TOPICAL IODOPHOR USE IN CHRONIC WOUNDS: A LITERATURE REVIEW[1]

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This study aimed to do a review of the literature regarding the use of topic iodine and/or compounds in the treatment of chronic wounds. The clinical trials were searched in the Cochrane database. Fourteen (58.3%) among 24 studies fulfilled the inclusion criteria. The articles were analyzed regarding journal and study characteristics and classified into three groups: Iodine versus other topic agents (7/ 50%); Iodine versus different dressings (6/ 42.9%); Iodine versus without Iodine (1/ 7.1%). Favorable results for the use of Iodine or similar product occurred in 50% of the analyzed studies. Six out of 8 trials showed favorable results for healing and infection prevention/ treatment; 4 out of 5 were not favorable when the healing objective was investigated and 1 study for infection treatment showed no favorable result.

DESCRIPTORS: iodine compounds; wound healing; review

USO DE YODO TÓPICO Y/O COMPUESTOS EN HERIDAS CRÓNICAS: REVISIÓN DE LA LITERATURA

La investigación trata de una revisión de la literatura a cerca de la utilización del yodo tópico y/o compuestos en el tratamiento de las heridas crónicas. Se buscaran los ensayos clínicos en el Cochrane. Catorce (n=24) publicaciones estaban de acuerdo con los criterios de inclusión, y fueran analizadas según las características de las revistas y ensayos y clasificadas como: yodo versus otros agentes tópicos (7/ 50%); yodo versus curativos (6/ 42,9%) y yodo versus sin yodo (1/ 7,1%). Fueran obtenidos resultados favorables a la utilización del yodo y/o compuestos en 50% de los artículos analizados. Cuanto a las tendencias de los resultados, 6 de 8 publicaciones, a cerca de la de cicatrización de las heridas y prevención de infección, fueran favorables; 4 de 5 fueran no favorables solamente para la cicatrización, y el resultado del único trabajo con indicación del uso para tratamiento de infección de herida fue no favorable.

DESCRIPTORES: compuestos de yodo; cicatrización de heridas; literatura de revisión

USO DE IODÓFORO TÓPICO EM FERIDAS CRÔNICAS: REVISÃO DA LITERATURA

Trata-se de revisão de literatura relacionada ao uso de iodóforos tópicos no tratamento de feridas crônicas. Os ensaios clínicos foram localizados por meio da Base de Dados Cochrane de Revisões Sistemáticas e Registro Cochrane Central de Ensayos Controlados. Quatorze (58,3%), dentre 24 artigos, atenderam os critérios de inclusão, analisados quanto às características dos periódicos e dos estudos e classificados em três grupos: iodóforo versus outros agentes tópicos (7 ou 50%); iodóforo versus coberturas (6 ou 42,9%) e iodóforo versus sem iodóforo (1 ou 7,1%). Resultados favoráveis à utilização dos iodóforos ocorreram em 50% dos artigos analisados. Quanto às tendências dos resultados, seis, dentre oito artigos, que tratavam de cicatrização de feridas e prevenção de infecção, foram favoráveis; quatro, dentre cinco, foram desfavoráveis somente para a cicatrização e no único ensaio em que houve indicação do seu uso para tratamento de infecção de ferida o resultado foi desfavorável.

DESCRITORES: compostos de iodo; cicatrização de feridas; literatura de revisão

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INTRODUCTION

The development of antiseptics is related to the history of wound treatment. Their basic objectives are to reduce risks and prevent or reduce infectious complications.

Antiseptics are hypoallergic substances, of low causticity, which possess lethal or inhibiting action of microbial reproduction, for application on skin and mucous tissues[1].

For more than a century, iodine was considered one of the most efficacious antiseptics. Although discovered in 1812 by the French scientist Dijon Bernad Courtors, it was only denominated iodine in 1814 by Gay Loussac. The word originates from the Greek word *ioidés* and refers to the purple color of its vapor[2]. It was officially recognized by the United States Pharmacopea in 1830. Some years later, in 1839, the first report was made of its specific use in wounds.

Despite the antimicrobial advantages obtained through its use, several disadvantages were observed in its clinical application[2], making pharmaceutical industries develop new research and formulations that led to the production of iodophors.

The term iodophor literally means iodine carrier. Iodophors consist of a stable combination of molecular iodine or triiodide with a transporter of high molecular weight. In aqueous solution, iodophors free iodine molecules, as found in pure solutions. The most known iodophor is the polyvinylpyrrolidone, a complex of 1-vinyl-2-polymers-pyrrolidone with iodine (PVP-I)[2-3].

For many authors and in the specific Brazilian legislation, the use of PVP-I on healthy skin is a consensus, especially in the preoperative phase[4]. However, authors show different and controversial results[5] for topical wound treatment.

Because of all this controversy and considering the indiscriminate use of antiseptics by several health professionals, especially iodinated formulations, whether due to a lack of technical knowledge, ignorance or devaluation of potential environmental and direct toxicological effects to patients and professional agents, we decided to elaborate this study, aiming to carry out a literature review related to the use of iodophors in chronic wound treatment.

METHOD

The literature review is considered an ample and critical revision of the most important specialized studies about a specific theme, whose specific aim depends on the reviewer's role, for example, acquisition of knowledge on a topic, preparation of critiques about existing nursing practices and recommendations for innovations, development of clinical protocols and interventions based on research in order to improve clinical practice, among others[6]. It is also considered indispensable in all steps of the quantitative research process[7].

There were seven phases that guided the procedures in this study, similar to those used in the systematic literature review process, ranging from the research question, definition of inclusion criteria and search strategies, search per se, selection of obtained studies and critical assessment of the studies, to the collection and synthesis of specific collected data[6]. In this study, the seventh phase was modified and developed through the analysis of scope, methodological design, study results and conclusions[8].

Given that the literature that involves the study of iodophors in chronic wounds - as the object of this research - is vast and reasonably old, we decided to include all clinical trial research articles published in journals indexed in the Cochrane Systematic Reviews database and Cochrane Central Register of Controlled Trials in the study sample. The decision to use only this database was because it contains a significant quantity of controlled clinical trials, considered sufficient to meet the study objective.

For the inclusion and analysis of the articles, the following criteria were established: clinical trials published in full text in English, Portuguese and Spanish. Articles related to mucous tissues were excluded, as well as those written in other languages, even with the abstract in English, and also editorials, letters and works published in the form of abstracts.

The bibliographic review was performed electronically from July, 2003 to June, 2004. The access to the Cochrane database was done through the Cochrane library*, available on the BIREME - Medical Regional Library (http://www.bireme.br) website, using the following grouped descriptors, in English: iodine, acute wound, treatment, healing, infection, surgery, surgical.

* Brazilian Cochrane Center - Brazilian section of the Cochrane Collaboration - updated collection of information sources on evidence-based medicine, for health care providers as well as professionals active in research, education and public administration, at all levels.

For data collection, a specific instrument was used, composed of: *journal data* (name, year, issue, number, original language, country); *researcher data* (quantity, name(s), profession(s) and place of activity); and *article data* (title; year and research site; case identification; scope; methodological design; results and conclusions).

RESULTS

Among 24 full text articles, 14 met the inclusion criteria and composed the research sample.

The results show that the first publication on the use of iodophors in chronic wounds occurred in 1980 and that the largest number of publications appeared in the 1980s (9/64.3%). All articles analyzed were written in English. The countries where the studies were performed are mostly European (9/64.2%), especially Sweden (3), Finland, England and Germany (with two studies in each of these countries). The trials analyzed were published in 12 different journals. Two of them - *Acta Chirurgica Scandinavica*/ *Supplementum* and *Dermatology* - published two articles each, that is, the largest number of articles considering isolated journals. The United States and England were leaders regarding the origin of the periodicals (four in each) the articles were published in. Regarding the authors of the trials, the clear presence of physicians stood out in all studies. The majority of publications (71.4%) was about patients with vasculogenic ulcers, of venous origin.

For the quantitative analysis, the studies were initially classified according to the product used for comparison with the iodophor: Group I - Iodophors x Other Topical Agents - 7 articles (50%); Group II - Iodophors x Dressings - 6 articles (42.9%); Group III - Iodophors x no Iodophors - 1 article (7.1%).

Regarding the formulation of the iodophors used in the clinical trials, Cadexomer-iodine (CI) 0.9% was the most frequent (57.2%). PVP-I at 5% solution was used in 14.3% of the studies. Varied solutions used for wound cleansing, with physiological solution as the most frequently used (50%). The solutions used in this procedure were not described in four of the studies.

The use of iodophors in chronic wounds met two main objectives: infection prevention/treatment (1 study) and wound healing (5 studies). For the remaining 8 articles, both objectives were proposed.

From the 14 studies analyzed, half (seven) were favorable to the use of iodophors in chronic wounds. Five were performed on venous ulcers in the inferior limbs and two on patients with skin grafts. In addition, six out of eight investigations that tested both objectives - infection prevention and/or treatment and wound healing - showed favorable results. In summary, positive results were found in only one of the five studies whose objective was to perform isolated evaluation of healing. The largest number of publications with unfavorable results regarding the use of iodophors occurred in 1987 [2]. After the first half of the 1990s, all results of these studies were favorable to the use of iodophors in chronic wound care.

DISCUSSION

Iodophors are antiseptic of wide antimicrobial range, available in several formulations. Several studies have been developed to investigate their efficacy, in different formulations and presentations, for wound infection prevention or treatment, as well as their influence in the healing process, comparing them with other products used in this therapeutic procedure or with no products. Nevertheless, the topical use of iodophors is still controversial.

Therefore, this study proposed to review clinical trials related to the use of iodophors in the topical treatment of chronic wounds, evaluating the objectives and methods, as well as the results and conclusions, whether favorable or not, with a view to establishing tendencies for its adoption in these clinical conditions.

A total of 14 clinical trials about the use of iodophors in chronic wound treatment for infection prevention or treatment or to assess its influence in the healing process were included in this review. The studies were performed in several countries, especially European, while no research had been developed in Brazil or any other South American country.

A total of seven clinical trials compared the use of the PVP-I iodophor solution or CI with other topical agents in chronic wounds (Group I), considering the healing or reduction of wound size[9-15].

In one of the studies*[9-10], at the end of eight weeks, 65% of patients in the CI Group showed

* The same study was published in two different journals (references 9 and 10).

completely healed venous ulcers, against 50% in the Dextranomer Group (D). Although the authors observed higher wound reduction levels among CI patients, no statistically significant difference was found, concluding that the use of PVP-I was not superior in the treatment of venous ulcers. In addition, in another study[11], the authors reached similar conclusions, since no significant reduction in ulcer size was observed in the first six weeks of treatment with CI or D, according to statistical tests.

As opposed to these results, when studying the use of PVP-I compared to D, the author[12] demonstrated the superiority of Dextranomer regarding the smaller average time for ulcer cleansing - wound with no exsudate, pus or devitalized tissue - reduction of microbial load and formation of granulated tissue and epithelization, with a statistically significant difference.

Comparing CI with other conventional treatments, the authors[13] achieved similar results to those found in previous studies[9-11], with no significant difference between the groups regarding the reduction of venous ulcer area sizes. However, a significant reduction of pain was found during the first weeks of treatment with CI.

Nevertheless, in a similar study[14], results favorable to the use of CI were described. After eight weeks of treatment, 13 ulcers of the CI group were healed, showing a statistically significant difference with the Group of Conventional Treatments - TC (which included different agents). In the fourth week of treatment, the CI Group was also significantly more effective than the TC in several evaluated criteria: ulcer size, edema, erythema, exsudate, odor, pus and pain. It is interesting to observe that, in the fourth week, the patients had the option to change the treatment and this change was also significant in favor of the group CI.

For other chronic ulcers, the trial[15] compared the topical use of Silver Sulfadiazine (SS), PVP-I and physiological solution (PS), considering the reduction of the microbial load and of the size of the pressure ulcer. Its results showed a significant difference in favor of the group that used SS for both objectives.

In the comparative analysis of iodophors with different dressings (Group II), researchers from the University der Rohr[16-17] compared the use of a new formulation of PVP-I - liposomal hydrogel - and of a dressing impregnated with chlorhexidine (C) in patients after skin grafting. One of the relevant criteria used was the loss of the graft, which occurred in only one patient in the PVP-I Group, in comparison with five in the C Group ($p=0.01$). The level of re-epithelization and the quality of tissue in the healing process were also evaluated and were significantly higher in the PVP-I Group ($p<0.04$). The use of PVP-I liposomal hydrogel also showed higher efficacy in local and systemic tolerability, without significantly altering the thyroidal hormones, confirming the efficacy of its use.

In two other studies[18-19], the use of iodinated solutions (CI or PVP-I, respectively) in venous ulcer treatment was compared to the use of coverings: hydrocoloid dressings (HD) in both, besides the use of paraffin gauze (PG) in the first study. In the first research[18], the reduction of the wound and quantity of slough were analyzed and both criteria were significantly higher among patients of the CI group in comparison with the other two groups (HD and PG). Regarding the impact on the thyroidal function, there was no glandular dysfunction. Costs were similar between groups CI, HD and PG, although the frequency of dressing changes was higher in the CI group. The other study[19], which used the patients themselves as controls, also showed favorable results regarding the use of PVP-I associated to HD in comparison with isolated treatment with HD. Similarly to a previous study, these studies concluded that the PVP-I contributed to the acceleration in the healing level of the venous ulcers, besides diminishing the microbial load.

Other authors[20-21] also presented favorable conclusions in their studies regarding the use of CI in the treatment of venous ulcers compared to several conventional treatments (TC), when considering infection healing and prevention, through the reduction of microbial load, besides the absence of significant alterations in the thyroidal hormones.

Only one clinical trial evaluated the isolated efficacy of PVP-I (Group III) in the treatment of post cardiac surgical mediastinitis[22]. Its results did not show significant differences between the groups (with and without PVP-I) regarding the level of mortality and time of hospital treatment, concluding that the use of irrigation with PVP-I does not present benefits in this treatment. The authors suggest that better results are obtained through early diagnosis, debridement and wound re-suture, combined with systemic antibiotics.

Aiming to establish the tendencies in the use of iodophors in chronic wounds, it was verified that, in half of the studies, the authors were favorable to its use, especially in those studies in which the iodophors were compared to several types of

dressings. In addition, half of the studies that involved patients with venous ulcers and the two trials with skin grafting appointed favorable results for the use of iodophors, independently of the objective to be tested. However, the studies with patients with infected surgical wounds and pressure ulcers were unfavorable to the use of the iodophors.

Despite the use of clinical trials, some considerations should be described. In some of the studies, the use of different types of products[13-14] was observed, which composed the TC, with different influences on the tissue healing process. In addition, in some of them, different products were used for cleansing or for the maintenance of the wound[12,20-21], which could cause interaction with the topical products used previously or afterwards, or yet distinct influence on the healing process. On the other hand, half the clinical trials did not describe the randomization process for the composition of treatment groups[10-12,14,18-20]. It is also important to consider the restricted size of the sample in the studies analyzed.

CONCLUSIONS

These investigation results did not allow for a definition regarding the tendencies of iodophor use in topical chronic wound therapy, especially due to the number of studies that composed it and the impossibility of performing the meta-analysis because of the different methods employed, as well as the lack of relevant information.

The search for new formulations of iodophors, more effective and with lesser adverse effects, probably composes one of the alternatives for future research, as a recent study*[16-17] indicates favorable and promising results for the use of PVP-I liposomal hydrogel in wound healing. Besides, the development of new experimental, controlled and randomized studies, involving larger samples will add to the evidences available here, with a view to a more precise and safe determination of the use of these products in chronic wounds, in terms of infection prevention and treatment and acceleration of the tissue healing process.

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