Randomized Double-Blinked Placebo-Controlled Trial of Retapamulin for Nasal Decolonization of Mupirocin-Resistant MRSA Carriers

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BACKGROUND

• Decolonization of the nasal reservoir has been extensively used to clear both methicillin-resistant S. aureus (MRSA) and methicillin-sensitive S. aureus (MSSA) to reduce surgical site infections, prevent recurrent S. aureus infections, and prevent infections as a part of routine ICU care.

• Decolonization regimens most commonly involve 5 days of twice daily nasal mupirocin ointment with or without chlorhexidine bathing.

• Mupirocin-resistance, both low-level (LL-MupR) and high-level (HL-MupR), have been reported. LL-MupR is due to mutations in 16S rRNA synthetase and has unclear clinical significance. HL-MupR is due to a plasmid-based novel 16S rRNA synthetase which is associated with clinical failure of nasal decolonization.

• Concern for emerging resistance has raised questions about alternatives to mupirocin for S. aureus decolonization.

• Retapamulin is a topically first-in-class pleuromutilin antibiotic that inhibits protein synthesis by interacting with the 50S bacterial ribosomal subunit. It was FDA approved in 2007 for the treatment of non-MRSA skin infections, but has good activity against mupirocin-resistant MRSA in vitro.

• We sought to evaluate whether retapamulin could decolonize the nose of patients harboring mupirocin-resistant MRSA.

OUTCOMES

• Primary Outcome: MRSA carriage at 6 weeks after completing initial regimen (Day 47)

• Secondary Outcome: MRSA carriage at 1 week after completing initial regimen (Day 12)

• Retapamulin cleared mupirocin-resistant MRSA nasal strains significantly more effectively than placebo 1 week after treatment (68% vs 24%).

• By 6 weeks after treatment, MRSA clearance in the retapamulin and placebo arms did not statistically differ (32% vs 16%), but sample size was limited.

• There was a significant 84% reduction in odds of MRSA carriage at one week post-therapy with retapamulin compared to placebo.

• There was a non-significant 59% reduction in odds of MRSA carriage at six weeks post-therapy with retapamulin versus placebo, given our sample size.

• There were no adverse events.

• No evidence of retapamulin resistance in any MRSA strains

CONCLUSIONS

• In a small randomized double-blinded placebo-controlled trial, retapamulin cleared mupirocin-resistant MRSA nasal strains significantly more effectively than placebo 1 week after treatment (68% vs 24%).

• By 6 weeks after treatment, MRSA clearance in the retapamulin and placebo arms did not statistically differ (32% vs 16%), but sample size was limited.

• Retapamulin appeared equally effective against both low-level and high-level mupirocin-resistant MRSA strains.

• Retapamulin was well tolerated without reported side effects.

• Retapamulin resistance was not identified in any study strains.

https://clinicaltrials.gov/ct2/show/NCT01461668