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RESEARCH ARTICLE

PAIN MANAGEMENT WITH PENTHROX INHALER IN PREHOSPITAL CARE:LITERATURE REVIEW

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Key words:-
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Abstract

Introduction: Traumas that give symptoms of severe pains could lead to stress induced pain if not given an immediate pain relief. Penthroxinhaler an immediate pain reliever, can be given in pre-hospital services by ambulance officers (paramedics or ambulance nurses). Penthroxinhaler is a low-dose Methoxyflurane single-use inhaler, and has been used for more than 40 years in the medical field in managing trauma pain.
Aim: The purpose of this study was to explore the original research related to the prospects of trauma pain management with Penthrox Inhaler, the benefits of using Penthrox inhaler in pre-hospital trauma pain management, and to identify the side effects from using Penthrox Inhaler based on researches published in international journals.
Method: The method used in this literature review is the PICO method a type of systematic literature review. Problem/patient: Severe pain. Intervention: Penthrox Inhaler, Comparison: none. Outcome: Pain relief, *Keyword : Pain relief.*
Result: The administration of Low Dose Methoxyflurane in cases of trauma pain showed a very significant effect.GivingLow Dose Methoxyflurane was given faster to the patientcompared to other drugs. With the provision of LDM, the pain reduction was with a VAS value, which stated very satisfying by 42.8% and satisfying 67.3%. The side effects of using gas drugs are generally seen, whether it causes neprotoxicity and the level of tolerability by the patient himself.Before giving Methoxyflurane to patients, must ensure that the oxygen saturation level is above 90% and the maximum dosage given must be 6 ml in the span of 2 hours to reduce side effects.Ambulance officers can be safe with an exposure time of 8 hours while administering Penthrox to patients.

Introduction:-

Trafic accident, industrial accident, and domestic accident, may cause severe traumatic pain, the evaluation of pain uses a pain scale, where the commonly used pain scale ranges from 1 to 10 a scale of one indicates free from pain while a scale of ten indicates severe pain, trauma cases with complaints of pain must be evaluated for acuity level using the Visual Analogue Scale(Martin et al., 2018).

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Severe pain not addressed immediately can induce stress, increased the concentration of catecholamine, vasoconstriction, impaired tissue perfusion, tissue of oxygen pressure, hyperglycemia, lipolysis, protein catabolism, disrupted in the wound healing process, risk of wound infection, disturbance in the immune system, disruption of sodium and potassium activities in cells, decrease in cytotoxic T lymphocyte and reduced phagocytes activities (Kotfis et al., 2017).

Penthrox inhaler containing Methoxyflurane which serves asa non-narcotic analgesic effect and can easily be given through inhalation, single-use inhalermaygivenimmedeatlyin pre-hospital services by ambulance officers for relief a severe of trauma painand has been of use for more than 40 years in cases of pain management in Australia and New Zealand(Porter et al., 2018).

Since 1915the Authorities in the UK, allowed to use the methoxyflurane in ambulance services in handling cases of moderate to severe pain in cases of trauma or injury (Forrest et al., 2019), and Methoxyflurane is wide used in other mainland of Europe(Fabbri et al., 2019).

Methoxyflurane is a type of fluorinated hydrocarbon anesthetic, first produced by the company Abbott Laboratories under the trade name Penthrane in the early 1960s,
Since 1970 the company About Laboratories developed Methoxyflurane in the form of a single-use inhaler package, and it can be used independently by patients for pain relief,especially in cases of minor and obstetric surgery(Porter et al., 2018).

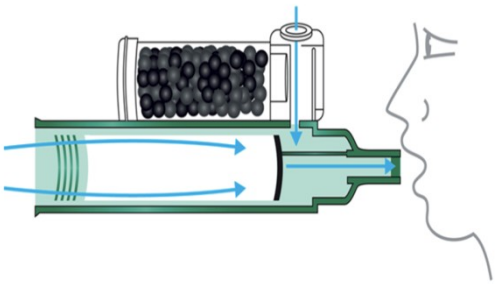
Low-dose methoxyflurane has been approved by the authorities in Canada, for use in cases of severe acute pain associated with trauma an also for carrying out medical procedures in conscious patients(Campbell et al., 2020).

Methoxyfluraneis a nonnarcoticanelgesic drug, common used for relief severe pain due to injury of musculoskeletal trauma(Kenworthy et al., 2018).Penthorx inhaler is easy to use for handling pain cases in the Ambulance Helicopter service and very helpful in the process of handling pain quickly. Patients will get maximal 2 times 3 ml of Methoxyflurane can be done by the patient himself under medical supervision (Marinangeli et al., 2018).

*Picture 1*shows the Penthrox Inhaler. Penthrox inhaler contains 3 ml Methoxyflurane substances, which is inserted into the cavity of the inhaler tube, and then rotated around before inhaled through the mouth by the patient(Crankshaw, 2015).

Picture 1:- Penthrox Inhaler Unit.

*Picture 2*describes how the Penthrox Inhaler works, where after the Penthrox drug is put into the suction tube, the air that is sucked in from the outside will push the penthrox substance into the respiratory tract, the respiratory tract then absorbs the Methoxyflurane quickly.



Picture 2:- Workflow Penthrox Inhaler.

Although Low-dose Penthrox Inhaler (3 ml) can be simply given, it also quickly reduces pain compared to the administration of analsegic drugs by injection (Mercadante et al., 2019).Penthrox Inhaler inhalation gives a faster effect on pain reduction compared to Tramadol injection, Tramadol is an analgesic drug that is given by injection into the intramuscular(Lim et al., 2020).

Aimof The Research
The purpose of this study was to explore the original research related of prospect of trauma pain management with Penthrox Inhaler, what are the benefits of using Penthrox inhaler in pre-hospital trauma pain management, and to identify the side effects of using Penthrox Inhaler based on research published in international journals.

Research Methods:-

PICO Method is used to identify of the Pain management with Penthrox Inhaler, in pre-hospital care.

Problem/patient:
Severe pain.*Keyword: Pain OR trauma AND prehopital*

Intervention:
Penthrox Inhaler, *Keyword: Penthrox inhaler OR Methoxyflurane*

Comparison:-
Outcome:
Pain relief, *Keyword :Pain relief*

Research question:
1. How is Traumatic pain managed with Penthrox Inhaler?
2. What are the Benefits of Penthrox Inhaler in the management of trauma pain ?
3. What are the Side effects of Penthrox Inhaler in the management of trauma pain?
4. How is the Penthrox Inhaler Level of the Ambulance Staff when administering Penthrox, is it safe?

Literature Research:-

The literature search was carried out by identifying all types of international articles that are related to pain management with Penthrox inhalation in the pre-hospital care. The electronic database used is the Penthrox Inhaler based on research that has been published in international journals such as PubMed, Wiley, Springer, and Google Scholar with the search strategy usingthe PICO method (patient, intervention, comparison and outcome)(Smith & Noble, 2016).

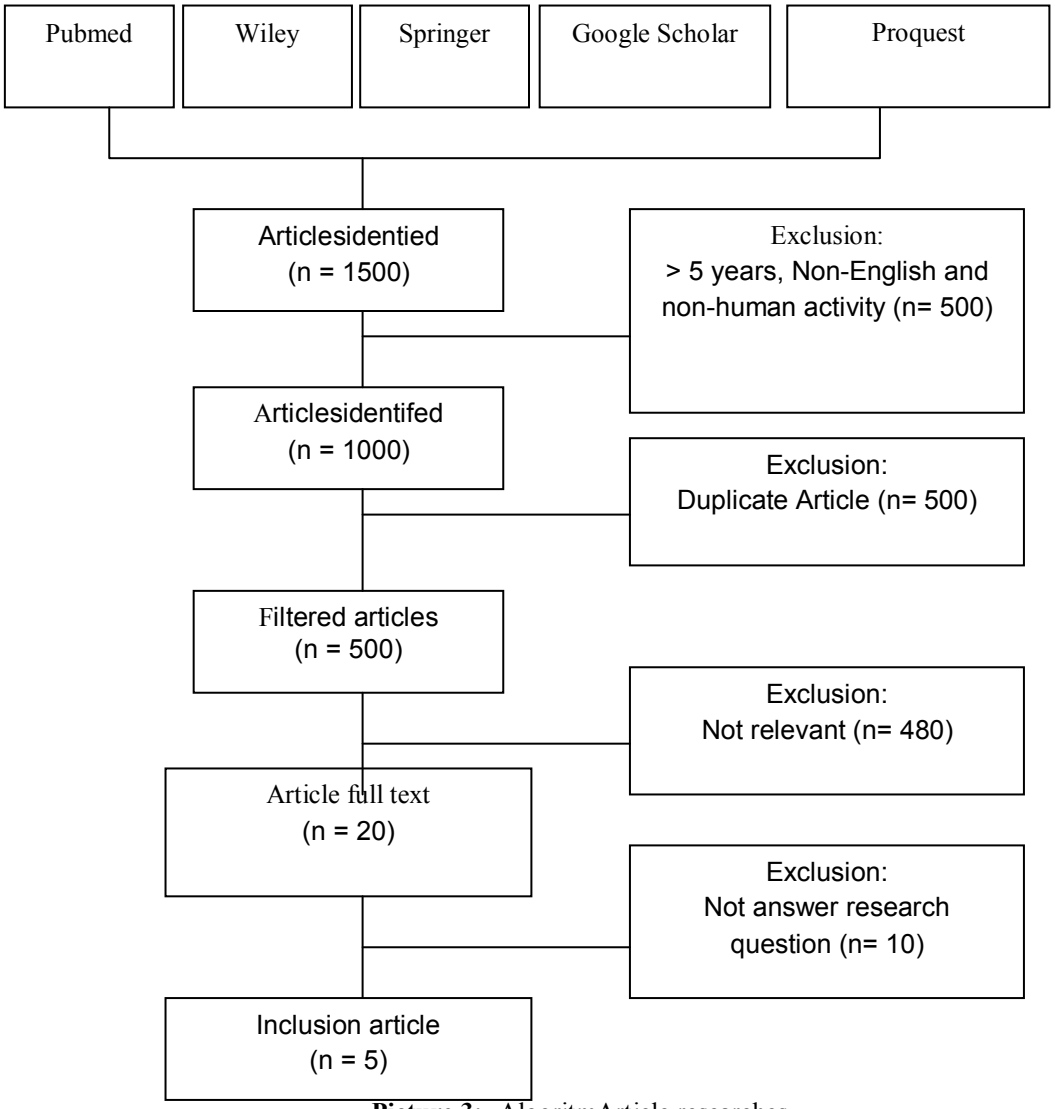
Key word
The keywords used in the literature searches are a combination of keywords that are as follows:pain, trauma, penthroxinhaler,Methoxyfluraneandprehospital. Literature search limitation from 2015 up to 2019,as well as manually selecting articles that are relevant and according to the research question(*picture 3*).

Inclusion Critera

The article inclusion criteria were: (1) Participants were adult cases with pain in trauma at the pre-hospital service, (2) The intervention used was Penthrox inhalation, (3) the results of the study showed the effect of reducing pain in trauma cases.

Exclusion criteria

The articles exclusion criteria are as follows: articles that are less than 5 years, Non-English articles, non-human activity, duplicate articles, non-relevant articles, and articles that don't answer research questions.



Picture 3:- AlgoritmArticle researches.

Evaluation Quality of Article research

Tabel 1:- Result of Literature Reviews.

No	Author	Name Journal Vol, No, Year	Title	Metode	Result
1	Patrick D. Dißmann, Maxime Maignan, Paul D. Cloves, Blanca Gutierrez Parres, Sara Dickerson, Alice Eberhardt.	Pain Ther (2018) 7:179–192 doi.org/10.1007/s40122-018-0101-1	*A Review of the Burden of Trauma Pain in EmergencySettings in Europe*	A literature review of pain management in prehospital and ED in Europe.	ER: Mild to moderate pain, treated with Paracetamol and / or NSAIDs, N2O inhalation, Metamizole (dipyrone) inj, codeine and tramadol. Severe pain is treated with Fentanyl inj, oxycodone inj or Ketamine inj. Ambulance paramedics: only use LDM in pain management, and are not allowed to use injectable drugs. Failure to assess pain acuity leads to delays in pain management.
2	John Frangos, Anissa Belbachir, Sandrine Dautheville, Christiane Jung, Key Herklotz, Freya Amon, Sara Dickerson, BerangereChomier.	BMJ Open (2020);10:e034647. doi:10.1136/bmjopen-2019-034647	*Non-interventional study evaluating exposure to inhaled, low-dose ethoxyflurane experienced by hospital emergency department personnel in France*	Non-Interventional Study. Evaluation of exposure to inhalation of LDM by a nurse-supervised patient in the French emergency department for the next 2 weeks and 3 weeks.	The results of observations on 138 cases of trauma pain given by Penthrox inhaler, showed that the concentration of Penthrox exposure to officers was a median value of 8 hours: 0.017 (0.008, 0.736) ppm, the maximum LDM exposure level was 15 ppm / 8 hours.
3	Keith M Porter, Anthony D Dayan, Sara Dickerson, Paul M Middleton	Open Access Emergency Medicine (2019) Https://www.dovepress.com 165.215.209.15 25-May-2019	*The role of inhaled methoxyflurane in acute painmanagement*	Literaturreviuw	Methoxyflurane in cases of trauma and other medical measures, is very effective in reducing pain levels, good tolerance, is widely used as an analgesia. Low-dose methoxyflurane has good safety, minimal side effects, does not interfere with vital signs and level of consciousness. No nephrotoxicitas were found.
No	**Author**	**Name Journal**	**Title**	**Metode**	**Result**

		Vol, No, Year			
4	Andrew D Xia, Sara L Dickerson, Andrew Watson, Mika Nokela, Sam Colman, AgotaSzende	Open Access Emergency Medicine (2019):11 229–240	*Evaluation of pain relief treatment and timelines inemergency care in six European countries and Australia*	Observational of the medical records of patients who entered the ER with cases of musculoskeletal trauma and administered analgesics with LDM. Looking at the speed of Paramedics compared to ER officers in pain management.	Pain management in Europe was longer than that in Australia (mean [SD] 38.1 [34.7] vs 29.9 [35.5] mins; P = 0.0017). Australia was faster in administering LDM compared to other analgesic drugs in the management of pain cases than European countries: (propensity score matched [n = 85] per group: 21.7 [24.2] vs 39.1 [43.0] mins; P = 0.0013). Paramedics decided to administer LDM more quickly than hospital emergency staff (15.7 [14.7] vs 49.1 [38.4] mins).
5	Antonio Voza, GermanaRuggiano, Sossio Serra, Giuseppe Carpinteri, GianfilippoGangitano, Fabio Intelligente, Elisabetta Bonafede, Antonella Sblendido, Alberto Farina, Amedeo Soldi, Andrea Fabbri		*Inhaled Methoxyflurane versus Intravenous Morphine for Severe Trauma Pain in the Emergency Setting: Subgroup Analysis of MEDITA, a Multicenter, Randomized, Controlled, Open-Label Trial*	Investigate the efficiency and safety of using LDM compared to injecting morphine in severe cases of trauma pain.	Pain decreased 10 minutes after LDM administration compared with morphine inj (adjusted mean treatment difference: −5.54mm; 95% CI: −10.49, −0.59mm; p = 0.029). Patients said “Excellent” or “Very good” to doctors more with LDM (42.8% to 7.3%) than those with morphine inj (18.1% to 22.8%). Non-serious side effects of using LDM were 20.4%, whereas with morphine inj 4.8%.

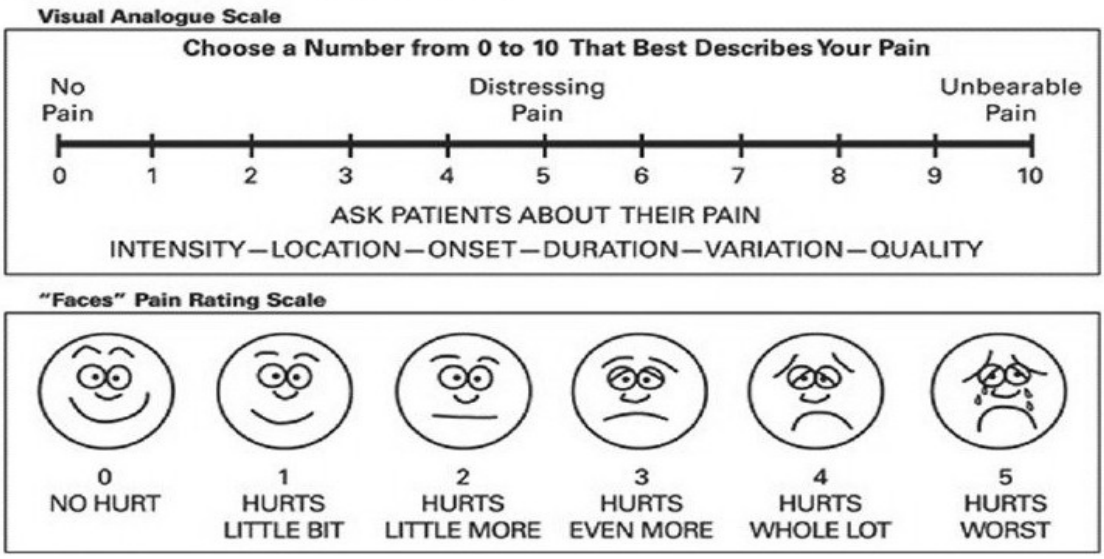
Result and Disccusion: -

Pain management with Penthrox Inhaler

A common problem in pain management in the emergency department and pre-hospital is the difficulty in injecting patients, especially in intravenous administration or patients who do not want to take oral medications because of nausea and vomiting. Failure to put the infusion in the ambulance can affect the delay in handling trauma pain, as well as the limited authority of ambulance officers to administer pain medication injections, penthrox inhaler is the choice of ambulance officers in handling trauma pain(Dißmann et al., 2018).Penthroxinhaleris an anesthetic drug as a trademark of Methoxyflurane, which has been used for more than 40 years in Australia in the management of traumatic pain, both in the pre-hospital and in the emergency department(Porter et al., 2018). Methoxyflurane is a fluorinated hydrocarbon anesthetic, where Penthtrox inhaler contains 3 ml per unit package or in terms of the low dose drug Methoxyflurane that can be used up to 6 ml in the treatment of trauma pain, when inhaled for 25-30 minutes, can provide analgesic effect(Porter et al., 2018). Penthrox inhaler is an alternative treatment for trauma pain and in minor surgical procedures or other medical procedures for both adults and children to treat pain due to the procedure(Porter et al., 2018).

Benefit of PenthroxInhaler

The administration of Low Dose Methoxyflurane in cases of trauma pain showed a very significant effect, seen from the length of pain relief (mean 38.1 minutes with SD 34.7 minutes) compared to other analgesic drugs (mean 29.9 minutes with a SD 35.5 minute)(Xia et al., 2019).Giving Low Dose Methoxyflurane was given faster to the patient (mean 21.7 minutes with a SD 24.2 minutes) compared to other drugs (mean 39.2 with SD 43 minutes)(Xia et al., 2019).Traumatic pain was measured using the VAS (Visual analogue Scale) model, figure 4 is a form of VAS that is often used in the emergency department to measure the quality of pain levels(Karcioglu et al., 2018). With the provision of LDM, the pain reduction was with a VAS value, which stated very satisfying by 42.8% and satisfying 67.3%, while the VAS level with the administration of morphine injection showed very satisfying by 18.1% and a satisfactory level of 22. 8%(Voza et al., 2020).



Gambar 3:- Visual Analogue Scale.

Side effect of Penthrox Inhaler

The side effects of using gas drugs are generally seen, whether it causes neprotoxicity and the level of tolerability by the patient himself. Neprotoxicity occurs, depending on how long the drug is given and at what dose. The safe dose for using Pentrox inhaler is 3 ml, and can be repeated for 0.3 hours, the results show that the fluoride level in the serum is 4.7 micro mol/l, while the blood level is between 0.006-0.026 micro mol/l(Porter et al., 2018). The maximum point for safe use of Penthrox inhaler is a maximum of 2 hours (serum level 50 micro mol/l), if given between 2.5 - 3 hours will cause sub-clinical symptoms of toxicity, and toxic levels occur when given more than 5 hours (serum level 90 micro mol/l)(Porter et al., 2018).The level of tolerability of drug use can be expressed by patients in the form of side effects. Side effects occurred when 3 ml of Penthrox inhaler was given with oxygen saturation less than 90%, some patients complained of mild headache and mild somnolence. Some patients complain of the smell of rotten fruit(Porter et al., 2018). 18.1% complained of nausea, euphoria, lightheadedness, hallucinations, dry throat, and paresthesia on the lips. Complaints in children after being given Penthrox inhaler, 25.7% experienced drowsiness and 6.7% experienced mild hallucinations(Porter et al., 2018).It can be concluded that giving Methoxyflurane to patients, must ensure the oxygen saturation level is above 90%, the maximum dose is 6 ml, can be given for 2 hours to reduce side effects.

Penthrox Inhaler Exposure Level to the Ambulance Staff

Every use of a drug in the form of gas, can undeniably give negative exposure to the officer who gave it. The results of observations of giving Penthrox inhaler in 8 hours in a room without cold air conditioning showed that methoxyflurane gas exposure was 0.23 PPM while in a closed room, exposure to Methoxyflurane gas showed 1.5 PPM, the median of 0.017 (0.008-0.736) PPM, the maximum exposure limit the Methoxyflurane gas is 15 PPM. It can be concluded that giving Methoxyflurane during working hours,specifically 8 hours a day, is safe for use by ambulance officers in the handling of cases of trauma pain(Frangos et al., 2020).

Conclusion:-

Common problems and difficulties in pain management in the emergency department and pre-hospital can be resolved easily and quickly by administering Penthrox inhalers compared to giving the patient injection, especially during intravenous administration or when the patient does not want to take oral medication. Penthrox inhaler when inhaled for 25-30 minutes, can provide an analgesic effect on traumatic pain, and provide a fast pain management effect and a longer analgesic effect compared to other methods of pain relief.Penthrox inhaler which contains a dose of 3 ml per package, is safe to use and can be administered by ambulance officers. Before administering the use of Penthrox inhaler, the oxygen saturation of the patients must be above 90% to reduce any possible side effects. The maximum dose of Penthrox inhaler for cases of trauma pain is 6 ml given for 2 hours. Penthrox inhaler does not expose the ambulance officers to lethal levels of exposure limit for Methoxyflurane gas when administering for 8 working hours to the patient.

Suggestion:-

It is recommended that the authorities, namely the Ministry of Health and the Food and Drug Supervisory Agency, to conduct a clinical study of the use of Pentrox inhalers for patients of Asian ethnicity, especially Indonesians and give special permission to ambulance officers (paramedics or ambulance nurses) to use Pentrox inhalers in handling trauma pain cases, without a doctor's prescription.

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