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CLINICS & DRUG THERAPY 2000 Vol.19 No.10

◆ Special Feature ◆
The Future of Osteoporosis Treatment in Primary Care

◆ Drug of the Month ◆
Anti-epileptic drugs

◆ THE TOPICS ◆
Japanese Psychogeriatric Society Specialist System

From the Clinic / Evaluation of New Drugs by Clinicians

Evaluation of New Drugs by Clinicians

● **Non-steroidal anti-inflammatory ophthalmic solution**

Bromfenac sodium hydrate

Start of sales: July 2000

Bronuck ophthalmic solution
(Senju Pharmaceutical Co., Ltd. – Takeda Pharmaceutical Co., Ltd.)

Commentary

Sumitomo Hospital, Department of Ophthalmology, Chief Director
Yoshiyuki Hara

Adrenocortical hormone (steroid) drugs are the most commonly used anti-inflammatory drugs to treat local inflammation in the field of ophthalmology. Steroids show superior pharmacological efficacy, and are used very frequently in everyday ophthalmological applications. However, there have also been many reports of adverse drug reactions such as corneal ulcers or corticosteroid glaucoma, etc. In consideration of these types of adverse drug reactions to steroids, there is also significant demand for non-steroidal anti-inflammatory drugs (NSAIDs). Currently, there are fewer types of NSAID ophthalmic drugs in comparison to steroid ophthalmic drugs, resulting in limited choices.

Bromfenac sodium hydrate is a type of NSAID that was developed in order to address the needs of clinical sites, and it is indicated for use in a broad range of conditions, from inflammation of the outer ocular area to post-operative inflammation of the anterior ocular segment.

The active ingredient in this drug is bromfenac sodium hydrate. Enhancement of anti-inflammatory action and maintenance of analgesic action is achieved through the addition of a bromine atom (Br) to the 4th position of the basic amfenac structure. The drug was given the name Bronuck by taking part of the name of the active ingredient.

The mechanism of activity of this drug involves activity to inhibit cyclooxygenase (COX) during the arachidonic acid cascade that is involved in the induction of inflammation. This activity is said to be 11 times greater than that of indomethacin, which is synonymous with NSAIDs. [1)]

● **Comparison with existing analogues**

There are 3 types of NSAID ophthalmic drugs that are currently available on the market: pranoprofen, indomethacin and diclofenac sodium.

Pranoprofen (Niflan) is an anti-inflammatory drug that is indicated for use in treating inflammation of the outer ocular and anterior ocular areas, and it is the most commonly used drug today. However, the efficacy of pranoprofen is weaker than that of this drug, and pranoprofen cannot completely inhibit the generation of fibrin in uveitis such as iritis, or in post-operative inflammation.

Indomethacin (Indomelol) is used to prevent the generation of fibrin following surgery and to maintain mydriasis during surgery. However, it is an oil-based drug, and therefore, an oil film may remain on the operative field during the procedure as a result of pre-operative instillation, which can sometimes prevent the progress of the surgery. Though this product resulted in a marked decrease in the generation of fibrin following surgery, it is mostly no longer used.

Diclofenac sodium (Diclod) is an NSAID drug that is indicated for use in treating anterior ocular segment inflammation following cataract surgery, and it shows particular efficacy in preventing the generation of fibrin, with superior anti-inflammatory efficacy. As is the case with bromfenac sodium hydrate, diclofenac sodium has a chemical structure in which two chlorine atoms (Cl) have been added to the basic structure. Problems with the generation of fibrin following surgery have mostly disappeared. Based on the pharmacological activity of the drug, it is believed to be effective in treating not only post-operative inflammation but also in treating outer ocular area inflammation and uveitis of the anterior ocular area, such as iritis. However, the range of

applications is limited because the drug is indicated only for use in treating inflammation following cataract surgery.

● **Tips in using the drug**

Aqueous ophthalmic solutions of bromfenac sodium hydrate contain 0.1% of the drug, and are clear, yellow solutions with a pH of 8.0 ~ 8.6. The solutions also contain benzalkonium chloride in addition to buffers and stabilizers. These solutions are used twice a day, with the instillation of 1 ~ 2 drops per dose. [2)]

It is necessary to keep in mind the fact that this drug is used not to treat the underlying disease, but as symptomatic therapy. Therefore, in the case of eye inflammation resulting from an infectious disease or the like, the fundamental treatment should involve localized or systemic dosing of antibiotics or antibacterial drugs.

With eye inflammation, once the arachidonic acid cascade has started, the inflammation can worsen suddenly, and the arachidonic acid that has been released can cause an inflammatory response based on COX. With drugs such as steroids that inhibit the release of an arachidonic acid cascade by being taken up into cells, it is necessary to administer sufficient drug during the early stage of the inflammation, or before the inflammation starts. In contrast, this drug acts on COX, and therefore, it will inhibit the production of prostaglandin, which is a phlogogenic substance, by free arachidonic acid in the presence of COX. Therefore, one of the strengths of this drug is that sufficient efficacy can be expected even after the inflammation has been induced. [3)]

● **Precautions**

Adverse drug reactions include blepharitis and corneal erosion, corneal edema, corneal abrasion and conjunctival hyperemia, etc. The frequency of the occurrence of adverse drug reactions was 16 out of a total of 423 cases (3.78%) in a Phase III clinical study. In terms of the occurrence of corneal disorders, COX inhibitory activity is said to be involved, even in healthy tissue such as the cornea. Therefore, sufficient care is required when using this drug. [2)]

Also, there have been foreign reports of serious liver disorders, including cases of death, when oral bromfenac sodium was used for at least one month. Therefore, this drug is meant to be used for less than one month.

Comments

This drug shows superior efficacy in treating anterior eye inflammation and post-operative inflammation. Unfortunately, this drug has not been approved for use in the treatment of anterior uveitis. This is due to the fact that, in the clinical studies, steroid drugs were used as the control in the comparisons, and therefore, there was insufficient significant difference in order to obtain approval. Based on the fact that the drug shows results that are not inferior to other NSAIDs when used to treat anterior uveitis, there are hopes that additional indications will be approved for the drug in the future. [3 ~ 5)]

■ Literature

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4) Usui, M, Masuda K: Efficacy of Bromfenac Sodium (AHR-10282B) ophthalmic solution in treating anterior uveitis. Folia Japonica de Ophthalmologica Clinica 91: 739-744, 1997
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臨床と薬物治療 10

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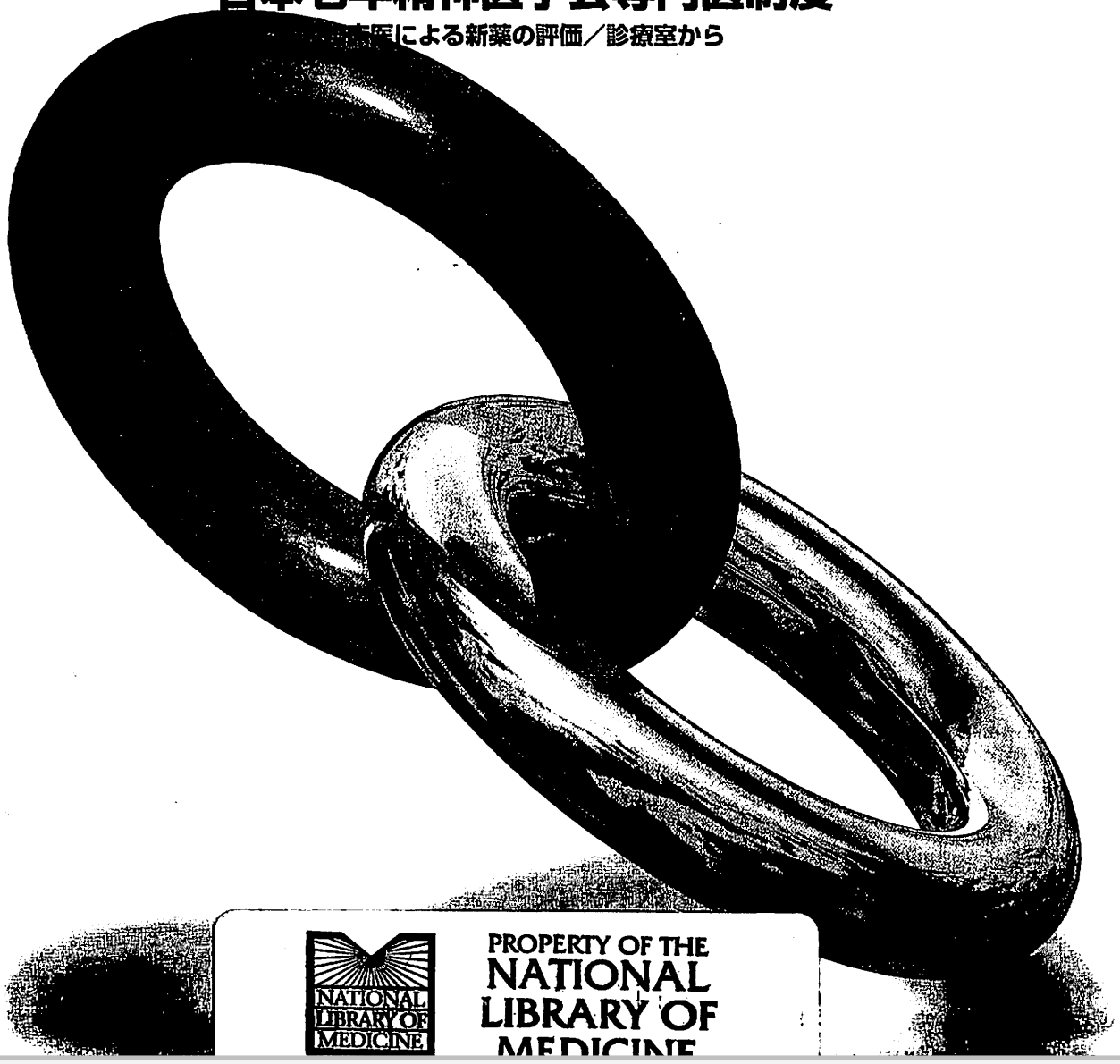
◆特集◆
プライマリケアにおける骨粗鬆症診療のこれから

◆今月の薬剤◆
抗てんかん薬

◆THE TOPICS◆
日本老年精神医学会専門医制度

医による新薬の評価／診療室から



●非ステロイド性抗炎症点眼薬

ブロムフェナクナトリウム水和物

bromfenac sodium hydrate

2000年7月発売

ブロナック点眼液

Bronuck

（千寿製薬ー武田薬品）

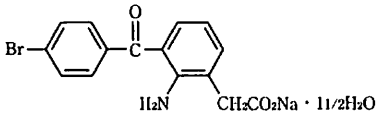
解説

住友病院眼科・主任部長

原　吉幸

Oはら　よしゆき

［構造式］



［効能・効果］

外眼部および前眼部の炎症性疾患の対症療法：眼瞼炎，結膜炎，強膜炎（上強膜炎を含む），術後炎症

［用法・用量］

通常，1回1～2滴，1日2回点眼する

［治験番号］

AHR-10282B

眼科領域における局所の抗炎症薬としては，副腎皮質ホルモン（ステロイド）薬が主流となっている。ステロイドの薬理効果は非常に優れており，日常眼科臨床での使用頻度は高い。しかし角膜潰瘍やステロイド緑内障などの副作用もまた多く報告されている。こういったステロイドの副作用を考慮し，非ステロイド系抗炎症薬（NSAIDs）の点眼薬の需要も多い。現在NSAIDsの点眼薬はステロイド点眼薬に比べると種類が少なく，選択肢が限られている。

ブロムフェナクナトリウム水和物は，臨床現場からのニーズに応えるべく開発されたNSAIDsで，外眼部炎症から前眼部の術後炎症に対して幅広い適応効能を有する。

本剤の有効成分はブロムフェナクナトリウム水和物で，基本骨格のアムフェナクの4位に臭素（Br）を修飾することで抗炎症作用の増強と鎮痛作用の持続が図られている。この有効成分の文字の一部をとってブロナックと命名された。

本剤の作用機序は，炎症惹起に関わるアラキドン酸カスケードにおけるシクロオキシゲナーゼ（COX）に対する阻害効果で，これはNSAIDsの代名詞でもあるインドメタシンの約11倍にもあたる[1]。

●既存類似薬との比較

現在市販されているNSAIDs点眼薬は，プラノプロフェン，インドメタシン，ジクロフェナクナトリウムの3種類である。

プラノプロフェン（ニフラン）点眼薬は，外眼部および前眼部炎症に対する抗炎症薬で，現在最も汎用されているが，その効果は本剤よりも弱く，術後炎症や虹彩炎などのぶどう膜炎においては，フィブリンの発生を完全に阻止することはできない。

インドメタシン（インドメロール）点眼薬は，術後のフィブリン発生予防と手術中の散瞳維持効果を目的として使用されていたが，油性であるがゆえに術前点眼によって手術中に術野に油膜が残り，ときに手術の進行を妨げることもあった。この製品によって術後のフィブリン発生は著しく低下したが，現在使用されることはほとんどない。

ジクロフェナクナトリウム（ジクロード）点眼薬は，白内障手術後の前眼部炎症，とくにフィブリン発生防止を効能とするNSAIDsで，その抗炎症効果は優れている。ブロムフェナクナトリウム水和物と同じ基本骨格に二つの塩素（Cl）を修飾した構造式をもっている。術後のフィブリン発生で悩まされることはほとんどなくなった。薬理作用からは術後炎症のみならず外眼部炎症や虹彩炎などの前眼部のぶ

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