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ORIGINAL ARTICLE

PARACETAMOL OVERDOSE FOLLOWING IMMUNIZATION IN TAMIL NADU, 2024: FROM RELIEF TO RISK – LESSONS FROM A CASE SERIES AND PUBLIC HEALTH INTERVENTIONS

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ABSTRACT

INTRODUCTION : Adverse Events Following Immunization (AEFI) range from more frequent minor side effects, such as fever or pain at the injection site, to rare but serious adverse reactions such as anaphylaxis, death, etc. For the children between 6 weeks to 6 years under the AEFI Surveillance Programme, syrup paracetamol (125mg/5ml) is recommended for uniformity and preventing dosing errors. However, AEFI cases due to paracetamol overdoses do occur. This study describes a series of five paracetamol overdose following immunization reported in Tamil Nadu during 2024 and enlists the state level interventions to prevent the occurrence of paracetamol overdose following immunization.

METHODS : AEFI cases are reported through the SAFEVAC portal in accordance with the AEFI Surveillance and Response Operational Guidelines (2024) and undergo causality assessment by the State Causality Assessment Committee. In 2024, of 454 cases reported in Tamil Nadu, five were identified as paracetamol overdose and assessed for causality.

RESULTS: Among the five cases, four children recovered, while one child died from severe toxicity leading to acute liver failure. The reasons attributed are incorrect dosing by health workers, repeated administration by caregivers, misinterpretation of prescriptions, and the availability of non-uniform paracetamol formulations. State-level corrective measures included, supply of a uniform paracetamol formulation (125 mg/5 ml syrup with measuring cups) through TNMSC, communication with the National AEFI Secretariat regarding the risks posed by multiple formulations, training of Medical Officers and Health Workers on safe dispensing with supportive supervision, and sensitisation of professional bodies (IMA, IAP) on overdose risks.

CONCLUSION: This case series illustrate how errors in dosage, misinterpretation by caregivers, and the use of multiple formulations can have serious consequences, including death. State level interventions demonstrate that coordinated policy decisions, capacity building, and stakeholder engagement are essential to safeguard child health and prevent recurrence of such adverse events.

KEY WORDS: Paracetamol overdose, Adverse events Following Immunisation, Public Health Interventions.

INTRODUCTION

Immunization is one of the most cost-effective health investments and a success story for global health and development1. Under the Universal Immunization Programme in Tamil Nadu, 11 Vaccines are being provided to children and pregnant mothers against the 12 Vaccine Preventable Diseases (VPDs). Annually, around 9.5 lakhs pregnant women and 8.77 lakhs children / infants are being covered under this UIP programme.[2]

Immunization sessions are being conducted both as Institutional in all days a week and on every Wednesday as Outreach sessions. Around 6.5 lakhs immunisation sessions are conducted in Tamil Nadu annually. Adverse Events Following Immunization (AEFI) are any untoward medical occurrences that follow immunization and do not necessarily have a causal relationship with the usage of the vaccine. These events can range from more frequent minor side effects, such as fever or pain at the injection site, to rare but serious adverse reactions such as anaphylaxis, death, etc.[3] The frequency of fever occurring within the first 24 hours following vaccination is highest following Pentavalent, DPT and IPV. For the children between 6 weeks to 6 years under the universal immunization programme, syrup paracetamol (acetaminophen) of strength 125mg/5ml is recommended for uniformity and preventing dosing errors.[3]Nevertheless, AEFI cases due to paracetamol overdoses do occur. This study describes a series of five paracetamol overdose following immunization reported in Tamil Nadu during 2024 and enlists the state level interventions to prevent the occurrence of paracetamol overdose following immunization.

METHODS

In accordance with AEFI Surveillance and Response Operational Guidelines 2024, AEFI cases occurring in districts

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are reported in SAFEVAC- Surveillance and Action For Events following Vaccination portal4. These cases are causally assessed by the State Causality Assessment Committee. Of the 454 cases reported in Tamil Nadu during 2024, five cases of paracetamol overdose are reported, and causally assessed by the State Causality Assessment Committee.

RESULTS

Among the five cases of paracetamol overdose reported, four cases recovered and one child died. Summary of the 5 cases are described in Table 1.

Contributing factors of paracetamol overdose	State level initiatives in preventing paracetamol overdose
▪ Dosage miscommunication between mother and health worker	▪ Trained Medical Officers and Health Workers on the Immunisation Manual, emphasizing supportive supervision and correct dispensing. ▪ Supplied paracetamol syrup (125 mg/5 ml) with calibrated measuring cups via TNMSC for immunisation sessions.
▪ Repeated oral administration by mother or caregiver ▪ Misinterpretation of prescribed doses	▪ Health workers and medical Officers sensitised to ensure parents and caregivers understand the right dosage.
Use of Paracetamol drops in field	▪ Addressed risks of multiple formulations with National AEFI Secretariat ▪ Requested supply of a single, uniform paracetamol syrup (125 mg/5 ml) for children
Additional doses of paracetamol administered by private practitioners without verifying prior doses given to the child	▪ Sensitised professional bodies (IMA, IAP) on overdose risks to strengthen awareness and safer prescribing practices, including verification of prior paracetamol intake before prescribing further doses.

Case 1 & 2:

1 month 13 days old twins who received bOPV 1, fIPV 1, PCV 1, Penta 1 and Rota 1 developed fever and seizures on the same day. Both were given excess doses of paracetamol (2.5 ml twice, 1 ml containing 150 mg of paracetamol, ~312 and 208 mg/kg respectively). Both children were hospitalized. Clinical examination was normal. Investigations revealed elevated CPP (59.4 mg/l), Serum Acetaminophen (134 mcg/ml). Diagnosed as simple febrile seizure and paracetamol overdose. Treated with antibiotics, antiepileptics, Vitamin K and N-acetyl cysteine (NAC). Both recovered.

Case 3:

3 months 10 days old male child vaccinated with bOPV 2, Penta 2 and Rota 2. On the same day baby developed fever with a background history of cold for 2 days and vomiting for 1 day (4 episodes). The mother administered 7.5 ml of paracetamol (150 mg/ml), instead of 0.4 ml advised by the health worker.

On the next day, baby developed fast breathing and was taken to a private clinic, where he was prescribed paracetamol 0.7 ml, oseltamivir, and nebulisation. Despite this, the symptoms persisted with poor feeding. The mother also gave 2 teaspoons of karpooravalli extract. The child was re-evaluated at the same clinic and referred to tertiary care hospital 2 days after vaccination.

On admission, the child had grunting respirations and was shifted to the PICU. He was intubated and started on NAC infusion, bicarbonate correction, and inotropes. During the course of management, child developed endotracheal bleeding, melena, and shock. Inotropes were escalated, and in view of fresh bleeding, packed red blood cells were transfused and steroids were initiated.

Despite all supportive measures, the child remained in refractory shock and suffered a cardiac arrest in the PICU. On day 3 of vaccination, the child had absent heart sounds, blood pressure, and palpable pulse. Pupils were 3 mm dilated and non-reactive, with no spontaneous respiration. Despite resuscitative efforts, the baby was declared dead.

Case 4:

3 months 15 days old female child vaccinated with bOPV 3, Penta 3, Rota 3, fIPV 2, PCV. Post vaccination, on the next day baby had fever, for which Paracetamol was given 4 times a day at a dose of 2.5 ml/dose (1ml~150 mg) ~1500mg/day ~ 348mg/kg. There was also a history of cough and cold for 1 day. The baby was referred from the PHC to Medical College Hospital and admitted. On examination, child was normal.

Initial investigations showed that liver enzymes were mildly elevated. However, from day 2 of admission, SGOT and SGPT levels became 370/166 U/L, which reduced on treatment with N-acetylcysteine, Vitamin K and intravenous fluids. The child recovered and later discharged.

Case 5:

4 months 11 days female child vaccinated with bOPV 3, Penta 3, Rota 3, fIPV 2, PCV 2. On the next day, baby had high grade fever, paracetamol was given 6th hourly for 2 days (cumulative dose: 360 mg/kg/day). On Day 2 of vaccination, child had seizure, taken to nearby hospital, loaded with antiepileptic drugs (AEDs) & paracetamol and referred to a private tertiary care hospital, where investigations revealed metabolic acidosis. NAC infusion started and child was referred to a Govt tertiary care hospital.

On admission, child had hematemesis and melena, treated with N acetyl cysteine, FFP and Vitamin K, levetiracetam. Serial CBC monitoring, liver enzyme monitoring done, which showed deranged coagulation profile. In view of prolonged derangement of coagulation profile, CT Brain done which showed mild diffuse hyperintensities in right cerebral hemisphere (suggestive of possible Encephalitis or Infarct). MRI Brain revealed Bilateral T2 globus pallidus hyperintensities, suggestive of secondary changes to liver failure. With treatment, child gradually improved and recovered.

Contributing factors for paracetamol overdose as identified in causality assessment and state level initiatives in preventing paracetamol overdose are outlined in Table 2.

DISCUSSION

Among the AEFIs, fever is the most common minor reaction attributed to most of the vaccines administered under UIP. The frequency of fever and local reaction (pain, swelling, redness) is highest following pentavalent, DPT and IPV. Paracetamol (acetaminophen) is commonly used as the first-line symptomatic medication for fever and pain management in the paediatric population, and it is the only drug recommended to treat fever in neonates5. When used in recommended doses and for a short duration (<72 hours), paracetamol has a good safety profile in infants. However, hepatotoxicity may occur after intake of a single high oral dose (> 150 mg/kg/ dose) or multiple excessive doses.[6,7]

Accidental paracetamol-induced hepatotoxicity owing to errors in dosage in infants has been reported globally. The reasons for overdosing include repeated oral administration by caregivers for persistent fever, and use of unsuitable formulations. Liver failure after repeated doses of paracetamol has been rarely reported, resulting from drug accumulation.[5]

This case series reports 5 cases of accidental paracetamol overdose, including one death due to paracetamol toxicity resulting in liver failure, disseminated intravascular coagulation and refractory shock. The reasons attributed are miscommunicated dosage by health worker, repeated oral administration by mother or caregiver, misinterpretation of prescribed doses and use of non-uniform formulations.

AEFI Surveillance and Response Operational Guidelines 2024 recommends that under UIP, syrup paracetamol of strength 125mg/5ml is preferable for uniformity and preventing dosing errors for the children aged between 6 weeks to 6 years. Despite this, field observations revealed that Paracetamol drops (supplied through National Health Programs as part of Kit A) are frequently used in practice. Drops pose challenges in dosing comprehension, particularly for mothers and caregivers who may already be distressed post-vaccination. This increases the likelihood of unintentional overdosing.

As observed in cases 3 and 5, additional doses of paracetamol were administered in private hospitals. This underscores the need to sensitise private practitioners to verify prior paracetamol intake before prescribing further doses. The State Causality Assessment Committee reviewing these cases emphasized the responsibility of health workers to ensure that caregivers understand dosing instructions clearly. Communication failures, especially in situations where the caregiver is anxious, can have catastrophic consequences, as illustrated by all the cases in this series. These findings underscore the importance of health workers not only prescribing the correct formulation but also verifying caregiver comprehension before dispensing.

State causality Assessment Committee insisted that it is the responsibility of health workers to ensure that mothers and caregivers clearly understand the correct dosage, particularly when they are anxious and distressed after their child's vaccination. The Committee also recommended that supportive supervision need to be strengthened.

From a programmatic perspective, five key actions are warranted. First, health workers should document the dosage of paracetamol advised for managing adverse events following immunisation in health records. Second, policy measures should enforce the supply of a single, uniform paracetamol formulation (125 mg/5 ml syrup) under UIP and National Health Programs to prevent confusion arising from multiple formulations across different supply kits. Third, supportive supervision needs to be strengthened at all levels of the health system to ensure adherence to guidelines. Fourth, continuous training and refresher training for health workers and supervisors should be institutionalized to build capacity for safe prescribing, dispensing, and caregiver education. Fifth, Sensitisation of private practitioners and paediatricians to verify prior paracetamol intake before prescribing further doses.

At the state level, several corrective measures were undertaken to address the issue of paracetamol overdose following immunisation. First, risks posed by multiple paracetamol formulations was addressed with the National AEFI Secretariat and requested to ensure the supply of a single, uniform formulation of paracetamol syrup (125 mg/5 ml) for the paediatric population, thereby preventing confusion arising from multiple formulations across different

supply kits. Second, to ensure accurate administration, paracetamol syrup (125 mg/5 ml) with calibrated measuring cups was supplied through the Tamil Nadu Medical Services Corporation (TNMSC) for use during immunisation sessions. Third, training of Medical Officers and Health Workers on the Immunisation Manual was completed, with emphasis on supportive supervision and appropriate dispensing of paracetamol for AEFI management. Fourth, Professional bodies, including the Indian Medical Association (IMA) and the Indian Academy of Paediatrics (IAP), were also sensitised on the risks associated with paracetamol overdose to strengthen awareness and promote safer prescribing practices.

CONCLUSION

This case series highlights the preventable risk of paracetamol overdose following immunisation. The reported cases illustrate how miscommunication in dosage, misinterpretation by caregivers, and the use of multiple formulations can have serious consequences, including death. In response, Tamil Nadu implemented a series of corrective measures, including ensuring uniform paracetamol formulations with calibrated measuring cups, training of health workers on safe dispensing and supportive supervision, and sensitisation of professional bodies on overdose risks. These interventions demonstrate that coordinated policy decisions, capacity building, and stakeholder engagement are essential to safeguard child health and prevent recurrence of such adverse events.

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