Transdermal Clonidine for Mucositis Pain

A retrospective observational study to determine whether transdermal clonidine improves analgesia for patients with severe mucositis

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INTRODUCTION

Pain caused by severe mucositis can be extremely challenging to manage[1]. The most severe oral ulceration, and severe pain, tends to occur when the patients reach the nadir of their white blood cell count[2].

It is thought that ulcers generally resolve when the absolute neutrophil count (ANC) recovers to a level greater than 500cells/ml but in patients who develop severe ulcerations some oral ulcers persist after recovery of the ANC[3].

In our institution, mucositis patients often need intravenous opioid, sometimes with additional ketamine via NCA/PCA (Nurse Controlled Analgesia/Patient Controlled Analgesia) for up to 14 days. For some patients, pain control remains problematic. We hypothesised that transdermal clonidine may be a useful analgesic adjunct.

On application of a clonidine patch, plasma levels rise gradually and stable levels are achieved after 72 hours.

METHOD

This retrospective analysis included data from 28 patients:

· 14 children who had transdermal clonidine (Group 1) prescribed in addition to PCA/NCA

· Matched historical control group managed only with PCA/NCA (Group 2).

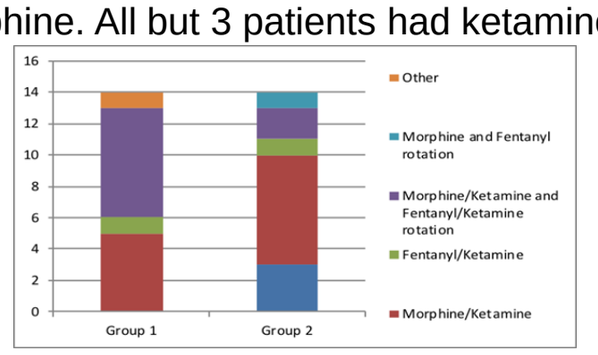
Data collected included:

· patient demographics
· maximum daily pain scores
· daily opioid consumption
· daily ketamine consumption
·daily white blood cell count and neutrophil count
·sedation scores and respiratory rates

Data was analysed to establish if there was a temporal relationship between analgesia requirement and neutrophil count.

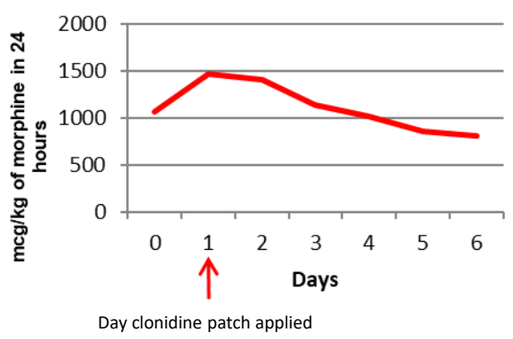
RESULTS

All the patients received an opioid PCA/NCA with the majority receiving morphine. All but 3 patients had ketamine added.

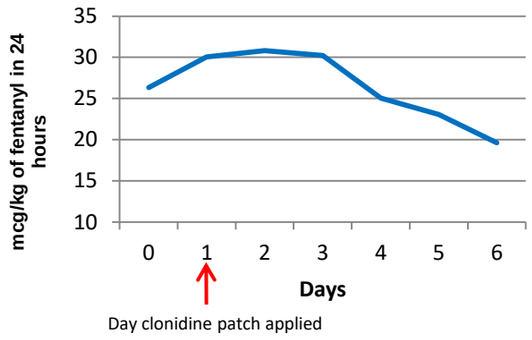


Maximum daily pain scores appeared to be independent of daily PCA/NCA opioid consumption in both groups.

In Group 1, 71% of patients reduced their opioid consumption within 72 hours of the patch being applied and 86% within 96 hours:



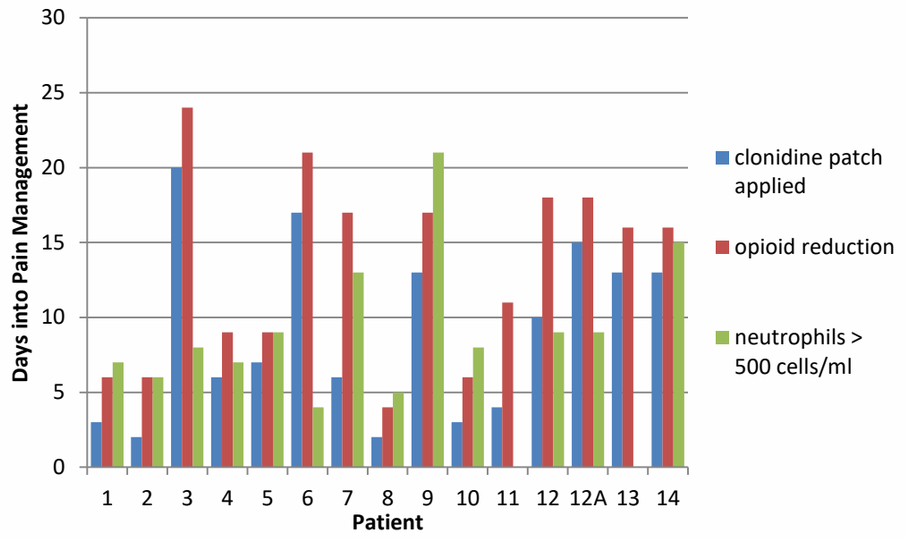
Day clonidine patch applied



Day clonidine patch applied

OPIOID REDUCTION AND NEUTROPHIL RECOVERY:

- 6 patients had opioid reduction prior to neutrophil recovery
- 3 patients had neutrophil recovery before patch application and opioid reduction then occurred within 96 hours
- 4 patients had opioid reduction on the same day or within 48 hours of neutrophil recovery but always within 72 hours of patch application

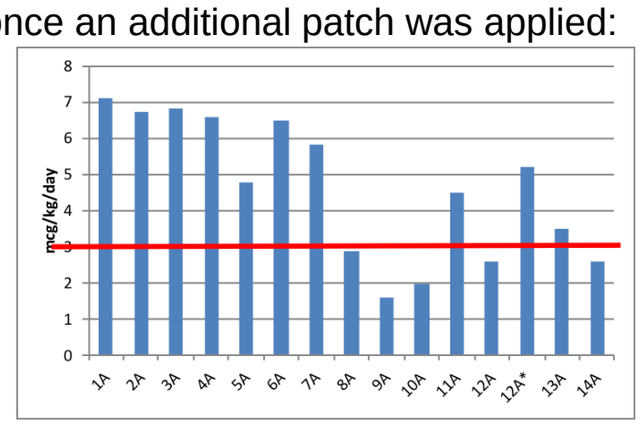


DISCUSSION

10 of the 14 patients in group 1 had reduced opioid consumption within 72 hours of the clonidine patch being applied. A further 2 patients reduced their opioid consumption within 96 hours of application.

The relationship between ANC and mucositis pain is complex and not completely understood. A significant proportion of patients in this study had opioid reduction prior to neutrophil recovery.

The dose of clonidine prescribed varied from 1.6microgram/kg/day to 7.1microgram/kg/day. The therapeutic dose is believed to be 3microgram/kg/day[4]. Initial caution at prescribing it potentially led to underdosing; one teenage patient (12/12A) had significantly better pain control once an additional patch was applied:



Red line denotes therapeutic dose

CONCLUSION

No patients receiving transdermal clonidine had any adverse side effects, specifically no increased sedation or hypotension.

The study demonstrated that transdermal clonidine can be a useful adjunct in this field of paediatric pain management allowing a reduction in opioid consumption and analgesic benefit that may be independent of the biological markers indicating resolution of the mucositis.

The study, although it involved a limited number of patients, also suggests that transdermal clonidine can be helpful for complex pain management in patients in the ward setting. Indeed the technique has been extended to patients from other specialities in the authors' Trust.

References: 1.Ribeiro, I. et al 2017. Oral mucositis in pediatric patients in treatment for acute lymphoblastic leukemia. *International journal of environmental research and public health*, *14*(12), 2. James, P.J. et al The addition of ketamine to a morphine nurse-or patient-controlled analgesia infusion (PCA/NCA) increases analgesic efficacy in children with mucositis pain. *Pediatric Anesthesia*, *20*(9), pp.805-811. 3. Woo, S.B. et al 1993. A longitudinal study of oral ulcerative mucositis in bone marrow transplant recipients. *Cancer*, *72*(5), pp.1612-1617. 4. Boehringer (2010) https://medsafe.govt.nz/profs/Datasheet/c/CatapresTTS.pdf Accessed on: 23/04/2019

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