subsequently exaggerated constriction of blood vessels and rise in blood pressure. Data demonstrate that the two medications may interact with each other in a clinically significant manner. A patient-specific assessment must be conducted to determine whether the benefits of concomitant therapy outweigh the risk. Specific actions

must be taken in order to realize the benefits or minimize the toxicity resulting from the concomitant use of the agents. These actions may include aggressive monitoring, empiric dosage changes and choosing alternative agents" [15].

CONCLUSION

Since the probability of acute hypertensive episode may be due to drug interaction, most of the catecholamines are not reliable for co-administering with Linezolid. In such cases Dopamine should start at a low dose or if the possible spacing between the interacting drugs should be prolonged to minimize anticipated toxicity.

ACKNOWLEDGEMENT

We obtained permission from patient parents to publish this case report.

ABBREVIATION

MAOI: Monoamine Oxidase Inhibitor; NICU: Neonatal Intensive Care Unit; SSRIs: Selective Serotonin Reuptake Inhibitors; $5HT_1$: Serotonin; TCA: Tricyclic Antidepressant.

CONFLICT OF INTERESTS

Declared None

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