NICE advice

Desflurane for maintenance of anaesthesia

Evidence summary
Published: 26 March 2024

www.nice.org.uk/guidance/es41

Overall summary

This evidence review found no high quality evidence to suggest that desflurane has any significant therapeutic advantage over other general anaesthetic agents in 2 specified populations. Other commonly used anaesthetic agents have a significantly lower global warming potential than desflurane.

Product overview

The content of this evidence summary was up to date in August 2023. See summaries of product characteristics (SPCs), British National Formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites for up-to-date information.

Desflurane has a marketing authorisation for induction and maintenance of general anaesthesia for inpatient and outpatient surgery in adults, and for the maintenance of

anaesthesia in infants and children. It is administered by inhalation (see the desflurane SPCs).

During general anaesthesia, several different types of medicines are given together (including anaesthetics, opioids and neuromuscular blocking agents). Anaesthesia is usually induced with an intravenously administered anaesthetic (such as propofol), but an inhaled volatile anaesthetic (such as sevoflurane) is sometimes used. Anaesthesia is then maintained with an intravenous or inhaled anaesthetic (such as desflurane, isoflurane or sevoflurane). Total intravenous anaesthesia (TIVA) is a technique in which surgery or procedures are carried out with all anaesthetic drugs given intravenously (see the BNF treatment summary for anaesthesia).

Desflurane has a global warming potential 2,500 times greater than carbon dioxide, which is significantly higher than alternative volatile anaesthetic agents (Sherman et al. 2012). It is the first medicine to be decommissioned by the NHS in England because of global warming potential. The purpose of this evidence summary is to support the implementation of the national policy to stop routine use of desflurane in anaesthetic practice in the NHS in England by early 2024 (Greener NHS Putting anaesthetic emissions to bed: commitment on desflurane, 13 January 2023). The evidence summary will inform decision making and, if necessary, guidance development on any exceptional circumstances where continuing to use desflurane is acceptable to ensure patient outcomes are not compromised.

The evidence review summarises the best available evidence on the clinical and cost benefits of using desflurane for maintenance of anaesthesia compared with other general anaesthetic agents in:

- people having neurological procedures
- people with a body mass index (BMI) of at least 30 kg/m^2 having any procedure.

The scope of the evidence review was agreed by NHS England, the Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland. The 2 populations included within the scope of the review were identified by NHS England from extensive clinical engagement and consultation with experts. These 2 populations have been most frequently and consistently raised by anaesthetists within the NHS in England as cases where patient outcomes and use of NHS resources could possibly benefit from the use of desflurane over alternatives and, therefore, where an evidence review into the use of desflurane would be most beneficial.

Key messages

Neurological procedures

No evidence was identified to suggest that using desflurane instead of other general anaesthetic agents for maintenance of anaesthesia is associated with improved clinical or cost outcomes in people undergoing neurological procedures. Overall, results of the studies included in the evidence review did not favour 1 general anaesthetic over another.

Overall, 5 randomised controlled trials found no statistically significant differences between desflurane and other general anaesthetic agents for all but 1 of the outcome measures relevant to the population, intervention, comparator and outcomes (PICO) framework, which are core outcome measures for perioperative and anaesthetic care. The only statistically significant difference was in mean cognitive impairment scores (using the Montreal Cognitive Assessment Scale) at discharge or 2 weeks after surgery in 1 study. Mean scores were statistically significantly worse in the desflurane group than in the propofol group (p=0.013). However, the quality assessment raised concerns about this study, which failed to recruit sufficient participants and probably lacked statistical power to detect any true differences between the treatment groups.

The quality assessment also raised some concerns about 2 other studies, and analyses of secondary outcomes in all 4 of the other studies may lack statistical power to detect differences between the groups. This means the evidence is uncertain and we cannot exclude the possibility that clinically important differences may be seen in larger, sufficiently powered studies. The evidence is available for a limited number of neurological procedures only, which may limit their applicability more widely (such as in extremely long duration surgeries).

BMI at least 30 kg/m^2 having any procedure

No evidence was identified to suggest that using desflurane instead of other general anaesthetic agents for maintenance of anaesthesia is associated with improved clinical or cost outcomes in people with a BMI of at least 30 kg/m^2 having any procedure. Overall, results of the studies included in the evidence review did not favour 1 general anaesthetic over another.

Overall, 2 randomised controlled trials and 1 large retrospective cohort study found no

statistically significant differences between desflurane and other general anaesthetic agents for outcome measures relevant to the PICO. The quality assessment raised some concerns about 1 randomised controlled trial, which lacked statistical power for all outcomes, and the other was considered to be at high risk of bias. The cohort study was assessed as being good quality but is an observational study with many inherent limitations. In all studies, secondary outcomes may lack statistical power to detect differences between the groups meaning the evidence is uncertain and we cannot exclude the possibility that clinically important differences may be seen in larger, sufficiently powered studies.

Factors for decision making: neurological procedures

Five randomised controlled trials that assessed desflurane for neurological procedures are included in this evidence review. Three studies compared desflurane inhalation and propofol infusion in adults undergoing aneurysmal neck clipping after subarachnoid haemorrhage (Bhagat et al. 2021, Bhardwaj et al. 2018 and Sharma et al. 2020). The other 2 studies compared inhaled anaesthetics. Dube et al. (2015) compared desflurane and sevoflurane in adults undergoing elective craniotomy for supratentorial lesions. Joys et al. (2019) compared desflurane and isoflurane in adults undergoing spine surgery.

Mortality or survival

Mortality was not reported in any of the papers on neurological procedures included in the evidence review.

Perioperative complications

Bhardwaj et al. (2018) found no statistically significant differences between desflurane and propofol in the incidence of vasospasm, infarct, tracheostomy, decompressive craniectomy or new onset neurological deficit at 24 hours. In Joys et al. (2019), there were no statistically significant differences between desflurane and isoflurane in the incidence or severity of postoperative delirium on day 1 or day 3.

Resource use

No studies reporting resource use in terms of monetary costs were identified. Studies by Bhagat et al. (2021) and Bhardwaj et al. (2018) found no statistically significant differences between desflurane and propofol in length of hospital stay. Similarly, Dube et al. (2015) found no statistically significant differences between desflurane and sevoflurane in length of hospital or intensive care unit stays.

Short-term recovery

At discharge, Bhagat et al. (2021), Bhardwaj et al. (2018) and Dube et al. (2015) found no statistically significant differences in the degree of disability or dependence on others for help with daily activities. Bhardwaj et al. (2018) also found that similar proportions of people in the desflurane and propofol groups had a good outcome, with no or only slight disability or dependence.

Sharma et al. (2020) found no statistically significant difference between desflurane and propofol in the proportion of people with cognitive impairment (defined as a score of less than 26 on the Montreal Cognitive Assessment Scale, a 30-point scale, with lower scores indicating a higher degree of cognitive impairment) at discharge or 2 weeks after surgery (81.6% compared with 65.4% respectively, $p>0.05$). By contrast, the mean cognitive impairment score was statistically significantly worse in the desflurane group than the propofol group at the same timepoint (19.09 compared with 22.81 respectively, $p=0.013$). It is unclear if the difference is clinically significant.

Longer-term recovery

Bhagat et al. (2021) found that, 3 months after discharge, there were no statistically significant differences between desflurane and propofol in 3 different measures of disability and dependence.

Limitations of the evidence

Four of the 5 randomised controlled trials that assessed desflurane for neurological procedures were generally well-designed and reported, but Sharma et al. (2020) failed to recruit sufficient participants and probably lacked statistical power. All studies were undertaken in India, which may limit their generalisability to the UK because of differences

in, for example, ethnicity and genetics, socio-economic factors, healthcare systems and clinical practice. The generalisability of the results may also be limited for people undergoing some types of neurosurgery; for example, surgeries that last much longer than those in the studies. One of the studies compared desflurane with isoflurane, which specialist reviewers advised is not widely used in the UK. This means this study may have limited applicability to wider UK practice.

Two of the studies were considered to be at low risk of bias (Bhardwaj et al. 2018 and Joys et al. 2019), but there were some concerns over the other 3 (Bhagat et al. 2021, Dube et al. 2015 and Sharma et al. 2020). All 5 studies were small, with results analysed for between 49 and 91 participants only, divided across 2 groups. Therefore, some analyses may lack statistical power, particularly secondary outcomes in all the studies and all outcomes in Sharma et al. (2020), which means that this evidence is uncertain and we cannot exclude the possibility that clinically important differences may be seen in larger, sufficiently powered studies. Nevertheless, point estimates did not consistently favour 1 general anaesthetic over another.

Participants in all 5 studies were aged between 18 years and 60 or 65 years and were assessed as being relatively healthy, fully responsive with only minor brain injury, or at low risk of mortality. The results of the studies may not be applicable to children or older adults, or people with poor health status, severe brain injury or at higher risk of mortality.

In Bhagat et al. (2021), around 10% of people in each group were lost to follow up. Although the proportions were balanced across the groups, no reasons are reported so it is unclear if outcomes such as mortality were similar in the groups.

Blinding was generally adequate in the studies. However, only the neurosurgeons who measured intracranial pressure were blinded in Dube et al. (2015), and assessors for the outcomes relevant to the PICO were not blinded. This may be a source of bias in this study, but the relevant outcomes are reasonably objective.

In Sharma et al. (2020), the sample size was estimated based on the mean difference in cerebral metabolic rate with propofol compared with desflurane; however, cerebral metabolic rate was not reported in the study, suggesting the study was not powered correctly. Also, a large proportion of people were excluded from the study after randomisation, which was not addressed sufficiently in the sample size calculation.

Factors for decision making: BMI at least 30 kg/m^2 having any procedure

Three studies that assessed desflurane in people with a BMI of at least 30 kg/m^2 having any type of procedure are included in this evidence review. One study is a randomised controlled trial (Tanaka et al. 2017), another is a sub-study of a randomised controlled trial (Aftab et al. 2019a), and the other is a retrospective cohort study (Zucco et al. 2021).

The study by Aftab et al. (2019a) compared desflurane and propofol infusion in adults with a BMI of at least 35 kg/m^2 who had laparoscopic gastric sleeve resection. Tanaka et al. (2017) compared desflurane and propofol infusion in adults aged over 65 years with a BMI over 30 kg/m^2 who had total knee replacement. BMI was not an inclusion criterion in Zucco et al. (2021), which compared desflurane and sevoflurane in adults who had any type of surgery (except cardiac surgery). However, various analyses were undertaken to control for confounding factors, including BMI of at least 35 kg/m^2 (around 9% of the study population).

Mortality or survival

Mortality was not reported in any of the papers on surgical procedures in people with a BMI of at least 30 kg/m^2 included in the evidence review.

Perioperative complications

Aftab et al. (2019a) found no significant difference between desflurane and propofol in the incidence of postoperative complications.

In Zucco et al. (2021), there was no statistically significant difference between desflurane and sevoflurane in the incidence of postoperative respiratory complications in either the entire study population or the subgroup of people with a BMI of at least 35 kg/m^2.

Up to 48 hours after surgery, the study by Tanaka et al. (2017) found no statistically significant difference in the incidence of postoperative delirium between desflurane and propofol.

Resource use

No studies reporting resource use in terms of monetary costs were identified. In the study by Aftab et al. (2019a), a similar number of people in the desflurane and propofol groups were discharged the same day as surgery (no statistically significant difference).

Short-term recovery

Tanaka et al. (2017) found no statistically significant differences between desflurane and propofol in 4 measures of cognitive function assessed 48 hours after surgery.

Longer-term recovery

Longer-term recovery was not reported in the papers on procedures in people with a BMI of at least 30 kg/m^2 included in this evidence review.

Limitations of the evidence

The quality assessment raised some concerns over the randomised controlled trial by Tanaka et al. (2017), and the randomised controlled trial by Aftab et al. (2019a) was considered to be at high risk of bias.

The sub-study included in this evidence review (Aftab et al. 2019a) included only 92% of participants who had sleeve gastrectomy in the original randomised controlled trial by Aftab et al. (2019b). No reasons for this are reported in the paper. There was also a difference in the proportions of missing outcome data in the desflurane and propofol groups. It is unclear whether the omissions and imbalance may have affected the results of the study.

The randomised controlled trials were small, with results analysed for around 90 participants only, divided across 2 groups. Therefore, some analyses, particularly for secondary outcomes, may lack statistical power to detect differences between the groups. This means that the evidence on the relative effects of the anaesthetic agents is uncertain. In particular, Tanaka et al. (2017) note that their study may have been underpowered to detect a difference between desflurane and propofol. This means we cannot exclude the possibility that clinically important differences may be seen in larger, sufficiently powered studies. Nevertheless, point estimates did not consistently favour

1 general anaesthetic over another.

The third study was a large retrospective cohort study (Zucco et al. 2021) in 108,438 participants. Observational studies such as cohort studies are subject to bias and confounding and cannot prove that an intervention caused an outcome, only that it is associated with that outcome. Nevertheless, the quality assessment found the study to be of good quality for a non-randomised study.

Two of the studies were undertaken in the USA and 1 in Norway. Their results are probably generalisable to the UK, although all were undertaken in single centres only and ethnicity, which can affect generalisability, was not reported. The studies included adults who were assessed as having mild or severe systemic disease. The results of the studies may not be applicable to children or adults with a worse health status at higher risk of mortality.

See the full evidence review for more information.

Evidence review commissioned by NHS England.

ISBN: 978-1-4731-5739-2