N-ACETYLCYSTEINE IN THE PREVENTION OF CONTRAST-INDUCED ACUTE KIDNEY INJURY (CIAKI)
Executive Summary

[Adapted from the report by Madam Maharita Abd. Rahman]

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2016

Introduction

Acute kidney injury (AKI) is one of health problems that affect kidney structure and function. It is common, harmful and potentially treatable. Even a minor acute reduction in kidney function has an adverse prognosis. Contrast-induced acute kidney injury (CIAKI) is uncommon among people with normal kidney function. It is accepted that, in patients with normal renal function; even in the presence of diabetes, the risk for CIAKI is low (1 – 2%). Usually it is defined as a rise in serum creatinine (srCr) of ≥ 0.5mg/dl (≥ 44µmol/l) or a 25% increase from baseline value, assessed at 48 hours after a radiological procedure. This definition was based on the observation that creatinine elevation after contrast administration typically peaks within three days.

There are several approaches for CIAKI prevention, either pharmacological strategies (N-acetylcysteine (NAC), theophylline, fenoldopam, statins and ascorbic acid) or non-pharmacological (haemodialysis or hemofiltration and hydration). N-acetylcysteine is a treatment of choice in CIAKI prevention, as it is inexpensive and appears to be safe; many studies did show potential benefits of NAC towards reducing CIAKI incidence especially among high risk patient.

Currently, there is no standard operating procedure for the prevention of CIAKI during and after radio-contrast procedure in Ministry of Health (MOH). This review was requested in order to determine the efficacy or effectiveness of NAC in prevention of CIAKI.

Objective/Aim

i. To assess the efficacy/effectiveness of NAC in the prevention of CIAKI
ii. To assess the safety of NAC in the prevention of CIAKI
iii. To assess the economic implications related to NAC in the prevention of CIAKI
iv. To assess the ethical, legal, and organizational implications related to NAC in the prevention of CIAKI

Methods

Literature search strategy

Studies were identified by searching electronic databases. The following databases were searched through the Ovid interface: MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to present. Parallel searches were run in PubMed and EMBASE. Appendix 2 shows the detailed search strategies. No limits were applied to the search. The last search was run in September 2016. Additional studies were identified from reviewing the references of retrieved articles.

Study Selection

Based on the inclusion and exclusion criteria, study selection was carried out independently by two reviewers. The titles and abstracts of all studies were assessed for the above eligibility criteria by first reviewer. If it was absolutely clear from the title and / or abstract that the study was not relevant, it was excluded. If it was unclear from the title and / or the abstract, the full text article was retrieved. The selected articles were assessed by first reviewer and second reviewer verified the content of the articles. Any disagreement and issues were resolved by discussion.

Results and Conclusions
A total of 538 titles were identified. After removal of 139 irrelevant titles, a potential of 399 relevant titles were screened for abstracts. Out of 399 abstracts, only 185 abstracts were retrieved for full text articles. Of these, 39 full texts could be not retrieved and 146 articles were appraised. Although the full text of 39 relevant abstracts could not be retrieved, the abstracts showed that the results reported were not much different from the study retrieved**.** Ten relevant full text articles were identified from references of retrieved articles and while updating the search. After critically appraised and discussion with second reviewer and expert committees only 10 articles were included in the review. The included articles consisted of seven systematic reviews (SRs) with meta-analysis (MAs), one systematic review (SR) and two randomised controlled trials (RCTs).

Conclusion
Good level of evidences was retrieved to show the effects of NAC in CIAKI prevention. However patients underlying problems, NAC dose and type of contrast media use may influence the overall effects of NAC in CIAKI preventions. The findings of this review were concluded as follows:

Efficacy

- In patients with renal insufficiency, oral NAC may reduce CIAKI incidence compared with placebo. However, the optimum dose of NAC required cannot be determined.
- In diabetes patients, use of NAC has no significant effects in CIAKI prevention
- In patients undergoing cardiac angiography, the role of NAC in CIAKI prevention was inconsistent. However, high dose NAC seems to be more effective compared to low dose NAC.
- Use of NAC with LOCM showed better outcome in CIAKI prevention compared to NAC with IOCM
- NAC single use has no significant difference in prevention of CIAKI compared to combination of NAC with other alternatives

Safety

- No adverse events were reported with the use of oral NAC but i.v NAC was associated with mild adverse events such as itching, flushing and rash

Cost

- No retrievable evidence on cost-effectiveness
- Local price of NAC injection (200mg/ml of 10ml vial) is about RM11.29 and in tablet formulation of 100mg, 200mg and 600mg is about RM2.00 to RM 5.00 per tablet

Ethical, legal and Organizational

- No standard guideline for CIAKI prevention in MOH
- In Malaysia, NAC is not indicated for CIAKI prevention. The off label use for CIAKI prevention require approval from the Director General of Health.
- Oral NAC is not listed in MOH Drug Formulary thus patients buy their own oral NAC tablet from a retail pharmacy
- Adverse events which may occur pertaining to off-label use of NAC for CIAKI

prevention may have legal implications

Recommendation

Based on the available evidence, oral NAC may be used in prevention of CIAKI in renal insufficiency patients. Other factors that may influence CIAKI incidence should be considered in patients undergoing radio-contrast procedure such as types of contrast media and patients' hydration status.