In adults, the diagnosis of these duplications can occur as complications (occlusion, bleeding, pain) and surgical resection is also indicated by the risk of malignancy.

The diagnosis of malignancy on these lesions is rare, with a small number of published case reports. It occurs more frequently in the colon, with a percentage of malignancy for this type of cysts of up to 68% in some published series,[8] and 23% in ileal cysts.[9] The most common histological type is adenocarcinoma, followed by squamous carcinoma and carcinoid tumor.[10] The diagnosis is also usually made in advanced stages, as in the case of our patient, frequently with the presence of lymph node involvement.

Surgery must be radical, with a curative intent from the outset.[1,2]

Although rare, intestinal duplication cysts can be diagnosed in adults, and this diagnosis must be contemplated in cases of abdominal mass of unknown origin. Knowing that malignization is possible, surgery should be the initial therapeutic option, and radical resection should always be carried out with curative intent.

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REFERENCES

1. Blank G, Königsrainer A, Sipos B, Ladurner R. Adenocarcinoma arising in a cystic duplication of the small bowel: case report and review of literature. World J Surg Oncol. 2012;10:55.
2. Jeziorczak PM, Warner BW. Enteric duplication. Clin Colon Rectal Surg. 2018;31:127–31.
3. Liu R, Adler DG. Duplication cysts: diagnosis, management, and the role of endoscopic ultrasound. Endosc Ultrasound. 2014;3:152–60.
4. Beltrán MA, Barría C, Contreras MA, Wilson CS, Cruces KS. Adenocarcinoma en duplicación intestinal del íleon: caso clínico. Rev Med Chil. 2009;137:1341–5.
5. Hata H, Hiraoka N, Ojima H, Shimada K, Kosuge T, Shimoda T. Carcinoid tumor arising in a duplication cyst of the duodenum. Pathol Int. 2006;56:272–8.
6. Tew K, Soans BK, Millar EA. Adenocarcinoma in an ileal duplication cyst: ultrasound and computed tomography findings. Australas Radiol. 2000;44:228–31.
7. Kusunoki N, Shimada Y, Fukumoto S, Iwatani Y, Ohshima T, Arahi E, et al. Adenocarcinoma arising in a tubular duplication of the jejunum. J Gastroenterol. 2003;38:781–5.
8. Inoue Y, Nakamura H. Adenocarcinoma arising in colonic duplication cysts with calcification: CT findings of two cases. Abdom Imaging. 1998;23:135–7.
9. Johnson JA, Poole GV. Ileal duplications in adults: presentation and treatment. Arch Surg. 1994;129:659–61.
10. Ricciardolo AA, Iaquinta T, Tarantini A, Sforza N, Mosca D, Serra F, et al. A rare case of acute abdomen in the adult: the intestinal duplication cyst. Case report and review of the literature. Ann Med Surg. 2019;40:18–21.

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# Are we overdosing parenteral metamizole?☆

## ¿Estamos sobredosificando el metamizol por vía parenteral?

Metamizole magnesium is one of the most frequently used analgesics in the treatment of perioperative pain.[1] This drug came on the market in 1921 and is currently authorized in South America and in 10 countries of the European Union (EU), including Spain. In October 2018, the Spanish Agency for Medicines and Health Products (AEMPS) published a communication on the risk of agranulocytosis and the growing use of metamizole in Spain, as its consumption has doubled in the last 10 years.[2] We are concerned about the dosage of metamizole, due to its well-known serious adverse effects. A recently published review has analyzed a total of 1448 cases reported from 1985 to 2017,[3] with a mortality rate of 16%. No lethal dose

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**Table 1 – Marketed presentations in Spain for parenteral dosage and posology according to the drug data sheet.**

| | Presentation | Standard parenteral posology | Maximum parenteral dose |
|---|---|---|---|
| Metamizole magnesium EFG (Normon®) | 2 g ampoule/5 m L | 2 g every 8 h | 6 g |
| Metamizol magnésico EFG (Mabo®) | 2 g ampoule/5 m L | 2 g every 12 h | 4 g |
| Nolotil® | 2 g ampoule/5 m L | 1 g every 6–8 h | 5 g |

has been established, but doses greater than 10 g or in a short period of time can cause nausea, vomiting, abdominal pain, renal function deterioration, central nervous system symptoms, and even shock.[4] The most common adverse effects are hypotension (frequency ≥ 1/100), followed by dermatological reactions (≥1/1000), leukopenia, anaphylactic reaction, asthma, maculopapular rash (≥1/10 000), agranulocytosis (including case fatalities), thrombocytopenia, toxic epidermal necrolysis, Stevens-Johnson syndrome, shock and phlebitis (<1/10 000).[5]

In clinical practice, metamizole is used at a parenteral dosage of 2 g every 8 h, which is changed to an oral dose of 575 mg every 8 h when the clinical situation improves. As a result of this difference and the AEMPS communication on metamizole and its adverse effects, a review was conducted of the pharmacokinetics, expert consensus and technical specifications of the different presentations marketed in Spain in order to determine the most appropriate dosage of metamizole.

At the pharmacokinetic level,[5,6] when administered orally, metamizole undergoes non-enzymatic hydrolysis in the stomach acid, transforming into its main active metabolite, 4-methyl-amino-antipyrine (4-MAA). Once absorbed, it is metabolized in the liver by oxidation, demethylation and acetylation. Intravenous administration

is the fastest to reach maximum levels, followed by intramuscular and oral routes, the latter having almost 100% absorption. Therefore, pharmacokinetics do not justify a four-fold higher dosage parenterally versus orally. The difference in the dosage of both formulations seems to be related to the indications, meaning that it may be associated with greater clinical benefit in patients whose pain is more intense, a faster effect is required, and the patient is also usually intolerant to oral administration. However, this reasoning does not determine the most appropriate pattern.

On December 13, 2018, after a review of medicines containing metamizole and given that their adverse effects may be dose-related, the European Medicines Agency (EMA) made a consensus recommendation of the maximum daily dose in the European Union (EU)[7] and addressed inconsistencies in product information marketed in many EU member states. The recommendations included a maximum single oral dose of 1 g up to 4 times a day in patients over the age of 15, and a maximum daily dosage of 5 g when the formulation is parenteral. These recommendations were sent to the European Commission (EC), which issued a final legally binding decision on March 20, 2019 that is valid throughout the EU.

Table 1 shows the presentations marketed in Spain and the dosage according to the drug data sheets. The biggest differences are in the Normon® metamizole magnesium data sheet,[6] which recommends a 2 g vial/8 h (exceeding EU recommendations), versus the Mabo® date sheet,[8] which recommends 2 g/12 h, or the Nolotil® data sheet,[5] which recommends 1 g/6–8 h and a possible maximum daily dose of up to 5 g. Regardless of the presentations, the dose of 2 g/8 h frequently continues to be used in hospitals. This exceeds the maximum daily dose of 5 g and the usual pattern of 1 g every 6–8 h or 2 g/12 h. In our opinion, with these dosages, the equivalence to the oral dose of 1–2 capsules every 8 h makes more sense.

We conclude that we are overdosing parenteral metamizole in routine daily practice. After a multidisciplinary consensus was reached at our hospital, we recommend a dosage of 1 g/6–8 h, thus guaranteeing adherence to the binding decision of the EC. It is true that the current presentations of 2 g ampoules do not facilitate its applicability, and we hope that pharmaceutical companies will revise their drug data sheets in order to unify criteria, adjusted to the recommended dosage and to promote the safe use of metamizole. Lastly, this information should be transmitted to all medical professionals in order to correct this extended clinical practice, because, in this instance, common practice is not always the best practice.

## REFERENCES


1. Cháfer Rudilla M, Domínguez Rodríguez JP, Reyes Santana A, Gorchs Molist M, Ocaña Gómez MA, Martín Conde JA, et al. Recomendaciones sobre el tratamiento farmacológico perioperatorio. Cir Esp. 2009;86:130–8.
2. Agencia Española de Medicamentos y Productos Sanitarios AEMPS. Metamizol y riesgo de agranulocitosis. MUH (FV), 15 / 2018. Oct 30, 2018. [Internet] [Accessed 28 January 2020] Available at: https://www.aemps.gob.es/informa/notasinformativas/medicamentosusohumano-3/seguridad-1/2018/ni_muh_fv-15-2018-metamizol-agranulocitosis/.
3. Hoffmann F, Bantel C, Jobski K. Agranulocytosis attributed to metamizole: An analysis of spontaneous reports in EudraVigilance 1985–2017. Basic Clin Pharmacol Toxicol. 2020;126:116–25. http://dx.doi.org/10.1111/bcpt.13310.
4. Marcos Sánchez F, Marcos Fernández F, Árbol Linde F, Fernández García E. Intoxicación con dosis elevadas de metamizol de evolución rápidamente favorable. Emergencias. 1997;9:310–1.
5. Ficha técnica Nolotil® 0,4 g/ml solución inyectable y para perfusión. [Internet]. [Accessed 29 September 2019]. Available at: https://cima.aemps.es/cima/dochtml/ft/42304/FT_42304.html.
6. Ficha técnica Metamizol Normon 2 g/5 ml solucioón inyectable EFG. [Accessed 29 September 2019]. Available at: https://cima.aemps.es/cima/pdfs/ft/63430/FT_63430.pdf.
7. EMA recommends aligning doses of metamizole medicines and their use during pregnancy and breastfeeding. EMEA/191666/2019 Mar 20, 2019 [Accessed 28 November 2019] Available at: https://www.ema.europa.eu/en/medicines/human/referrals/metamizole-containing-medicinal-products.
8. Ficha técnica Algi-Mabo® ampollas, 6 ampollas de 5 ml [Internet]. [Accessed 29 de September 2019]. Available at: https://cima.aemps.es/cima/pdfs/ft/51345/FT_51345.pdf.

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# Degeneration of Barrett's esophagus after sleeve gastrectomy☆

## Degeneración del esófago de Barrett tras gastrectomía vertical

Bariatric surgery is the most effective and long-lasting therapeutic option for the treatment of morbid obesity and its comorbidities. In the last decade, sleeve gastrectomy has been established as the most widely used surgical procedure in bariatric surgery, showing exponential growth.[1] Even so, gastric bypass is the technique of choice when sleeve gastrectomy is not an absolute contraindication but should be indicated with caution, especially in cases of previous gastroesophageal reflux.[2]

Compared to the population at large, people with morbid obesity have a higher incidence of gastroesophageal reflux, esophagitis, Barrett's esophagus, and esophageal adenocarcinoma.[3] Although some studies describe a decrease in gastroesophageal reflux after sleeve gastrectomy,[4] recent studies show the high risk of developing *de novo* reflux, esophagitis and Barrett's esophagus in the medium to long term after this procedure,[1,2,5–7] with the subsequent risk of malignancy. Table 1 shows the percentage of esophagitis and Barrett's esophagus after sleeve gastrectomy observed in several studies. A recent meta-analysis has indicated that, after sleeve gastrectomy, 23% of patients have *de novo* gastroesophageal reflux, 28% esophagitis, and 8% develop Barrett's esophagus[7] (compared to 1.6% of the general population[5]). The increased incidence of reflux is probably due to an imbalance between intragastric pressure and the pressure of the lower esophageal sphincter. A directly proportional relationship has also been observed between the diameter of the tubular stomach and the incidence of reflux.[8]

Another notable feature is that the endoscopic findings do not correlate with the severity of the gastroesophageal reflux symptoms perceived by the patient.[6] In fact, some authors suggest performing systematic follow-up endoscopies to screen for lesions associated with reflux, regardless of whether there are symptoms or not.[1,5,6,8]

Given that sleeve gastrectomy is widely used around the world, this is a topic of special interest in young patients, who have many years ahead to develop complications. It is unknown whether the progression to Barrett's esophagus and adenocarcinoma occurs identically in patients who undergo sleeve gastrectomy compared to the rest of the population.[8] The optimal approach to follow after the diagnosis of Barrett's esophagus in a patient with sleeve gastrectomy is also unclear: follow-up, or conversion to gastric bypass?

Despite the above, the literature published on cases of esophageal adenocarcinomas in patients treated with sleeve gastrectomy is very limited. Khoury et al. described a patient who already had Barrett's esophagus before sleeve gastrectomy.[9] Wright et al. reported a case of a patient with a normal preoperative endoscopy study, who developed reflux after surgery and had developed esophageal adenocarcinoma 5 years later.[10]

We present the case of a 60-year-old patient with a history of hypertension, diabetes, dyslipidemia, acute myocardial infarction and stent placement in 2002, depression and morbid obesity, with a body mass index of 39, no symptoms of gastroesophageal reflux and previous fibrogastroscopy that was normal. In May 2011, the patient underwent sleeve gastrectomy.

Given the latest publications on esophagitis and Barrett's esophagus after sleeve gastrectomy in asymptomatic patients, at our hospital we carried out a follow-up study of patients who had undergone sleeve gastrectomy (all of them with previous fibrogastroscopy) with more than 4 years of evolution. We analyzed both symptoms and endoscopic findings.

In the context of this study, our patient was studied by fibrogastroscopy in January 2019, which found evidence of a 9-mm lesion in the distal esophagus. Barrett's esophagus was confirmed with high-grade epithelial dysplasia. An immunohistochemical study showed marked positivity with a component of high-grade dysplasia (CK CAM5.2), high proliferative index (Ki-67), and nuclear positivity for p53 in the high-grade component. In March 2019, endoscopic resection of the mucosa was performed; the pathological study showed Barrett's esophagus with foci of high-grade dysplasia with free margins, and no infiltrative component. Fibrogastroscopy was repeated 2 months later and demons-

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