Best evidence topic - Cardiac general

Low dose (renal dose) dopamine in the critically ill patient

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Summary

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was whether low dose (renal dose) dopamine in the critically ill patient prevents acute renal failure. Altogether 141 papers were found using the reported search, of which three presented the best evidence to answer the clinical question. The author, journal, date and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these papers are tabulated. We conclude that there is no evidence to support the use of low-dose dopamine to treat acute renal failure in critically ill patients.

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Keywords: Evidence-based medicine; Thoracic surgery; Dopamine; Renal failure; Acute

1. Introduction

A best evidence topic was constructed according to a structured protocol. This protocol is fully described in the ICVTS [1].

2. Clinical scenario

You are asked to review a 75-year-old patient who is 1 day post coronary arterial bypass surgery. He has passed 8 ml of urine in the last hour and only 70 ml in the last 6 h. Of note he had 40 mg of Frusemide 1 h ago. His pulse is 95 and he is in sinus rhythm, his blood pressure is 105/70 and his CVP is 5 cm. He has no history of renal failure and he is on no reno-toxic drugs, although he is on a small dose of noradrenaline. You note that it had been a difficult operation and there had been a long bypass time. You suggest an increase in the noradrenaline to increase his blood pressure and thus his renal perfusion pressure. The nurse suggests that you try a ‘renal dose of dopamine’ instead. You do not believe that dopamine is actually reno-protective and thus you elect to search for the evidence for or against this commonly held view.

3. Three part question

In [a critically ill patient] is [low dose (renal dose) dopamine effective] at [preventing renal failure].

4. Search strategy


5. Search outcome

One hundred and forty-one papers were found of which 24 were included in the meta-analysis reported below [2]. Two further papers were found which were relevant [3–4]. One hundred and twelve abstracts were irrelevant and three were of insufficient quality for inclusion. The relevant papers are presented in Table 1.

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<table>
<thead>
<tr>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kellum and Decker (2001), Crit Care Med, USA [2]</td>
<td>Medline search 1966 to December 1999 of papers reporting the effects on the kidney (drug effects) of low dose dopamine &lt;5 μg/kg per ml; 24 studies found (n = 1019) of which 17 were RCTs (n = 854).</td>
<td>Meta-analysis (level 1a)</td>
<td>Mortality in treatment and control group n = 508</td>
<td>Dopamine 4.7%, placebo 5.6%, N/S</td>
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<td>Requirement for haemodialysis n = 618</td>
<td>Dopamine 13.9%, placebo 16.5%, N/S</td>
<td>Power calculations showed that they could confidently exclude that dopamine reduces renal failure by over 50%. But even this meta-analysis cannot detect more subtle differences</td>
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<td></td>
<td>Acute renal failure n = 508</td>
<td>Dopamine 15.3%, placebo 19.5%, N/S</td>
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<tr>
<td>Australia and New Zealand intensive care society clinical trial group (2000), Lancet, Australia [3]</td>
<td>328 critically ill adults with early renal dysfunction from 23 intensive care units; 161 patients received continuous infusion of low dose dopamine (2 μg/kg per min) via a central line; 163 patients received placebo infusion</td>
<td>Double-blind PRCT (level 1b)</td>
<td>Peak creatinine μmol/l</td>
<td>Dopamine 245, placebo 249</td>
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<td>No. patients with creatinine concentration &gt; 300</td>
<td>Dopamine 56, placebo 56</td>
<td>Large amount of diuretic used by physicians during the study: dopamine group mean dose 192 mg but placebo group mean dose 268 mg</td>
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<td>No. patients requiring renal replacement therapy</td>
<td>Dopamine 35, placebo 40</td>
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<td>Urine output (ml/h) after 24 h</td>
<td>Dopamine 96 ml/h, placebo 92 ml/h</td>
<td>The dopamine group had a lower baseline urine output that almost reached significance (37 ml/h vs. 50 ml/h, difference 13 (CI – 1 to 27 ml/h)</td>
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<td>Output after 48 h</td>
<td>Dopamine 99 ml/h Placebo 109 ml/h</td>
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<td>Marik and Iglesias for The NORASEPT II Study (1999), Am J Med, USA [4]</td>
<td>A sub-study of 395 oliguric patients with septic shock; three groups identified: Group 1, 174 patients receiving dopamine at &lt;3 μg/kg per min; Group 2, 127 patients receiving dopamine at &gt;3 μg/kg per min; Group 3, 94 patients receiving no dopamine</td>
<td>Non-randomised case-control study (level 4)</td>
<td>Development of acute renal failure</td>
<td>Group 1, 29%; Group 2, 31%; Group 3, 29%; N/S</td>
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<td>Requirement for dialysis or ultrafiltration</td>
<td>Group 1, 13%; Group 2, 14%; Group 3, 13%; N/S</td>
<td>This is a sub-study of the NORASEPT II study that was a PRCT looking at monoclonal antibody to TNF in sepsis). This analysis is retrospective, non-randomised, non-matched, and did not have prospective data collection regarding adverse events</td>
</tr>
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<td>28-day survival</td>
<td>Group 1, 64%; Group 2, 58%; Group 3, 66%; N/S</td>
<td>Included here as it is a similar quality paper to those in the meta-analysis but this was not included by Kellum and Decker [2]</td>
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</table>
6. Comment(s)

The meta-analysis by Kellum et al. could demonstrate no benefit of low dose dopamine for the preservation of renal function. This was a well conducted meta-analysis, however, of 53 relevant papers found, data could only be extracted from half of the reviewed papers.

We also found two more recently published trials not included in this meta-analysis. These also presented negative results. The ANZICS trial found no reno-protective effect with dopamine, and the NORASEPT II study also found no reno-protective effect.

The meta-analysis and the two randomised controlled trials presented here find that there is no reno-protective effect with dopamine. To ensure that there has not been a type I error (finding no difference when in fact one does exist) the papers must be adequately powered. Kellum et al. provide power calculations showing that they are very unlikely to have missed benefits to renal failure of over 50%.

However, even this meta-analysis is not able to exclude smaller effects than this. Our calculations show that to detect a 20% difference in acute renal failure (control event rate from this meta-analysis was 19.5%) with a power of 80%, one would need 4100 patients for a double blind RCT, or meta-analysis.

Thus, while it can firmly concluded that dopamine does not halve the rate of acute renal failure, it is currently unknown as to whether dopamine might have a smaller positive effect than this. In order to exclude a 20% reduction in acute renal failure with dopamine, a randomised controlled trial would have to recruit 4100 critically ill patients.

7. Clinical bottom line

There is no evidence to support the use of low-dose dopamine to treat acute renal failure in critically ill patients.

References


Appendix A. ICVTS on-line discussion

Author: Dr. Murat Ozeren, Cardiovascular Surgeon, SSK Ankara Training Hospital, Department of Cardiovascular Surgery, kizilirmak cad 61/5, Kizil, Ankara, 06640 Turkey

Date: 10-Jan-2004

Message: I thank Dr. Dunning and colleagues for their evidence-based analysis regarding usage of renal-dose dopamine in the critically ill patient. Lack of renoprotective effect of renal-dose dopamine in cardiac surgery is shown by the recent prospective randomized study of Dr. Woo et al. [1]. These insufficient results also found in the clinical studies of neonatal and pediatric cases following cardiac surgery [2]. In this paper, the clinical scenario is about a 75-year-old patient with renal problems after cardiac surgery. The Authors are searching evidence for the usage of renal-dose dopamine in this patient, but their evidence-based paper is about critically ill non-cardiac surgery patients. I wonder why the authors did not discuss the papers which are primarily in combination "cardiac surgery" and "renal-dose dopamine".

References


Response

Author: Mr. Joel Dunning, SpR Cardiothoracic Surgery, Freeman Hospital, Newcastle-upon-Tyne, Freeman Road, Newcastle-upon-Tyne, UK

Date: 12-Jan-2004

Message: A useful comment regarding the methodology of our selection procedures for the papers included here. Of note Best Evidence Topics are designed to be as transparent as possible, which is why all included papers are tabulated and also why the search strategy is also included. Thus if, as Dr. Ozeren may have done, the reader considers that important evidence may have been missed it is possible for the reader to quickly run the search strategy themselves. The reader can then look through the abstracts to see if they consider any of the papers not included by may in fact be important to them to help them answer the question addressed. Alert readers such as Dr.Ozeren may note that neither of the papers that he mentions got picked up by our search strategy.

The second strength of our Best Evidence Topics now comes in to play, namely our review process. Each of our Best Evidence Topics are reviewed by an Evidence Based Journal Club. This is a group of consultants and registrars with an interest in Evidence Based Medicine and expertise in Cardiothoracic Surgery that meets weekly to review Journals and these topics. When this topic was reviewed, the paper by Woo et al was mentioned to us by the group. However after looking at this paper we found that Woo et al studied prophylactic dopamine in the prevention of renal failure, rather than Renal Dose Dopamine in patients post-operatively with evidence of impending renal failure. Of note although their patients were high risk, none of them went into renal failure so the question of whether renal dose dopamine prevented renal failure was not answered with the same strength of evidence that the included papers did. Dr.Ozeren also illustrates the final strength of these topics. After each topic is checked by a second author and the journal club, the topic is posted on the internet at www.icvts.org prior to publication. If a reader knows of a paper that may contribute to the topic, this can easily be added by that reader, by posting a comment on the website for inclusion with the original article. Dr.Ozeren mentions the survey and review of 7 studies in critically ill neonates and children by
Prins et al, and this paper would certainly help clinicians working with neonates to answer their questions on the effectiveness of low dose dopamine for renoprotection.

BestBET topics are not systematic reviews but we believe that with our multi-stage checking process and sensitive and reproducible search strategies that we can quickly answer relevant clinical questions that we see in our daily practise and that the findings will be robust and reliable. The true strength however is that these topics can be written by everyone who has an interest in improving their clinical practise. So if you have a question that you want answering just read how to write a BET [1], sit down with Medline, get writing and send it to the ICVTS!

Reference