Improving Outcomes in Necrotising Otitis Externa (IONOE) study: initial results from a UK prospective multicentre observational study

Contact: junko.takata@ndm.ox.ac.uk

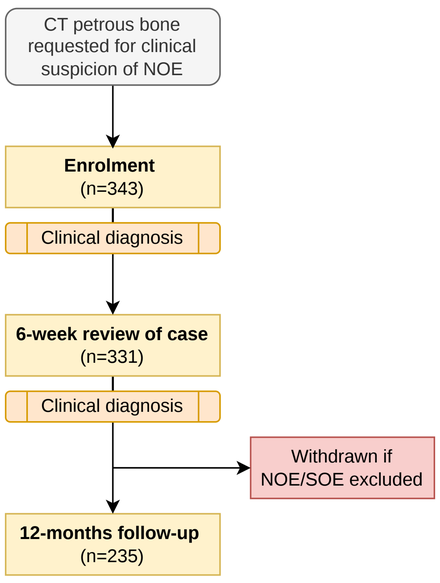
Junko Takata[1,2], Victoria Sinclair[1], Manu Shrivastava[3], Oliver Bannister[1], Michelle Kümin[2], Claire Scarborough[2], Pieter Pretorius[1], Monique I. Andersson[1,4], Susanne H. Hodgson[1,2], *on behalf of the IONOE Study Team*

[1] Oxford University Hospitals NHS Foundation Trust, Oxford, UK [2] Nuffield Department of Medicine, University of Oxford, UK [3] London North West University Healthcare NHS Trust, London, UK [4] Radcliffe Department of Medicine, University of Oxford, UK

Background

- Necrotising otitis externa (NOE) is a severe infection of the external ear canal (EAC).
- Early NOE can be difficult to distinguish from severe otitis externa (SOE).
- Approaches to diagnosis and treatment vary widely, with limited data to guide the creation of consensus guidelines.
- The IONOE study is the largest multicentre, prospective, observational cohort study of severe EAC infection to date.

Methods



23 sites in England, Wales and Scotland

Data collected on:

- Demographics, co-morbidities
- Presenting symptoms, initial blood results
- Radiology reports
- Treatment (antimicrobial therapy, surgery)
- Outcomes

Results

1. Diagnosis and baseline characteristics

- 343 patients were enrolled from 23 UK sites.
- At the 6-week timepoint, 14% (47/331) patients had a change in their clinical diagnosis from time of initial CT.
- Of the patients for whom diagnosis was unchanged, 68% (193/284) had NOE and 24% (69/284) SOE.
- NOE and SOE groups had similar presenting symptoms, but cranial nerve palsy and fever was more common in the NOE group (**Table 1**).

Symptoms	NOE (n=151)	SOE (n=52)
Otalgia	145 (96%)	49 (94%)
Otorrhoea	125 (83%)	42 (81%)
Granulation tissue in EAC	109 (72%)	36 (69%)
Oedema in EAC	107 (71%)	38 (73%)
Worse/new hearing loss	102 (68%)	43 (83%)
Cranial nerve palsy	28 (19%)	2 (4%)
Reported fever	15 (10%)	3 (6%)

Table 1. *Comparison of clinical presentation (if recorded) at time of initial CT (+/- 7 days), between NOE and SOE patients who had a consistent clinical diagnosis between enrolment and 6-week review.*

Results (continued)

2. Microbiology

97% (254/262) patients had at least one microbiology sample.

- 13% (35/254) patients had no growth, and 4% (9/254) no significant growth, on any sample (**Fig. 1A**).
- 63% (160/254) patients had >1 sample sent; of these, 15% (25/160) had growth following an initial result of no growth.
- Median samples sent per patient was 2 (range: 1-10) in both groups.
- 81% (206/254) patients only had superficial swabs sent (**Fig. 1B**).

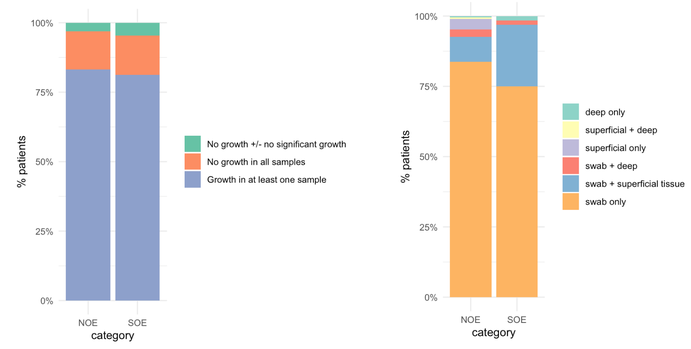


Figure 1. (A) *Sample growth, and* ***(B)*** *sample type in NOE vs. SOE.*

82% (210/254) patients with a sample sent had positive growth.

- 38% (80/210) patients had more than one organism isolated.
- 29% (61/210) patients had at least one sample with fungal growth.
- Of positive isolates (deduplicated per patient), *Pseudomonas aeruginosa* was the most common in both groups, followed by *Candida spp* (**Fig. 2**).
- More non- *P. aeruginosa* organisms were found in the SOE group.

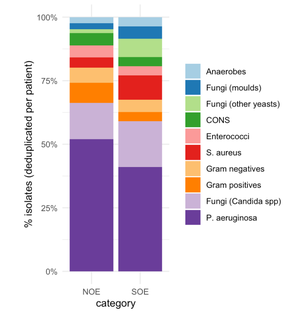


Figure 2. *Organisms isolated, deduplicated per patient, in NOE vs. SOE groups.*

3. Antimicrobial therapy

Antimicrobial choice

- 100% (193/193) of NOE and 86% (59/69) of SOE patients received parenteral or oral antibiotics.
- Of these, 99% (192/193) of NOE and 95% (56/59) SOE patients received an antipseudomonal antimicrobial; most common empirical choice was piperacillin-tazobactam for NOE and ciprofloxacin for SOE (**Table 2**).
- 31% (60/193) of NOE and 10% (6/59) of SOE patients received more than one antipseudomonal concurrently over the course of their treatment (**Fig. 3A**).
- 11% (6/61) patients with fungal growth received antifungal therapy; a further 2 patients received antifungal therapy without fungal growth on sampling.

Duration of treatment

- Excluding cases that relapsed, median duration of treatment was 50 days (IQR: 42-82.5) in NOE, and 19 days (IQR: 10-37) in SOE (**Fig. 3B**).

Empirical therapy	NOE	SOE
Piperacillin-tazobactam	89	18
Ciprofloxacin	37	26
Ceftazidime	28	8
Piperacillin-tazobactam + gentamicin	11	1
Piperacillin-tazobactam + ciprofloxacin	9	0
Ceftazidime + ciprofloxacin	6	2
Meropenem	5	1
Other combinations	7	0
Total	**192**	**56**

Table 2. *Empirical antipseudomonal for NOE and SOE groups, i.e. the first antibiotic course received.*

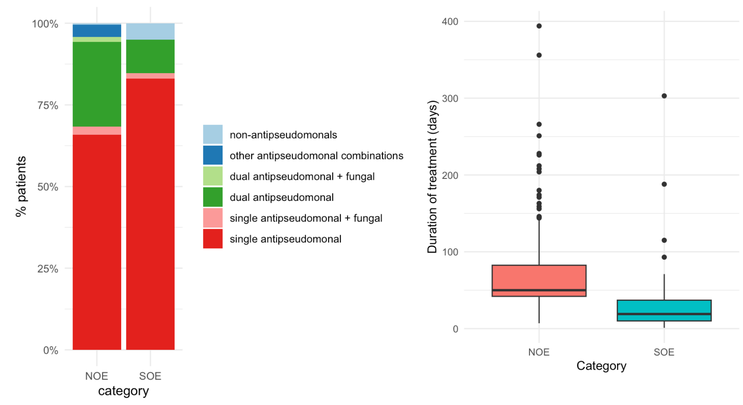


Figure 3. (A) *Antimicrobial course(s) received in NOE and SOE groups. Dual treatment was defined as courses that overlapped by >48 hours, i.e. concurrent rather than sequential prescribing.* ***(B)*** *Duration of treatment in NOE and SOE groups, excluding cases who relapsed.*

4. Outcomes

- 11% (21/172) NOE patients and 6% (4/69) SOE patients died.
- Among NOE patients, 6% (11/193) relapsed, and 35% (68/193) had complex disease*.
- Among NOE patients who survived and could be contacted at 12 months, 34% (47/138) reported long-term symptoms including hearing loss, chronic pain and facial weakness (**Fig. 4**).

* Complex disease includes cranial nerve palsy, TMJ involvement, skull base osteomyelitis, cerebral venous sinus thrombosis, or contralateral spread of disease.

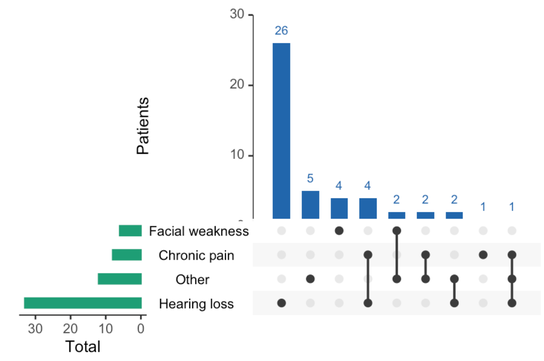


Figure 4. L*ong-term complications reported by NOE patients at 12 months of follow-up.*

Conclusions

- NOE and SOE can be difficult to distinguish clinically, and diagnostic uncertainty exists on initial presentation.
- Although classically associated with *Pseudomonas aeruginosa* infection, our findings indicate multiple organisms can be isolated in NOE, the significance of which is unclear.
- NOE and SOE in the UK are managed with markedly different antibiotic durations, suggesting improving diagnostic accuracy will contribute to antimicrobial stewardship.
- Antibiotic treatment of NOE varies nationally, with some centres implementing dual anti-pseudomonal therapy.
- High levels of mortality, morbidity and relapse associated with NOE highlight the need for future interventional studies to inform clinical guidelines.
- Further analysis will assess radiological findings and associations between treatment and outcomes.

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