

A Review On: Mucosal Atomization Device

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Abstract- Transmucosal nasal shipping is a promising drug shipping choice wherein common drug administrations (e.g., intravenous, intramuscular, or oral) are inapplicable. Recently, it's been proven that many tablets have higher bioavailability via way of means of nasal course than via way of means of oral course. This has been attributed to wealthy vasculature and a highly permeable shape of the nasal mucosa coupled with avoidance of hepatic first-pass elimination, intestine wall metabolism and/or destruction within the gastrointestinal tract. The purpose of this take a look at became to decide the effect of long-time period topical budesonide remedy thru the mucosal atomization device (MAD) at the hypothalamic-pituitary-adrenal axis (HPAA) and intraocular pressure (IOP). The Mucosal Atomization Device (MAD) distributes medicinal drug during the paranasal sinuses for sufferers with continual rhinosinusitis (CRS). Determining the premiere head position is vital to make sure maximal shipping of medicine to the sinus cavities. The goal of this painting became to decide the impact of the lying-head-back (LHB) and head-down forward (HDF) position, at the distribution of topical nasal medicinal drug thru MAD in cadaver specimens.

Keywords- Mucosal atomization devices,

I. INTRODUCTION

The Intranasal Mucosal Atomization Device (MAD) is an adapter that may be connected to a luer lock syringe to show liquid remedy into an atomized mist for intranasal transport of the drug. The era is much like Afrin and different nasal sprays. In veterinary medicinal drug the intranasal MAD may be used for in-health center or at-domestic transport of emergency medicinal drugs whilst IV get entry to isn't to be had. It would basically be used for at-domestic emergency transport of midazolam or diazepam during a seizure. The tool will also be used with saline for animals with very dry nasal passages, with DDA¹. Transmucosal routes of drug transport (i.e., the mucosal linings of the nasal, rectal, vagina, ocular and oral hollow space) provide wonderful blessings over peroral management for systemic drug transport. These blessings consists of possible pass of the primary bypass impact, avoidance of presystemic removal of gastrointestinal tract and relying at the unique drug. The nasal hollow space as a domain for neighborhood and systemic drug transport has been investigated with the aid of using many studies groups 1-

4 and the direction has already reached business popularity with numerous tablets including calcitonin^{5, 6}. However, the capability infection and irreversible harm to the ciliary movement software of nasal dosage forms, in addition to the huge intra and inter subject variability in mucus secretion within the nasal mucosa may want to substantially impact drug absorption from this site. Seizures are a not unusual place trouble in veterinary medicinal drug, affecting an envisioned 0.5–5.7% of all puppies, and comprising a great percentage of sufferers provided to each preferred and referral veterinary practices (Cunningham & Farnbach, 1988). Despite suitable anticonvulsant therapy, about 20–30% of canine epileptics continue to be poorly managed with presently to be had clinical therapy, and lots of those puppies expand repeat episodes of cluster seizures and popularity epilepticus (Farnbach, 1984; Schwartz-Porsche et al., 1985; Lane & Bunch, 1990; Podell, 1996). These situations may have excessive damaging scientific consequences including hyperthermia, metabolic acidosis, muscle necrosis, noncardiogenic pulmonary edema, aspiration pneumonia, renal failure, cerebral edema, neuronal necrosis, and death, and consequently represent a real clinical emergency. The emotional and economic toll of routine emergency hospitalization reasons many proprietors to elect euthanasia for those sufferers. Emergent remedy for seizures is normally initiated with intravenous (i.v.) management of a benzodiazepine drug, usually diazepam. Diazepam is fantastically lipid soluble, and movements unexpectedly throughout the blood–brain barrier into the apprehensive device to acquire its scientific effect. It is unexpectedly metabolized, predominantly with the aid of using the liver, to the fundamental metabolites desmethyl diazepam (nordiazepam) and oxazepam. These metabolites have among 20% and 50% of the hobby of diazepam itself (Randall et al., 1965; Frey & Loscher, 1982; Boothe, 1998). Although i.v. benzodiazepines often offer a fast and powerful scientific response, acquiring i.v. get right of entry to may be technically tough in a affected person with ongoing seizure hobby, hence delaying the time to drug management or stopping transport entirely. Rectal management of possible, which include in actively seizing sufferers and for at-domestic use in puppies with cluster seizures. Although this path may be powerful (Podell, 1995), rectal management may be inconvenient and ugly for owners, can bring about faulty transport or expulsion of the drug, and can bring about unpredictable systemic absorption (Mealey & Boothe, 1995). In addition, the presence

of feces within the rectum can impair accurate transport. In people, one gain of rectal management is to skip hepatic first-pass metabolism, generating excessive systemic concentrations, due to the fact venous drainage from the distal rectum flows to the vena cava in place of the portal vein. However, this isn't always a bonus in puppies. Importantly, venous drainage of the rectum of puppies dictates that almost all of rectally administered drug could be absorbed into the portal circulation, and go through first-pass hepatic metabolism. As a result, concentrations of the drug in the systemic stream can be very low, which precludes these of this direction for a few medicinal drugs (Podell et al., 1998; Barnhart et al., 2000). For diazepam, scientific effectiveness turns into depending on its much less-lively metabolites (Papich & Alcorn, 1995). In addition, animals receiving hepatic enzyme inducing medicinal drugs along with phenobarbital may have upregulated metabolism of diazepam, necessitating better doses to acquire the supposed scientific effect (Wagner et al., 1998). Intranasal (i.n.) management is an alternative direction for anticonvulsant drug remedy that circumvents a number of the barriers of i.v. and rectal drug management. Intranasal management is simple, effortlessly finished through individuals with out scientific training, and is much less awkward than rectal transport for lots of owners. The dense vascular plexus of the nasal mucosa permits for speedy absorption of drug into the systemic stream, with avoidance of first-pass hepatic metabolism (Harris et al., 1986; Jones et al., 1997). In addition, there may be great proof that a few compounds, along with antimigraine drugs, morphine and proteins/peptides such as nerve boom component, and vascular endothelial boom component absorbed via the olfactory mucosa can also additionally bypass immediately into the vital fearful gadget after i.n. transport (Rapoport & Winner, 2006; Westin et al., 2006; Hanson & Frey, 2007; Yang et al., 2009). Higher drug concentrations had been located in the cerebrospinal fluid compared with blood after intranasal transport of midazolam in preceding dog studies (Henry et al., 1998). Physiochemical drug houses such as lipophilicity and occasional molecular weight had been proven to facilitate each systemic and direct vital fearful gadget absorption after intranasal management of a lot of these drugs (Costantino et al., 2007). Intranasal management of medicinal drugs has been substantially documented within the human scientific literature for a number of indications such as the avoidance of needles, preanesthetic sedation in children, remedy of acute pain, and for the emergent transport of anticonvulsant and antimigraine medicinal drugs (Jones et al., 1997; Wolfe & Bernstone, 2004; Barton et al., 2005; Rapoport & Winner, 2006; Wermeling, 2009). Because intravenous management of diazepam isn't always usually possible and rectal management is related to tremendous barriers in dog patients, this take a look at changed into performed to assess the i.n. direction as

an greatest alternative. Absorption of i.n. diazepam in puppies after nasal drop management changed into formerly verified through Platt et al. (2000). However, the conclusions of that take a look at had been restricted due to the fact the benzodiazepines had been analyzed with a semi-quantitative fluorescence polarization immunoassay (FPIA) approach that couldn't correctly quantify diazepam. We hypothesized that i.n. management of diazepam with a mucosal atomization device could bring about advanced absorption and better blood ranges of the drug when as in comparison with a nasal drop approach. To correctly quantify diazepam plus the two predominant metabolites (desmethyldiazepam and oxazepam), certainly considered one among our particular changed into to apply a touchy and particular high-overall performance liquid chromatography (HPLC) assay, which could permit correct dedication of the pharmacokinetics of the stronger discern drug in addition to its lively metabolites¹⁴.

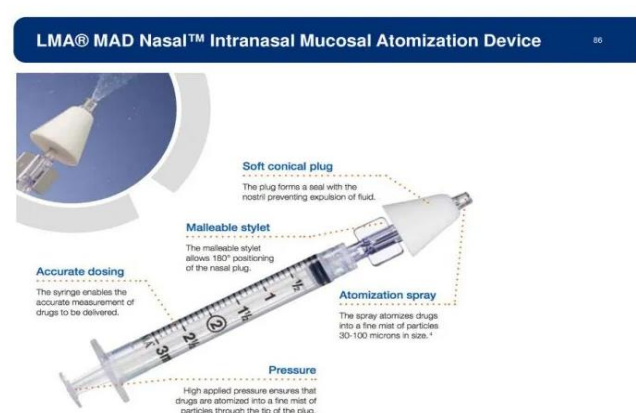


FIG. MUCOSAL ATOMIZATION DEVICE

Mucosal atomization tool (MAD) training to be greater tolerable. The MAD has been proven to very well distribute topical medicinal drug to the sinuses in cadaver fashions and correctly deal with sinus sickness in scientific studies. 5–7 Unfortunately, the equal best this is idea to make the MAD efficacious within the remedy of mucosal infection (ie, droplet distribution and retention) eight may additionally growth the potential for systemic aspect effects. Although the protection profile of well-known topical nasal corticosteroid sprays (INCs) has been properly established, 9, 10 the off-label use of budesonide respules for topical remedy of sinonasal infection has occupied a grey region within the past. A randomized, managed trial from our middle demonstrated short-term (60 days) protection of budesonide added through each the MAD and INSI. This tool is fine because it produces a nice mist, growing the potential touch floor region within the nasal hollow space and paranasal sinuses. Clinicians enjoy has located that sufferers administering medicinal drug within the lying-

head-backrole (LHB) can correctly deal with the edematous mucosa of the ethmoid roof and frontal sinus recess. Patients are mechanically told to lie supine and grasp their heads over the threshold in their mattress to quality simulate this role. Our goal become to decide if the LHB role accelerated medicinal drug dispersal inside sinonasal cavities as compared to the HDF role in a human cadaver model.

REASON FOR DEVELOPMENT OF NASAL DELIVERY

Nasal drug shipping is a beneficial shipping approach for capsules which might be energetic in low doses and display no or minimum oral bioavailability. The nasal path circumvent the hepatic first pass by skip removal related to the oral shipping: it's far without problems accessible and appropriate for self-medication. Currently, two lessons of nasally delivered therapeutics are at the market. The first one incorporates low molecular weight and hydrophobic capsules for the remedy of the nasal mucosa and sinus, including decongestants, topical steroids, antibiotics and other (OTC) products. These second class encompasses some capsules, that have enough nasal absorption for administered with the aid of using injection and rarely absorbed after oral management because of their instability in gastrointestinal tract, negative absorption properties, and their speedy and huge biotransformation

Table : Benefits of nasal drug shipping evaluation to exchange shipping strategies¹.

Key Features	Nasal	Oral	I.V.
High Drug Level	Yes	No	Yes
Rapid Onset	Yes	No	Yes
Painless	Yes	Yes	No
Self Administration	Yes	Yes	No
Low Resource Utilization	Yes	Yes	No
Bypasses BBB	Yes	No	No
Patient Compliance	High	Low	High
Hepatic First Pass Metabolism	No	Yes	No
After Taste	Low	No	High
Peptide drug Degradation	Low	High	No
Emesis	No	Yes	No

II. METHODS

This cross-sectional observational observe become performed at a tertiary rhinology middle in Vancouver, BC, Canada. The research become performed with approval from the University of British Columbia Clinical Research Ethics Board (H14-01608). Patients had been consented for enrollment among September 2014 and February 2016. Those sufferers who had been recognized with CRS without or with

nasal polyposis primarily based totally at the Canadian scientific exercise recommendations for sinusitis, eleven obtained FESS in the past, and had been actively being dealt with with every day intranasal budesonide through MAD for six months had been invited to participate. Patients had been excluded in the event that they were it. Patients simultaneously the usage of nasal saline irrigation are informed to manage budesonide through MAD half-hour after irrigation to keep away from washing out topical medication. Upon recruitment, demographic and scientific variables had been collected from clinical charts, which includes records of sinus surgery, nasal polyposis status, bronchial allergies status, present day medications, and different comorbidities. Subjects also finished a sequence of surveys that covered the 22-object Sino-Nasal Outcomes Test (SNOT-22), and pointed questions associated with scientific signs of adrenal suppression skilled during the route in their treatment (nausea, dizziness, vomiting, weakness, muscle aches, diarrhea). The SNOT-22 is a validated questionnaire used to subjectively verify sinonasal symptom severity.¹² A standard (high-dose) adrenocorticotropic hormone (ACTH) stimulation check (250 µg cosyntropin, deltoid intramuscular technique) become prepared on the recruitment visit. Tests had been preferentially finished within the morning among 8:00 and 10:00 AM while possible. Patients had been informed to chorus from administering budesonide on the morning of the check. Serum cortisol ranges had been suggested at baseline, then 30 and 60 mins after stimulation. Patients located to illustrate inadequate reaction to the ACTH stimulation check had been noted an endocrinologist for a extra thorough assessment of adrenal function. Criteria for secondary adrenal insufficiency had been satisfied if both of the subsequent situations had been met: inspired serum cortisol. Cadaver specimens have been collected from 2 superior sinus surgical operation course taking region in July and August 2012. Ethics approval changed into acquired from the University of British Columbia Research Ethics Board previous to the begin of this take a look at. Subjects protected have been cadaver specimens with out preceding sinus surgical operation, nasal polyposis, widespread septal deviations, septal perforations, or facial trauma. All specimens obtained entire endoscopic dissection, which protected bilateral uncinectomy, maxillary sinus antrostomy, ethmoidectomy, sphenoidotomy, and frontal sinusotomy (Draf Type IIa). Post dissection, 2 ml of fluorescein (Fluorescein Injection, Alcon Inc., Fort Worth, TX) changed into jumbled together a sterile emesis basin with ninety mL of sterile saline to provide a 0.20 mg/mL answer. This answer changed into then drawn into a 3-cc (3-mL) Luer-Lock syringe affixed to a MAD to distribute 1 mL of technique to the proper and left nasal valves. Cadaver specimens obtained remedy in both the LHB or HDF function. The LHB function changed into described because the chin being at the very best point of

the pinnacle, nine 60 stages underneath the horizontal aircraft. This attitude changed into decided on to simulate the location of a affected person as their head hangs over the threshold in their bed . The HDF function changed into described because the brow near the knees⁹ at an attitude off forty stages underneath the horizontal aircraft with the nostrils going through upwards. Nine An analog protractor correct to the closest diploma changed into used to affirm and standardize every orientation. Once positioned, three-quarters of the MAD tip changed into inserted at a 45-diploma attitude into the nasal aperture after which directed to the ipsilateral orbit. One milliliter (1 mL) of fluorescein answer changed into atomized thru the proper or left nostril (relying on take a look at arm) and the specimen remained in function for 30 seconds previous to endoscopy. Rigid nasal endoscopy changed into finished with a 0-diploma and 30- diploma pediatric endoscope with a blue-mild clear out out connected to the mild source (Karl Storz).

Images of the paranasal sinuses (maxillary, ethmoid, sphenoid, frontal) and different clinically applicable locations (inferior turbinate, anterior septum, center turbinate, olfactory cleft, frontal recess, sphenoidal recess, and nasopharynx) have been captured. The proper paranasal sinuses have been first to acquire the fluorescein spray for all specimens protected. Once the manner changed into finished on the proper side, the pinnacle changed into reoriented to the opportunity head function and the left paranasal sinuses obtained the fluorescein nasal spray. To save you retrograde regurgitation of the dye, the sinus cavities have been vigorously rinsed with regular saline and extra dye changed into eliminated from the endoscope with an alcohol swab, previous to spraying the alternative paranasal sinuses. Sinus cavities have been visualized to affirm the dye changed into eliminated. These tactics have been standardized for all specimens. Blinded assessment of all captured snap shots changed into carried out independently through 3 rhinologists (A.R.J., E.C.G., and A.V.T.)



FIGURE 1. LHB position angled approximately 60 degrees below the horizontal plane. LHB = lying head back.

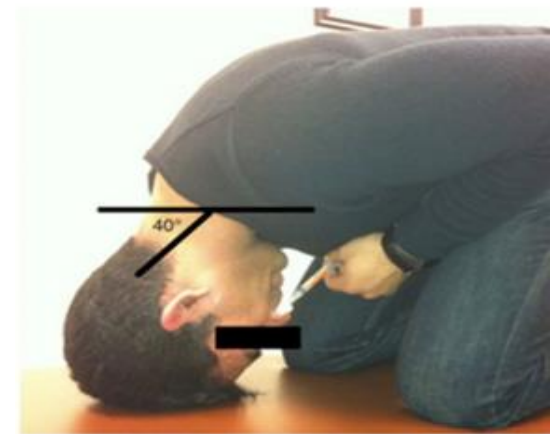


FIGURE 2. HDF position angled to approximately 40 degrees below the horizontal plane. HDF = head-down and forward.



fig.: The LMA MADgic airway with syringe and oxygen tubing Laryngo-Tracheal Mucosal Atomization Device: LMA MADgic⁵

III. STATISTICAL ANALYSIS

Data turned into collected, tabulated. Numerical variables had been supplied as imply and fashionable deviation (SD) at the same time as specific variables had been supplied as frequency and percentage. As regard numerical variables,

unpaired scholar² take a look at turned into used each time suitable among-organization comparisons; at the same time as for specific variables, chi² square take a look at turned into used. A distinction with sizeable level ($p < 0.05$) Descriptive analyses had been carried out to evaluate the adrenal suppression organization with the ordinary cortisol reaction organization, along side different key associations. All non-stop variables had been skewed, so the nonparametric Mann-Whitney U rank sum take a look at turned into used to check for variations among the two groups. Categorical variables had been assessed the use of the chi-square take a look at or Fisher's genuine take a look at while the range of instances in line with organization turned into < 0.2 on univariate analysis. STATA model 12.1 (StataCorp, College Station, TX) turned into used for the analysis, with $p < 0.05$ taken into consideration statistically sizeable.

IV. CURRENT ROLE AND FUTURE DIRECTIONS

As mentioned above, naloxone management thru the intranasal path has been proven to be a secure and powerful intervention for the preliminary control of opioid overdose.^{30,31} There stays a want for an powerful naloxone shipping machine that is more secure and simpler for each bystanders and scientific employees to manage than strategies presently in use. Forty four A needle-free, ready-to-use, unit dose shipping machine for the intranasal management of naloxone is presently withinside the scientific development stage, with an lively investigational new drug software submitted to FDA. Forty five This technology, which mixes a nasal spray tool with a naloxone solution particularly formulated for nasal shipping, Forty four will facilitate the secure and rapid management of naloxone thru the intranasal path. It is anticipated that this product will carry out higher than the prevailing preferred of take care of opioid overdoses¹².

V. DISCUSSION

Postoperative nasal irrigation and pharmacotherapy is an crucial element of consequences control following purposeful endoscopic sinus surgery (FESS). Depending at the institution, the usual of care can also additionally dictate that medicines be administered through impregnated nasal irrigation, or that separate gadgets be used to irrigate the nostril and follow topical medicines. Common nasal irrigators encompass the 240-mL Power Rinse bottle (Honeydoc Inc, Vancouver, Canada), the 240-mL NeilMed Sinus Rinse bottle (NeilMed Pharmaceuticals, Inc., Santa Rosa, CA), the 240-mL NetiPot (NeilMed Pharmaceuticals), and NasalCare Rinse bottle (TechWorldCorp Inc., Las Vegas, NV). Medications brought through nasal irrigation generally tend to get diluted

and are consequently much less effective. The atomization tool permits for a more focused dose to be brought to the place in want. There are a variety of atomization gadgets available in the marketplace and that they may be divided into three extraordinary types: squeeze, pump, and mechanical. The MAD is taken into consideration a pump atomization tool. The medical literature at the efficacy of the MAD is scarce. The simplest medical take a look at in otolaryngology assessing the efficacy of the MAD confirmed that topical budesonide through MAD can also additionally lessen the want for systemic prednisone and enhance each doctor and affected person international evaluation ratings in postsurgical CRS sufferers.¹ To our know-how, there are presently no posted facts withinside the literature at the consequences of various head positions at the distribution of topical medicinal drug withinside the sinuses the usage of the MAD. This is the first take a look at to evaluate the greatest head function for CRS sufferers the usage of the MAD. This take a look at indicates that specimens orientated withinside the LHB function have extra dispersal of medicinal drug for the duration of the sinonasal cavities than specimens orientated withinside the HDF function. The odds of standard staining withinside the LHB function are three.², while the chances of standard staining withinside the HDF function are 0.7. This also can be interpreted as; the odds of standard staining in LHB is 4.5 times extra than the chances withinside the HDF function. This know-how is critical to supplying greatest care to postsurgical sufferers. Senior et al.¹¹ confirmed that properly treating mucosal infection after surgery both medically or with debridement almost gets rid of risk of revision surgery. Moreover, recurrent frontal sinusitis is a not unusual place purpose for revision surgery.¹² Based at the consequences of our take a look at, the LHB function must be the recommended function for management of topical intranasal medicinal drug. We hypothesize that multiplied spatial distribution of drugs because of the LHB function can also additionally lessen international and frontal sinus-precise mucosal infection. However, this hypothesis have to be evaluated in next human trials accounting for versions in attitude of the head, sinonasal anatomy, and pressure of plunger depression. The diploma of dissection to open sinus cavities also can effect distribution. The diploma of opening into the maxillary sinus may be controversial. Grobler et al.¹³ decided that an ostia large than This become similarly supported with the aid of using Hyo et al.¹⁴ Sphenoid sinuses, on the opposite hand, do now no longer have a maximal ostial length and the penetration into the sphenoid sinus is correlated with length. Eight However, in our experience, it is prudent to restriction the sphenoidotomy to five to ten mm, due to the fact sufferers bitch of complications from inspiring bloodless air whilst the bulk in their sphenoid face has been removed. Much just like the sphenoid sinus,

multiplied penetration into the frontal sinuses happens with similarly dissection. Eight The most appropriate length of aerosolized debris has also been investigated and stays a debatable subject matter. Based at the effects of our study, the LHB role ought to be the recommended role for management of topical intranasal medication. We hypothesize that multiplied spatial distribution of drugs because of the LHB role might also additionally reduce worldwide and frontal sinus—precise mucosal inflammation. However, this hypothesis have to be evaluated in next human trials accounting for versions in perspective of the head, sinonasal anatomy, and pressure of plunger depression. The diploma of dissection to open sinus cavities also can effect distribution. The diploma of opening into the maxillary sinus may be debatable. Grobler et al. thirteen decided that anostia large .

VI. CONCLUSIONS

This cross-sectional look at has proven that a subgroup of recalcitrant CRS sufferers on long-time period renovation remedy with topical budesonide brought through MAD confirmed asymptomatic adrenal suppression (3%). A separate subgroup of those sufferers became determined to have expanded IOP (6%). Although the cross-sectional layout inherently limits our potential to ascribe those detrimental occasions to topical budesonide exclusively, the stringent measures taken to govern for potential confounders make this etiology plausible. These findings recommend that sufferers using the MAD to manage nasal budesonide can be vulnerable to growing those sequelae within the long time and must be monitored accordingly. Until specific screening pointers may be set up primarily based totally on potential research, a surveillance protocol for sufferers dealt with with long-time period budesonide through MAD may encompass annual adrenal feature and intraocular stress testing.

VII. RESULTS

A general of 946 patient-care data have been reviewed—518 within the pre-MAD organization and 428 within the put up-MAD organization. In the pre-MAD organization, of the 518 charts reviewed, one hundred thirty five sufferers (26.1%) met the standards for ache remedy administration; of these, forty one (30.4%) obtained fentanyl. In the put up-MAD organization, of the 428 charts reviewed, 98 sufferers (22.9%) met the standards, and of these, 36 (36.7%) obtained fentanyl. Only 13 (36.1%) sufferers of these receiving fentanyl have been dealt with with the MAD. Using then Kappa score, reviewer settlement for each the pre and put up MAD organizations became 86.7% (95% CI, 0.811-0.924). The suggest age, in years, of each the pre-MAD organization

and the put up-MAD organization became identical (9.9, SD 4.5). Both organizations have been predominantly male. There became no distinction within the suggest Glasgow Coma Scale or suggest preliminary pulse. The distinction among the suggest preliminary respiration price became giant: 22.3 (SD 6.1) in P, .05. Males tended to acquire fentanyl greater than girls in each the pre- and put up-MAD organizations (37.9% vs 26.9%). However, this fashion became now no longer statistically giant. Furthermore, there became a fashion closer to older kids receiving fentanyl while in comparison with younger kids. Just over 23% of these receiving fentanyl have been 0-5 years of age; 27.6% have been 6-10 years of age; and 39.8% have been 11-15 years of age. Again, even as there became a fashion, it did now no longer attain statistical significance. Mechanism of damage, however, became a statistically giant predictor of fentanyl administration. The percent of kids receiving fentanyl via way of means of mechanism of damage became assault, 16.7%; burn, 69.2%; cut, 20.0%; fall, 40.9%; motor car crash, 13.0%; struck via way of means of or against, 33.3%; and other, 33.6%; P, .001. Injuries within the "other" class covered animal bite, bicycle, pedestrian, penetrating, or sports activities damage. The logistic regression evaluation of the elements influencing fentanyl use is supplied in Table 1. As age increased, the probability of receiving fentanyl increased. Similar effects have been determined for preliminary pulse of the patient. Burn sufferers have been related to an growth in fentanyl use within the put up-MAD period (adjusted odds five 6.34; 95% CI, 1.14-35.41) even as motor car crash sufferers have been related to a lower in fentanyl use within the put up-MAD period (odds five 0.29; 95% CI, 0.09-0.89).

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