Iodoform (triiodomethane) - An Old, but Still Extremely Efficient Antiseptic

MIHAI DIMITRIU^{1,2}, BOGDAN SOCEA^{1,2*}, CRINGU ANTONIU IONESCU^{1,2}, LIANA PLES^{1,3}, DIANA-CLAUDIA GHEORGHIU², VLAD DENIS CONSTANTIN^{1,2}, CATALIN-GABRIEL CIRSTOVEANU^{1,4}, NICOLAE BACALBASA^{1,5}, CRISTIAN GEORGE FURAU^{6,7}, DRAGOS VIRGIL DAVITOIU^{1,2}, NICOLAE GHEORGHIU^{1,8}

¹ Carol Davila University of Medicine and Pharmacy, 37 Dionisie Lupu, 020021, Bucharest, Romania

²Sf. Pantelimon Emergency Clinical Hospital, 340-342 Soseaua Pantelimon, 021659, Bucharest, Romania

³Sf. Ioan Clinical Emergency Hospital, Bucur Obstetrics Department, 10 Intre Garle Str.,040292, Bucharest, Romania

⁴Maria Sklodowska Curie Emergency Clinical Pediatric Hospital, 20 Constantin Brancoveanu Str., 041451, Bucharest, Romania

⁵Dr. Ion Cantacuzino Clinical Hospital, 5-7 Ion Movila Str., 020475, Bucharest, Romania

Vasile Goldis West University Arad, Faculty of Medicine, 94 Revolutiei Blvd., 310025, Arad, Romania

⁷Emergency Clinical Arad County Hospital, 2-4 Andreny Karoly Str., 310037, Arad, Romania

⁸Elias Emergency Hospital, 17 Marasti Str., 011461, Bucharest, Romania

Iodoform (triiodomethane), a yellow crystalline solid, belonging to the family of organic halogen compounds, is used as an antiseptic. Its antiseptic action is due to the slow release of iodine under the action of catalase from wounds. Currently, it is widely used only in dentistry and in veterinary medicine. We have extended, with good results, the use of iodoform as an antiseptic for other types of surgical or traumatic wounds that have been infected with piogens. Between 2009 and 2018, on 242 cases of different wounds, we obtained good results, with no severe adverse effects.

Keywords: iodoform, triiodomethane, antiseptic, wounds

As it was natural, with the passage of time and the advances of world medicine, surgery has gained an increasingly important place in our daily medical practice. The number of surgical interventions of all types has steadily increased worldwide, sometimes even alarming (e.g. caesarean section) [1-5].

Obviously, even if the rate of infectious complications of these steadily increasing surgeries remained constant, with the increase in incidence, the number of cases of wound infection would also increase.

The rate of postoperative infections has improved worldwide over the years due to the progress of antisepsis, the antibiotics industry and the advancement of surgical techniques, but it has not become null.

We are still confronted with infections and suppurations of postoperative wounds of all kinds. In an era where stateof-the-art antiseptics and increasingly effective antibiotics are being used permanently, resistant infections and suppurations occurring naturally overload surgical services and specialist staff.

A solution for these wound infections and exudations can be the rehabilitation and reintroduction of some *forgotten* or *out of date* antiseptics.

Reinventing such an infection-fighting solution can counteract, at least partially (and in carefully selected cases), the resistance to today's antibiotics and antiseptics.

Our daily experience and practice has made us *rediscover* for some time such a long-forgotten antiseptic solution: Iodoform (Triiodomethan).

Iodoform or Triiodomethane is an iodine organic compound of the formula CHI $_3$, with a tetrahedral molecular geometry, with a molecular weight of 393,732 g / mol, being a bright crystalline powder of bright, odor-specific, unpleasant, and persistent [6].

It was first prepared in 1822 (1824 by other sources) by Georges Serullas [7, 8] and was synthesized from sodium

iodide (NaI), acetone and alkaline hypochlorite solution [7, 8]. In 1843 Dumas announced its composition. Its antiseptic action was discovered in 1880, which made it an important medicinal compound first used in practice by Bouchard [9]. It is a substance very slightly soluble in water, but soluble in ethanol and methanol and has been extensively used in the past centuries (XIXth and XXth) as a suppressant wound disinfectant, dermato-venereal disinfectant, antiseptic agent in dentistry, otorhinolaryngology and veterinary medicine [8]. It is used as crystalline powder coated in wounds or in the form of iodoform gauze dressings [6-8].

Its use was subsequently greatly limited due to its irritating qualities, the extremely strong smell, and the development of more effective disinfectants [6, 8, 10, 11].

Currently, it is widely used only in dentistry (iodoform gauzes) and, as etheric solutions of concentrations of 2-3%, in veterinary medicine, especially in large or medium sized animals (equines, sheep, cattle, goats, swine, canines and birds) [6, 8].

Triiodomethane, a yellow crystalline solid, belonging to the family of organic halogen compounds, is used as an antiseptic component of certain medications [12]. The open packing has been used successfully as a secondary healing method to help bone tissue healing [13, 14].

Some studies reported an effectiveness in removing necrotic tissue from wounds, although the mechanisms remain incompletely explained. It is supposed to have a lytic activity for collagen fibers. In a study of 60 wounds, more than 60% of iodoform gauze-treated wounds were completely debrided within 2 weeks [15]. The thyroid function and the levels of thyroid hormones were not affected.

Its antiseptic action is due to the slow release of iodine under the action of catalase from wounds.

^{*}email: bogdansocea@gmail.com, Phone: +40788491091 All the authors equally contributed to this manuscript and share first authorship

Experimental part

There is no experienced surgeon (irrespective of his subspecialty) who is not often confronted with infected or over-infected wounds, with several strains of resistant or very resistant piogene bacteria to usual antibiotics, and /or to the second-line antibiotics, and /or to the use of the most advanced substances and combinations of disinfectants.

These long-lasting supurations are extremely demanding for surgical and medical staff involvement in the treatment of this type of plagues. Often infections are nosocomial infections (associated with the medical act), which may further complicate the management of these difficult cases.

Being often confronted with the treatment of such cases, and with some treacherous abscesses, we reappeared in some of these situations to the *oldest surgeons' friend*, Iodoform.

Starting from the practice of dentists and of the othorynolarynologists to mesh cavities infected with piogens, we rehabilitated the antiseptic and re-adapted it to our current practice. Therefore, the most frequent use was in the cases of Bartholin's abscess. Starting from these abscesses, we have extended the use of iodoform as an antiseptic for other types of surgical or traumatic wounds that have been infected with piogens.

Thus, in the 2009-2018 period, we summed up 242 cases of wounds and abscesses of different types successfully treated by daily local Iodoform applications in all 7 departments that were included in our retrospective study. Obviously, after a prior surgical removal (removal of necrotic tissue) and chemical treatment (generally betadine solution) of these wounds and abscesses. Drainage has often been used, especially in the case of abscesses.

The departments in which our retrospective study was conducted (between 2009 and 2018) were: Clinical Department of Obstetrics Gynecology of the Emergency Clinical Hospital Sf. Pantelimon in Bucharest; Clinical Department of Pathological Obstetrics of the Emergency Clinical Hospital Sf. Pantelimon in Bucharest; Clinical Department of Obstetrics and Gynecology of the Emergency Clinical Hospital Sf. Ioan in Bucharest - Bucur Maternity; Clinical Department of Obstetrics and Gynecology of the Clinical Hospital Dr. Ion Cantacuzino in Bucharest; Clinical Department of Obstetrics and Gynecology of the Emergency County Clinical Hospital of Arad; Clinical Department of General Surgery of the Emergency Clinical Hospital Sf. Pantelimon Clinic in Bucharest and the Clinical Department of Orthopedics and Traumatology of the Emergency Clinical Hospital Elias in Bucharest.

The 242 cases treated by us are shown in table 1.

Results and discussions

All wounds included in our study were suprainfected wounds and required a local treatment of 7-39 days and a total hospitalization of 2 to 46 days.

Local treatment was accompanied by broad spectrum antibiotics (combination of two or more antibiotics, later adjusted with antibiotherapy according to the antibiogram of cultures of the respective wounds).

Drainage of wounds was used in 147 of the 242 cases included in the study (60.74% of cases). It was instituted from first intervention in 99 cases (67.34% of cases with surgical drainage) and per secundam (with a surgical gesture after the first intervention) in 48 cases (32,.65% of drained cases).

We did not record in our study any significant adverse reaction that we could directly attribute to local treatment with Iodoform (Triiodomethane).

All cases thus treated resulted in favorable or slow favorable progression and subsequent surgical healing.

The fact that most cases were gynecological in our study (139 of the 242 cases = 57.43% of cases) is, of course, due to the fact that the cases corresponding to a certain higher number of gynecologists have been included in the study compared to a lower number of surgeons or orthopedists. Also, most of the clinics included in the study with such cases were gynecological.

The distribution of the 242 cases over time is shown in table 2.

As can easily be seen in table no. 2, most cases treated by us were recorded in 2017 (29 cases) and 2015 (28 cases), and the fewest in 2012 (19 cases) and 2013 (20 cases).

Table 1							
THE 242 CASES OF SUPRAINFECTED WOUNDS, TREATED BY LOCAL DAILY IODOFORM							
POWDER APPLICATIONS (2009-2018 PERIOD)							

Obstetrics	Postoperative C-section wounds	23	139 (57.43%)
Gynecology	Perineal wounds (episiotomy)	15	1
	Postoperative gynecologic wounds	43	1
	Bartholin's suprainfected cavity	58	1
Surgery	Postoperative abdominal wounds	35	58 (23.96%)
	Posttraumatic abdominal wounds	23	
Orthopedics	Postoperative wounds	19	45 (18.59%)
	Posttraumatic wounds	26	1
Total	-	242	242

Table	2
-------	---

ANNUAL DISTRIBUTION OF 242 CASES OF ABSCESSES AND SUPRAINFECTED WOUNDS TREATED WITH IODOFORM + ANTIBIOTHERAPY +/- SURGICAL DRAINAGE

Year	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
Obstetrics-	15	17	12	10	11	14	17	11	15	17	139
Gynecological											
Cases											
Surgical Cases	7	4	6	4	5	7	4	8	9	4	58
Orthopedics cases	3	5	6	5	4	3	7	4	5	3	45
Total	25	26	24	19	20	24	28	23	29	24	242

Conclusions

Although the study did not include a very large number of cases (N = 242), our retrospective study demonstrates that under well-selected conditions, Iodoform (Triiodomethane) may be a valuable adjunct to the treatment of abscesses of all kinds (our cases predominated in abscesses of Bartholin's gland and in wounds infected with piogene germs), no matter if the infection was primary (traumatic wounds, for example), or if the superinfection was subsequently produced (localized purulent infection of post-operative wounds, meaning infections associated with the medical act).

Another valuable conclusion of our study is that we should never give up a treatment method just for the simple reason that it is *obsolete*. It is always necessary to individualize the treatment and weigh the risks and benefits of the therapeutic method used.

References

1. IONESCU, C.A., PLES, L., BANACU, M., POENARU, E., PANAITESCU, E., DIMITRIU, M.C.T., J Pak Med Assoc, **67**, no. 8, 2017, pp. 1248–1253. 2.PASC, A., NAVOLAN, D., PUSCASIU, L., IONESCU, C.A., SZASZ, F.A., CARABINEANU, A., DIMITRIU, M., CALIN, D., BOHILTEA, R., PLES, L., NEMESCU, D., J Eval Clin Pract, pp. 1-6, 2018, DOI: 10.1111/jep.13062. 3.. IONESCU, C.A., DIMITRIU, M., POENARU, E., BANACU, M., FURAU, G.O., NAVOLAN, D., PLES, L., J Eval Clin Pract, **25**, no. 1, 2019, pp. 111–116, DOI: 10.1111/jep.13025.

4. DIMITRIU, M., IONESCU, C.A., MATEI, A., VIEZUINA, R., ROSU, G., ILINCA, C., PLES, L., J Eval Clin Prac, **25**, no. 1, 2019, pp. 117-124, DOI: 10.1111/jep.13036.

5.IONESCU, C., NAVOLAN, D., CALIN, A., et al., Rev Chim (Bucharest), **69**, no. 2, 2018, pp. 478-483.

6.SOCEA, B., NICA, A.A., SMARANDA, A., BRATU, O.G., DIACONU, C.C., CARAP, A.C., NEAGU, T.P., BADIU, C.D., CONSTANTIN, V.D., Modern Medicine, **25**, no. 4, 2018, pp. 187-191.

7.***https://pubchem.ncbi.nlm.nih.gov/compound/iodoform #section=Top

8. COTTLE W., Br Med J, 1, no. 893, 1878, pp. 190-191, accessed on https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2220447/pdf/brmedj05286-0012.pdf

9. *** https://www.britannica.com/science/iodoform

10.*** The Ministry of Health, Labour and Welfare. The Japanese pharmacopoeia (The Ministry of Health, Labour and Welfare ed.), 15th ed., 2006.

11.*** Kirk-Othmer. Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984, pp. 779-803.

 $12.^{***https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+\ hsdb: \\ @term+@rn+@rel+75-47-8$

13.SINGH, V. , DAS, S. AND SHARMA, N., Open Journal of Stomatology, 2, 2012, pp. 322-325.

14.ORBAN, H.B., GHEORGHIU, N., CRISTESCU, V., Chirurgia (Bucharest), 105, no. 3, 2010, pp. 365-372.

15.ORBAN, H., STAN, G., GHEORGHIU, N., DRAGUSANU, M., MARES,

E., ORBAN, C., Chirurgia (Bucharest), **107**, no. 2, 2012, pp. 226-230. 16. MIZOKAMI, F., MURASAWA, Y., FURUTA, K., ISOGAI, Z., Biol Pharm Bull, **35**, no. 7, 2012, pp. 1048-1053.

Manuscript received: 28.11.2018