Methisoprinol (*Inosine Pranobex*) for Mumps During a Local Outbreak: Findings from a Descriptive Single-Center Study

*Rochman Mujayanto**

** Department Oral Medicine, Faculty of Dentistry, Universitas Islam Sultan Agung, Semarang – Indonesia*

Correspondence: rochman.mujayanto@unissula.ac.id

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ABSTRACT

Background: *Mumps is an acute infectious disease caused by the paramyxovirus, commonly found in many countries. In 2024, mumps outbreaks were reported globally, with significant cases in India (18,158), the USA (328), the Netherlands (578), and Indonesia (413). The current treatment guidelines for mumps are paracetamol or ibuprofen for pain relief. To describe clinical profiles and outcomes of mumps patients treated with methisoprinol in a single-center cross-sectional study.*

Methods: *A descriptive cross-sectional study of mumps patients treated with methisoprinol was conducted at the Islamic Dental Hospital Sultan Agung, Semarang, using retrospective data from August to December 2024. Mumps was defined by the WHO's clinical definition of parotid gland swelling.*

Results: *Among 35 mumps patients, there was an almost equal gender distribution, with most being under 18. The majority had a history of febrile illness, used symptomatic medication, and lacked MMR vaccination history. There was a significant difference in the duration of parotitis before and after methisoprinol medication. Factors like sex, age, parotitis location, and MMR vaccination history did not significantly affect recovery time.*

Conclusion: *Methisoprinol significantly reduced the duration of parotitis, while sex, age, parotitis location, and MMR vaccination history did not significantly influence recovery time.*

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INTRODUCTION

Mumps is an acute infectious disease caused by the paramyxovirus, which is still commonly found in many countries.[1] The World Health Organization reported that India experienced a surge in mumps cases from the beginning of 2024 to 30 March 2024, with a total of 18,158 cases.[2] The Centers for Disease Control and Prevention reported mumps outbreaks from November 2024, with 328 cases recorded by 5 December 2024.[1] The Dutch National Institute for Public Health and the Environment reported a spike in mumps cases in 2024 (578 cases) compared to 2023[3]. An overview of mumps cases in Indonesia from February to October 2024, 413 cases were reported across Indonesia.[4]

The paramyxovirus is transmitted through direct contact or airborne droplets from the upper respiratory tract of someone with mumps. The disease is commonly seen in children aged 5 to 9 years, but can also occur in teenagers or adults. Mumps lasts for 2 to 4 weeks after the incubation period of the paramyxovirus, with symptoms including myalgia, headache, malaise, and low-grade fever. Patients experience parotitis, characterized by pain and unilateral or bilateral swelling of the parotid glands. Mumps is a self-limiting disease. However, complications such as encephalitis, sensorineural deafness, or orchitis (painful swelling of the testes) in males may occur.[1,5,6] The aim of the study was to describe the clinical characteristics and outcomes of mumps patients treated with methisoprinol as an immunomodulatory agent in a single-center setting, using a descriptive cross-sectional study design

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted at the Islamic Dental Hospital Sultan Agung, Semarang, Indonesia. Medical records of mumps patients treated with methisoprinol were retrospectively reviewed over a five-month period from August to December 2024. Mumps was defined by the WHO's clinical definition of parotid gland swelling. Mumps definition base on World Health Organization clinical definition, unilateral or bilateral swelling of parotid glands[5].

RESULTS

In a sample of 35 individuals, there was an almost equal gender distribution with 48.6% males and 51.4% females. The majority were pediatric (under 18 years) at 85.7%, and adults (over 18 years) made up 14.3%. Most had a history of febrile illness (97.1%) and symptomatic medication use (paracetamol) (85.7%), with 77.1% reporting a family history of mumps. Regarding parotitis, 20% were affected on the left side, 17.1% on the right side, and 62.9% bilaterally. Submandibular lymphadenitis was noted in 22.9% of the sample, with 77.1% having no lymphadenitis, and the remainder having it on one or both sides. Additionally, a significant majority (97.1%) lacked a history of Mumps-Measles-Rubela (MMR) vaccination. The average length of days of complaints before methisoprinol treatment was 4 days (ranging from 1 to 10 days), while after treatment, the average increased to 5.34 days (ranging from 1 to 14 days). (table 1)

Table 1. Patient Charactheristics

Charactheristics	Total (n=35)
Sex	
• Male	17 (48.6%)
• Female	18 (51.4%)
Age	
• Pediatrics (age <18 years)	30 (85.7%)
• Adult (age >18 years)	5 (14.3%)
Febris History	
• No	1 (2.9%)
• Yes	34 (97.1%)
Symptomatic Medication History	
• No	5 (14.3%)
• Yes	30 (85.7%)
A Family History of mumps	
• No	8 (22.9%)
• Yes	27 (77.1%)
Parotitis	
• Left side	7 (20%)
• Right side	6 (17.1%)
• Bilateral	22 (62.9%)
Limfadenitis sub mandibula	
• No	27 (77.1%)
• Left side	1 (2.9%)
• Right side	1 (2.9%)
• Bilateral	6 (2.9%)
MMR Vaksin History	
• No	34 (97.1%)
• Yes	1 (2.9%)
Temperature (Celcius)	
• Mean	37.046
• Minimum	36
• Maximum	38
Days of parotitis before medication	
• Mean	4
• Minimum	1
• Maximum	10
Days of resolved parotitis after medication	
• Mean	5.34
• Minimum	1
• Maximum	14

The statistical tests conducted reveal significant results, indicating that the length of days of parotitis both before and after medication as evidenced by the Shapiro-Wilk test p-values of 0.006 and 0.005. The paired T-Test results (p-value of 0.023), suggest a statistically significant difference in the duration of parotitis pre- and post-medication, implying that medication (table 3) has an effect in reducing the length of days of parotitis complaints. (table 2)

Table 2. Days of parotitis before and after medication

Test	p-Value
Test of normality (Saphiro-Wilk)	
• Days of parotitis before medication	0.006
• Days of resolved parotitis after medication	0.005

Paired T-Test Analysis	0.023

Table 3. Medication

Medication	Total (n=35)
Methisoprinol	9 (25,7%)
Methisoprinol, Paracetamol	10 (28,6%)
Methisoprinol, Ibuprofen	15 (42,9%)
Methisoprinol, Paracetamol, Ibuprofen	1 (2,9%)

Sex, age, location of parotitis, and MMR vaccination history, not significance in affecting the recovery time of parotitis. The p-values of linear regression statistical tests for these factors (sex: 0.213, age: 0.283, location: 0.166, and MMR vaccination history: 0.901) indicate that there is no meaningful difference in recovery times based on these variables. Hence, these factors do not significantly influence how quickly patients recover from parotitis in this study. (table 4)

Table 4. Factors influencing the recovery time of parotitis

Linear Regression Analysis	p-Value
Sex	0.213
Age	0.283
Location parotitis	0.166
MMR vaksin history	0.901

DISCUSSION

The data shows that the majority of the sample consists of pediatric patients (85.7%), with a nearly equal gender distribution (48.6% male, 51.4% female). A significant proportion of the sample has a history of febrile illness (97.1%) and symptomatic medication use (85.7%), indicating a high prevalence of related health conditions. Additionally, 77.1% of the sample has a family history of mumps, which could suggest a genetic predisposition to the disease. The presence of parotitis in 62.9% of the sample, with 20% on the left side, 17.1% on the right side, and bilateral involvement in 62.9%, highlights the common symptomatology of mumps.

According to the World Health Organization (WHO), mumps is a highly contagious viral infection that primarily affects children aged 5 to 9 years, but can also occur in adolescents and adults.[5] The disease is characterized by symptoms such as myalgia, headache, malaise, and low-grade fever, followed by parotitis, which is the swelling of the parotid glands. Complications such as encephalitis, sensorineural deafness, and orchitis can occur, particularly in males.[5,7]

The lack of MMR vaccination in 97.1% of the sample could be a contributing factor to the high incidence of mumps in this group. (table 1) The efficacy of the mumps vaccine is relatively low, with a single dose being about 80% effective and two doses increasing efficacy to almost 90%. However, immunity can weaken over time, leading to outbreaks among vaccinated populations. The data from this sample aligns with these findings, as the high incidence of mumps and the lack of MMR

vaccination suggest a need for better immunization strategies.[1,5,7]

Mumps is a viral infection primarily managed through supportive care, as there is no specific antiviral treatment. The mainstay of treatment includes rest, hydration, and over-the-counter pain relievers such as paracetamol and ibuprofen to alleviate pain and fever. Applying cold or warm compresses to swollen areas can also provide relief.[1,5,7] All these patients were given treatment with paracetamol or ibuprofen, and methisoprinol. (table 3)

Methisoprinol (Inosine Pranobex) is an orally administered antiviral and immunomodulatory agent that inhibits viral replication. The dosing regimen is 100 mg/kg/day, divided into three doses, with a maximum dosage limit of 3000 mg/day. Methisoprinol enhances both the humoral and cell-mediated immune responses. It induces a Th1 cell-type response, characterized by an increase in pro-inflammatory cytokines such as IL-2 and IFN-γ. This response promotes the maturation and differentiation of T-lymphocytes and potentiates lymphoproliferative responses. Methisoprinol also decreases the production of anti-inflammatory cytokines like IL-10, thereby modulating the suppressive effects on immunity. Additionally, IP increases the population and activity of natural killer (NK) cells, and enhances neutrophil, monocyte, and macrophage chemotaxis and phagocytosis. On the humoral side, IP stimulates B lymphocyte differentiation into plasma cells and enhances antibody production.[8–11]

The antiviral properties of methisoprinol are believed to stem from its immunomodulatory effects. It boosts host immune responses upon activation by viral antigens, although it does not stimulate resting lymphocytes. Methisoprinol affects viral RNA synthesis by enhancing host cell RNA and protein synthesis while decreasing viral RNA synthesis. Methisoprinol components may interact with ribosomes in infected cells, causing incorrect transcription of viral genetic code, thus inhibiting viral replication. Another hypothesis involves inosine's ability to inhibit the synthesis of phosphoribosyl pyrophosphate, a key intermediate in viral RNA synthesis. Methisoprinol action is multifaceted, enhancing immune responses and exhibiting antiviral effects by promoting T-lymphocyte function, increasing cytokine production, and inhibiting viral RNA synthesis. These combined effects contribute to its efficacy in treating various viral infections.[8–11]

Methisoprinol was found to significantly reduce complaints of parotitis in a statistically meaningful manner. The mumps virus, part of the Paramyxoviridae family, causes parotitis and can lead to complications like orchitis, oophoritis, and meningitis. Controlling the immune response to the mumps virus is crucial to managing the infection and preventing complications. Methisoprinol enhances the immune response by stimulating T-cell activity and promoting cytokine production, essential for an effective antiviral response.[10,12,13] This effect can be particularly beneficial for mumps patients by strengthening the immune system's fight against the virus.

Studies have highlighted methisoprinol's antiviral properties against various viruses, such as herpes simplex virus and other infections[10,14,15] It enhances T-cell proliferation and activity, critical for an effective immune response against viral infections like

mumps.[10,13]This suggests methisoprinol could reduce mumps severity and duration by boosting the host's immune response.

Methisoprinol has also been studied for subacute sclerosing panencephalitis (SSPE), a serious complication of measles infection, sharing similarities with mumps in terms of viral family and neurological complications. Methisoprinol has shown promise in stabilizing the disease and improving patient outcomes, suggesting it could be useful in managing severe viral infections.[16,17] It could potentially mitigate mumps complications, especially in immunocompromised individuals or those with severe disease manifestations.

The safety profile of methisoprinol is well-documented, showing it is generally well-tolerated in both adults and children.[10,12] This is crucial for treating pediatric viral infections, where safety and tolerability are paramount. Its ability to enhance immune responses without significant adverse effects makes it a promising candidate for mumps treatment.

Despite promising data, more targeted research is needed to assess methisoprinol efficacy in treating mumps. Clinical trials evaluating its outcomes in mumps patients, especially those at risk for complications, would provide valuable insights into its clinical role. Understanding the optimal dosing and treatment duration for methisoprinol in mumps is essential for establishing evidence-based guidelines.

In conclusion, methisoprinol's immune-boosting and antiviral properties make it a compelling candidate for mumps treatment. Its ability to enhance T-cell responses and modulate inflammatory pathways could improve outcomes in mumps patients, particularly those with severe manifestations or complications. However, further research is needed to fully understand its efficacy and safety in this context.

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